RESTRICTIONS IN USE AND AVAILABILITY OF PHARMACEUTICALS

2010 - 2018

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Restrictions in use and availability of pharmaceuticals, 2010-2018

ISBN 978-92-4-001477-0 (electronic version)
ISBN 978-92-4-001478-7 (print version)

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Introduction

This text is the update to the Fourteenth Issue of the United Nations *Consolidated List of Products whose Consumption and/or Sale have been Banned, Withdrawn, Severely Restricted or Not Approved by Governments - Pharmaceuticals* (UN General Assembly Resolutions 37/137, 1982; 38/149, 1983; 39/229, 1984; 44/226, 1989). It is offered as a service to drug regulators, the pharmaceutical industry, and to everyone interested in assuring the safe and rational use of drugs. It complements *Pharmaceuticals: restrictions in use and availability, 2010* and WHO Pharmaceuticals Newsletter.

Scope and presentation

This volume presents information on new national regulatory decisions, and on voluntary withdrawal of products by manufacturers on grounds of safety, between 01 May 2010 and 31 December 2018, as were reported to WHO or listed on regulators' websites.

Products are listed alphabetically within sections. In addition to Monocomponent Products, Combination of Products, and Group Products, a new section, Other Products, is created for this Update to capture products such as extracts from herbal or animal sources, vaccines, etc. International Nonproprietary Names (INNs) have been used whenever possible. Each product entry includes, where available, the Chemical Abstracts Service registry number (CAS number), synonyms including other generic names and trade names, the effective date on which the regulation came into force, a summary of regulatory measures taken by governments with a brief explanatory comments where necessary, and legal and bibliographical references.

While the information cannot be regarded as exhaustive, either in terms of products or regulatory measures, it covers regulatory actions taken by a total of 32 governments on 725 products, listed chronologically by date of regulatory decision, where available, then alphabetically by country/region. It should be noted, nonetheless, that decisions taken by a limited number of governments on a specific product may not be representative of the positions of other governments. Moreover, the fact that a given product is not listed as regulated by a country does not necessarily mean that it is permitted in that country; it may mean that the relevant regulatory decision has not been communicated to WHO or that the product has not been submitted for registration. The efficacy of products listed is not addressed, but is an aspect that may be crucial when a government is considering regulatory action. Finally, it is strongly recommended to consult drug safety communications regularly released by various national and regional regulatory authorities, a list of which is included in the Annex.

Criteria for the inclusion of products in the *Consolidated List* were developed in 1985 and revised in light of the comments received from governments. However, governments' interpretation of the criterion continues to vary widely, leading to considerable unevenness in reporting. When necessary, additional information and/or clarification have been requested from governments. Products that clearly do not meet the criteria have been omitted after consultation with governments. Information received from non-governmental organizations has, in each case, been verified with governments.

The information provided also includes references to relevant legal or statutory documents that enable the user to ascertain the legal context and scope of the regulations. Such references cannot be given for most entries relating to specific pharmaceutical products since the relevant licenses are often made or amended by an administrative decision which is not published. Brief explanatory comments also appear, where necessary, to clarify certain regulatory actions and put them into broader context.

Monocomponent Products

PRODUCT NAME: acebutolol

C.A.S. NUMBER: 37517-30-9

OTHER NAMES: Sectral, Prent

Country	Effective Date	Description of action taken
United Arab Emirates		Sectral 100 mg capsules and 400 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: acetylcysteine

C.A.S. NUMBER: 616-91-1

OTHER NAMES: Mucomyst, Acetadote, Fluimucil

Country	Effective Date	Description of action taken
United Arab Emirates		The products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: acetylsalicylic acid (aspirin)

C.A.S. NUMBER: 50-78-2

OTHER NAMES: Aspirin, Aspro, etc.

Country	Effective Date	Description of action taken
United Arab Emirates		Tablet form Aspirin 100 mg, Aspirin Adult 0.3 g, Aspirin PROTECT 300 mg, Remin®300 mg, and Aspro 320 mg were withdrawn by the MAH before approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: aciclovir

C.A.S. NUMBER: 59277-89-3

OTHER NAMES: Supraviran

Country	Effective Date	Description of action taken
United Arab Emirates		Aciclovir-containing products were withdrawn by the MAH before approval. **References:**

		Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: acipimox

C.A.S. NUMBER: 51037-30-0

OTHER NAMES: Olbetam

Country	Effective Date	Description of action taken
United Arab Emirates		Olbetam 250 mg capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: acyclovir

C.A.S. NUMBER: 59277-89-3

OTHER NAMES: Zovirax, Aciclovir

Country	Effective Date	Description of action taken
Togo	22 March 2018	The MAH voluntarily withdrew the marketing authorisation of acyclovir in the form of 3% ophthalmic ointment. **References:**

PRODUCT NAME: agomelatine

C.A.S. NUMBER: 138112-76-2

OTHER NAMES: Melitor, Thymanax, Valdoxan

Country	Effective Date	Description of action taken
Indonesia	25 March 2015	The product information of all high dose agomelatine containing products should be revised due to risk of hepatotoxicity. **References:** Dear Healthcare Professional Communication SV.01.03.343.3.03.15.1488

PRODUCT NAME: albiglutide

C.A.S. NUMBER: 782500-75-8

OTHER NAMES: Eperzan, Tanzeum

Country	Effective Date	Description of action taken

United Arab Emirates		Eperzan 30 mg and 50 mg injection products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: alendronate sodium trihydrate

C.A.S. NUMBER: 121268-17-5

OTHER NAMES: Lendomax

Country	Effective Date	Description of action taken
United Arab Emirates		The products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: alglucosidase alfa

C.A.S. NUMBER: 420794-05-0

OTHER NAMES: Myozyme

Country	Effective Date	Description of action taken
United Arab Emirates		These products were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministrial Decree No. 366.

PRODUCT NAME: alimemazine (or trimeprazine)

C.A.S. NUMBER: 84-96-8

OTHER NAMES: Vallergan, Nedeltran, Panectyl, Repeltin, Therafene, Theralen, Vanectyl, Temaril

Country	Effective Date	Description of action taken
United Arab Emirates		Vallergan and Vallergan Forte syrup were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: aliskiren

C.A.S. NUMBER: 173334-57-1

OTHER NAMES: Tekturna, Rasilez

Country	Effective Date	Description of action taken
Brazil	January 2012	After a study concluded that aliskiren would probably not benefit patients with type 2 diabetics at high risk of cardiovascular and renal events in the reduction of cardiovascular risks, it was recommended to healthcare professionals that aliskiren-containing drugs should not be used in combination with enzyme-converting inhibitors of angiotensin or angiotensin receptor blockers in patients with diabetes. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).
Canada	23 January 2012	A contraindication is advised for patients with diabetes taking aliskiren or aliskiren-containing fixed combination products in combination with an angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB). Following interim results of the ALTITUDE trial there was a higher incidence of non-fatal strokes, renal complications, hyperkalemia and hypotension in aliskiren-treated patients. **References:** Advisories, Warnings and Recalls, Health Canada, 23 January 2012 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 1, 2012. WHO Pharmaceuticals Newsletter No. 2, 2014.
Europe	6 February 2012	The European Medicines Agency (EMA) recommends that aliskiren-containing medicines should be contraindicated in patients with diabetes or moderate to severe renal impairment who take angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs). The agency also recommends the inclusion of a warning that the combination of aliskiren and an ACE inhibitor or ARB is not recommended in all other patients because adverse outcomes cannot be excluded. The EMA advised that physicians should stop prescribing aliskiren-containing medicines to patients with diabetes (type 1 or 2) or with moderate to severe kidney impairment who are also taking an ACE inhibitor or ARB and that the risks and benefits should be weighed in continuing treatment for all other patients receiving aliskiren-containing medicines in combination with an ACE inhibitor or an ARB. **References:** Press Release, EMA, 16 Feb 2012 (www.ema.euopa.eu). WHO Pharmaceuticals Newsletter No. 1, 2012. WHO Pharmaceuticals Newsletter No. 2, 2012.
USA	22 April 2012	The U.S. Food and Drug Administration (FDA) added a new contraindication against the use of aliskiren with ARBs or ACEIs in patients with diabetes because of the risk of renal impairment, hypotension, and hyperkalemia. They have also added a warning to avoid use of aliskiren with ARBs or ACEIs

		in patients with moderate to severe renal impairment (i.e., where glomerular filtration rate [GFR] < 60 mL/min). The labels for the aliskiren drugs are being updated based on preliminary data from a clinical trial, "Aliskiren Trial in Type 2 Diabetes Using Cardio-Renal Endpoints (ALTITUDE)." **References:** FDA Drug Safety Communication, US FDA, 22 April 2012. (www.fda.gov). WHO Pharmaceuticals Newsletter No. 3, 2012.

PRODUCT NAME: alkaloid thiophosphoric acid derivative of Chelidonium majus L.

C.A.S. NUMBER:

OTHER NAMES: Ukrain

Country	Effective Date	Description of action taken
United Arab Emirates		Ukrain, an alkaloid thiophosphoric acid derivative of Chelidonium majus L. was withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: almagate

C.A.S. NUMBER: 66827-12-1

OTHER NAMES: Almax

Country	Effective Date	Description of action taken
United Arab Emirates		The application was rejected by the committee for various reasons. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: almitrine

C.A.S. NUMBER: 27469-53-0

OTHER NAMES: Duxil

Country	Effective Date	Description of action taken
Viet Nam	27 November 2012	The marketing authorisation for this product is suspended due to limited safety and efficacy data. **References:** Drug Administration of Viet Nam Official documents No. 18428/QLD-DK, 27 November 2012.

United Arab Emirates	The products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ambrisentan

C.A.S. NUMBER: 177036-94-1

OTHER NAMES: Volibris, Letairis, Pulmonext

Country	Effective Date	Description of action taken
Brazil	July 2012	Healthcare professionals have been informed that ambisentan should not be used in patients with idiopathic pulmonary fibrosis (IPF), after a clinical study in patients with IPF demonstrated high rates of hospitalizations due to respiratory causes, adverse events culminating in death, and decreased respiratory function in the study group versus placebo group. The medicine package leaflet was updated with this contraindication. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: ambroxol hydrochloride

C.A.S. NUMBER: 23828-92-4

OTHER NAMES:

Country	Effective Date	Description of action taken
Indonesia	17 May 2017	The indication for Ambroxol HCL should be revised to dismiss claim of asthma bronchiale, and to provide warning and precaution against adverse event. **References:** Dear Healthcare Professional Communication B-SV.01.05.343.3.05.17.2281
United Arab Emirates		Fedecol sugar free syrup were discontinued upon the request from the MAH. Bronchopront Retard 75 mg capsules, Bronchopront 15 mg/5 ml syrup, and 7.5 mg/ml drops were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: amikacin

C.A.S. NUMBER: 37517-28-5

OTHER NAMES: Amikin, Amiglyde-V, Arikayce

Country	Effective Date	Description of action taken
United Arab Emirates		The products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: amlodipine besylate

C.A.S. NUMBER: 111470-99-6

OTHER NAMES: Amlovasc, Norvasc

Country	Effective Date	Description of action taken
Brazil	July 2018	ANVISA communicated new safety information regarding alodipine besylate-containing products, following recommendations made by the EMA. Based on reviews of scientific literature, published clinical studies and databases of adverse event notifications, ANVISA confirmed the warnings of drug interaction between alodipin and rifampicin, as well as the risk of alodipine excretion in breast milk. The package leaflet of the drug has been updated. The inclusion of toxic epidermal necrolysis as an adverse reaction remained under evaluation. **References:** ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia). WHO Pharmaceuticals Newsletter No. 4, 2011.

PRODUCT NAME: amoxicillin

C.A.S. NUMBER: 26787-78-0

OTHER NAMES: Glomox, Ospamox, Ranoxyl, Enhancin, Amoxidin, Flemoxin

Country	Effective Date	Description of action taken
Armenia	2018	After an assessment by the Scientific Centre of Drug and Medical Technology Expertise after Academician E. Gabrielyan (SCDMTE), the product information of Flemoxin Solutab was updated to include information on posology and administration for reducing risk of fatal mechanical asphyxia due to inappropriate use of the medicine and ingestion of a whole tablet without prior dissolution in water. As a risk minimization measure a DHPC was circulated. **References:** Communication from Armenian National Pharmacovigilance Centre, 2018.

United Arab Emirates		Glomox 500 mg and Neomox 375 mg were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. Ospamox 100 mg and 375 mg, Ranoxyl 250 mg, Amoxidin 375 mg, Enhancin 375 mg and 625 mg tablets, Flemoxin 125 mg/5 ml suspension, Princimox and Hiconcil in various strengths and forms were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: amphotericin

C.A.S. NUMBER: 1397-89-3

OTHER NAMES: Fungilin, Fungizone

Country	Effective Date	Description of action taken
Madagascar	7 February 2011	For industrial purposes the product has been withdrawn. **References:** Communication from the Madagascar National Pharmacovigilance Centre July, 2012.
United Arab Emirates		Fungizone were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ampicillin

C.A.S. NUMBER: 69-53-4

OTHER NAMES: Ultracillin, Pentrexyl

Country	Effective Date	Description of action taken
United Arab Emirates		Ultracillin and Pentrexyl various form and strengths products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: aprotinin

C.A.S. NUMBER: 9087-70-1

OTHER NAMES: Trasylol

Country	Effective Date	Description of action taken

USA	1 September 2011	The Contraindications, Warnings and Precautions, Adverse Reactions, and Patient Counselling Information sections have been revised to include information about serious allergic type I hypersensitivity reactions which may include anaphylaxis, angioedema, low blood pressure, rapid heart rate, swollen tongue, difficulty breathing, wheezing, or rash. **References:** FDA Drug Safety Communication, US FDA, 1 September 2011 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 5, 2011.
Canada	21 September 2011	Health Canada concluded that the benefits of aprotinin outweigh the risks when aprotinin is used as authorized by Health Canada. Health Canada requested that strong warnings, in the form of a Boxed Warning, be added to the prescribing information emphasizing that there have been reports of an increased risk of death in some studies associated with aprotinin use outside of its authorized indication, and that aprotinin should only be used as authorized after careful consideration of the potential benefits and risks. Information on the risk of abnormal kidney function has also been added to the Boxed Warning. **References:** Advisories, Warnings and Recalls, Health Canada, 21 September 2011 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 5, 2011.

PRODUCT NAME: aripiprazole

C.A.S. NUMBER: 129722-12-9

OTHER NAMES: Aristab, Abilify

Country	Effective Date	Description of action taken
Brazil	August 2016	The health professionals were Informed of safety communication published by US FDA, regarding adverse reactions related to compulsive behavior during the post-marketing period of aripiprazole, with cessation of compulsive behavior with dose reduction or discontinuation of treatment. Health professionals were advised to monitor and alert patients and caregivers about the possibility of compulsive behavior. The medicine package leaflet has been updated. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).
United Arab Emirates		The products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: astemizole

C.A.S. NUMBER: 68844-77-9

OTHER NAMES: Hismanal

Country	Effective Date	Description of action taken
Bhutan	22 July 2015	All forms of astemizole-containing medicines are banned due to the risk of rare but serious side-effects on heart, primiray changes in heart rhythm. Pharmacies have been notified of the restrictions in their importation and sales. **References:** Bhutan Drug Regulatory Authority, List of Banned Drugs (www.dra.gov.bt).

PRODUCT NAME: atenonol

C.A.S. NUMBER: 29122-68-7

OTHER NAMES: Canar, Tenormin

Country	Effective Date	Description of action taken
United Arab Emirates		The products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: atezolizumab

C.A.S. NUMBER: 1380723-44-3

OTHER NAMES: Tecentriq

Country	Effective Date	Description of action taken
Brazil	August 2018	After classification of a new important risk, immunorelated nephritis, associated with the use of Tecentriq®, it was recommended that treatment with Tecentriq® be discontinued in cases of moderate immunorelated nephritis (Grade 2) and permanently discontinued in cases of severe nephritis (Grades 3 or 4). The product package leaflet has been updated. Additionally, based on preliminary data from an ongoing clinical study, the Tecentriq® leaflet was revised with its indication as a first-line monotherapy for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma after chemotherapy prior to platinum, or who are considered ineligible for cisplatin and whose tumor has a high expression of PD-L1 (greater than or equal to 5% of expression of PD-L1 in immune cells that infiltrate the tumor). The use of Tecentriq® remains unchanged after previous platinum-based chemotherapy.

		References: ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: atomoxetine

C.A.S. NUMBER: 83015-26-3

OTHER NAMES: Straterra

Country	Effective Date	Description of action taken
Canada	21 October 2011	Atomoxetine carries the risk of increasing blood pressure and heart rate and is therefore contraindicated in patients with symptomatic cardiovascular diseases, moderate to severe hypertension or severe cardiovascular disorders whose condition would be expected to deteriorate if they experienced increases in blood pressure or heart rate. Atomoxetine should be used in caution in patients with hypertension, tachycardia, cardiovascular or cerebrovascular disease, congenital or acquired long QT syndrome or a family history of QT prolongation. **References:** Advisories, Warnings and Recalls, Health Canada, 21 October 2011 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 6, 2011. WHO Pharmaceuticals Newsletter No. 1, 2012.
United Kingdom	January 2012	The Medicines and Healthcare products Regulatory Agency (MHRA) has advised that atomoxetine should not be used in patients with severe cardiovascular or cerebrovascular disorders. It is also recommended that patients who take atomoxetine for extended periods have their treatment reviewed at least annually to determine whether continuation is needed. **References:** Drug Safety Update, January 2012, Volume 5, issue 6, A1, MHRA, (www.mhra.gov.uk). WHO Pharmaceuticals Newsletter No. 1, 2012.
Australia	February 2012	The Therapeutic Goods Administration (TGA) advised health care professionals of the risk of clinically significant increases in blood pressure and/or heart rate with the use of atomoxetine. Health-care professionals are advised that atomoxetine is contraindicated in patients with symptomatic cardiovascular diseases, moderate to severe hypertension or severe cardiovascular disorders whose condition would be expected to deteriorate if they experienced clinically important increases in blood pressure or heart rate. Atomoxetine should be used with caution in patients whose underlying medical conditions could be worsened by increases in blood pressure or heart rate such as patients with hypertension, tachycardia, or cardiovascular or cerebrovascular disease. The drug should not be used in patients with a family history of congenital or acquired QT

		prolongation and patients should be screened for pre-existing or underlying cardiovascular or cerebrovascular conditions before initiating treatment with atomoxetine. **References:** Medicines Safety Update Vol. 3, No. 1, February 2012 (www.tga.gov.au). WHO Pharmaceuticals Newsletter No. 2, 2012. WHO Pharmaceuticals Newsletter No. 6, 2013.

PRODUCT NAME: atropine

C.A.S. NUMBER: 5908-99-6

OTHER NAMES: Atropine

Country	Effective Date	Description of action taken
United Arab Emirates		Atropine 1% ointment and other atropine-containing products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: azapentacene

C.A.S. NUMBER: 3863-80-7

OTHER NAMES: Quinax

Country	Effective Date	Description of action taken
Azerbaijan	15 November 2016	Marketing authorization is withdrawn due to stability issues. Azapentacene containing eye drops have been suspsended. **References:** Ministry of Health final desicion N 267-S, November 2016.

PRODUCT NAME: azathioprine

C.A.S. NUMBER: 446-86-6

OTHER NAMES: Azamun

Country	Effective Date	Description of action taken
United Arab Emirates		Azamun 50 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: azithromycin

C.A.S. NUMBER: 83905-01-5

OTHER NAMES: Zitromax, Astro, Azithrocin

Country	Effective Date	Description of action taken
Sudan	21 June 2012	Prescribers have been informed to avoid prescribing this antibiotic for: 1. Patients with known QT interval prolongation 2. Patients with low potassium levels 3. Those taking drugs that prolong the QT interval **References:** Communication from the Sudan National Pharmacovigilance Centre, July 2012.
Brazil	March 2013 August 2018	In 2013, following post-marketing observation of the risk of developing cardiac arrhythmia and Torsades de Pointes, healthcare professionals were recommended to weigh the risks and benefits of azithromycin for risk groups including: patients with congenital or documented QT interval prolongation; patients with electrolyte disorder; patients with clinically relevant bradycardia; cardiac arrhythmia or heart failure; elderly, etc. The product package leaflet was updated with the information. In 2018, ANVISA issued a warning regarding the potential risks associated with the use of azithromycin, following warnings from the FDA and Health Canada, as well as results from a clinical study conducted in France on the long-term off-label use of azithromycin in the prophylaxis of obliterating bronchiolitis in patients undergoing halogenic bone marrow transplantation in hematologic neoplasms, which identified an increase in the rate of cancer recurrence cases (including death). Healthcare professionals were recommended not to prescribe long-term off-label use of azithromycin for obliterating bronchiolitis prophylaxis in patients after hematopoietic stem cell transplantation. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: aztreonam

C.A.S. NUMBER: 78110-38-0

OTHER NAMES: Azactam

Country	Effective Date	Description of action taken
United Arab Emirates		Azactam 500 mg and 1 g were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: bacitracin

C.A.S. NUMBER: 1405-87-4

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		Bacitracin for IM injection were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: beclometasone

C.A.S. NUMBER:

5534-09-8

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		Viarex 50 mcg/dose inhaher were withdrawn by the MAH before getting approval. The application for Aerocort HFA inhaler was rejected by the committee for various reasons. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: belatacept

C.A.S. NUMBER: 706808-37-9

OTHER NAMES: Nulojix

Country	Effective Date	Description of action taken
USA	7 July 2011	Patients treated with belatacept are at an increased risk for developing post-transplant lymphoproliferative disorder (PTLD), predominantly involving the central nervous system. Progressive multifocal leukoencephalopathy (PML) has been reported in patients receiving belatacept at higher than recommended doses as part of an immunosuppressant regimen. **References:** FDA Drug Safety Communication, US FDA 7 July 2011 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 4, 2011.

PRODUCT NAME: belimumab

C.A.S. NUMBER: 356547-88-1

OTHER NAMES: Benlysta

Country	Effective Date	Description of action taken
Canada	3 May 2012	GlaxoSmithKline Inc., in consultation with Health Canada, informed health-care professionals of important new safety information related to hypersensitivity and infusion reactions associated with belimumab (BENLYSTA™) treatment. In the event of a severe reaction, belimumab administration must be interrupted and appropriate medical therapy administered. Patients treated with belimumab should be informed of the symptoms of hypersensitivity reactions, and the importance of immediately seeking medical attention. In addition, patients with a history of multiple drug allergies or significant hypersensitivity may be at increased risk. Health-care professionals should monitor patients during and for an appropriate amount of time after administration of belimumab, because a delay in the onset of acute hypersensitivity reactions has been observed. **References:** Advisories, Warnings and Recalls, Health Canada, 3 May 2012 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 3, 2012. WHO Pharmaceuticals Newsletter No. 3, 2014.

PRODUCT NAME: benazepril

C.A.S. NUMBER: 86541-75-5

OTHER NAMES: Cibacen

Country	Effective Date	Description of action taken
United Arab Emirates		Cebacen 5 mg, 10 mg, and 20 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: bendamustine

C.A.S. NUMBER: 16506-27-7

OTHER NAMES: Ribomustin, Treanda, Treakisym, Levact

Country	Effective Date	Description of action taken
Brazil	October 2017	Healthcare professionals were informed of an increased frequency of mortality when bendamustine was used non-approved treatment combinations or outside the approved indication. Fatal toxicities occurred mainly due to opportunistic infections, cardiac, neurological and respiratory toxicities. The medicine package leaflet has been

		reviewed. At the time of the publication of the Letter, Ribomustin was not yet commercially available in Brazil. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: benfluorex

C.A.S. NUMBER: 23602-78-0

OTHER NAMES:

Country	Effective Date	Description of action taken
Viet Nam	8 June 2010	The marketing authorisation of benfluorex-containing medicines is suspended due to cardiac valvulopathy (thickening of the heart valves) and pulmonary arterial hypertension (high blood pressure in the artery that leads from the heart to the lungs). The products are removed from the market. **References:** Drug Administration of Viet Nam Official documents No. 13691/QLD-CL, 30 August 2010.

PRODUCT NAME: benzathine benzylpenicillin

C.A.S. NUMBER: 1538-09-6

OTHER NAMES: Retarpen, Permapen

Country	Effective Date	Description of action taken
United Arab Emirates		Retarpen L.A. 0.6 MIU and 2.4 MIU solutions for injection were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: benzocaine

C.A.S. NUMBER: 1994-09-07

OTHER NAMES: Spec-T

Country	Effective Date	Description of action taken
United Arab Emirates		Spec-T troches were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: benzydamine

C.A.S. NUMBER: 642-72-8

OTHER NAMES: Benflogin, Flogo-rosa, Tantum Verde, Difflam, Septabene

Country	Effective Date	Description of action taken
Brazil	July 2013 June 2016	In 2013, upon receiving reports of abuse of benzidamine that almost caused the death of a patient, ANVISA conducted a search in its database, detecting other cases of adverse events associated with its misuse. Consultation of the scientific literature demonstrated the use of the substance for recreational purposes by young people and adolescents, since the drug, in high doses, can cause hallucinations and visual changes. Therefore, a warning was issued about the risk of death and serious adverse events related to the abuse of benzydamine. The markering authorisation of the oral solution and tablet forms were suspended in 2014. In 2016, ANVISA became aware of the accidental ingestion of Flogo-Rosa (benzidamine hydrochloride for vaginal use) and intoxication, especially in children. Guidance was given to patients, emphasizing that Flogo-Rosa is intended for vaginal use and should not be ingested. Measures were recommended to prevent accidental ingestion of the drug and the occurrence of intoxications, especially in children. A Risk Minimisation Plan was requested from the manufacturer. **References:** ANVISA Pharmacovigilance Alert, and Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia). Official Gazette, cancellation of registration, 24 February 2014 (Resolution-RE No. 681).

PRODUCT NAME: benzyl benzoate

C.A.S. NUMBER: 120-51-4

OTHER NAMES: Ascabiol

Country	Effective Date	Description of action taken
United Arab Emirates		Ascabiol lotion were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: benzylpenicillin

C.A.S. NUMBER: 61-33-6 (free acid); 69-57-8 (sodium salt)

OTHER NAMES: Penicillin G

Country	Effective Date	Description of action taken
United Arab Emirates		Penicillin G 1,000,000 IU, 500,000 IU and 200,000 IU were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: betahistine mesylate

C.A.S. NUMBER: 54856-23-4

OTHER NAMES: Merislon

Country	Effective Date	Description of action taken
United Arab Emirates		Merislon 6 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: betaxolol hydrochloride

C.A.S. NUMBER: 63659-19-8

OTHER NAMES: Kerlone

Country	Effective Date	Description of action taken
United Arab Emirates		Kerlone 20 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: bevacizumab

C.A.S. NUMBER: 216974-75-3

OTHER NAMES: Avastin

Country	Effective Date	Description of action taken
USA	16 December 2010	Communication from the Egypt National Pharmacovigilance Centre July, 2012. **References:** MedWatch Safety Information, US FDA, 16 December 2010 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 1, 2011.
New Zealand	September 2011	Ovarian failure occurs commonly in association with bevacizumab use. Medsafe advised prescribers to discuss the possibility of ovarian failure with all female patients prior to treatment with bevacizumab and that patients

		should also be monitored for the development of signs and symptoms of ovarian failure during treatment. **References:** Prescriber Update Vol. 32 No. 3, September 2011 (www.medsafe.govt.nz). WHO Pharmaceuticals Newsletter No. 5, 2011.
Canada	7 December 2011	Bevacizumab is not formulated for intravitreal use. Serious ocular complications including acute oclular inflammation, endophthalmitis, and infectious endophthalmitis resulting in blindness have been reported following intravitreal injection of bevacizumab. **References:** Advisories, Warnings and Recalls, Health Canada, 7 December 2011 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 1, 2012. WHO Pharmaceuticals Newsletter No. 3, 2013. WHO Pharmaceuticals Newsletter No. 1, 2016. WHO Pharmaceuticals Newsletter No. 3, 2017.
Brazil	December 2010 June 2011 April 2013	In 2010, ANVISA warned that the drug Avastin should be prescribed for the treatment of metastatic breast cancer only in combination with paclitaxel. This is in line with EMA evaluation, which confirmed that Avastin, in combination with paclitaxel, showed favorable benefit-risk profile for metastatic breast cancer treatment, as well as concluded that its use associated with docetaxel demonstrated a negative benefit-risk profile. In 2011, HCPs were informed of the reversible inhibition of dose-dependent ovarian function related to the use of Avastin® regarding, which can cause ovarian failure as an adverse event. It was recommended that strategies for fertility preservation be discussed with women of childbearing age prior to initiation of treatment. In 2013, ANVISA warned of reports of necrotizing fasciitis, including some cases with fatal outcome, in patients who received Avastin, both in clinical studies and in the post-commercialization period of the drug. Discontinuation of treatment with Avastin in these cases was recommended and the product label was updated. **References:** ANVISA Pharmacovigilance Alert, and Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: bifendate

C.A.S. NUMBER: 73536-69-3

OTHER NAMES:

Country	Effective Date	Description of action taken

Viet Nam	29 July 2015	The marketing authorisation for this product is suspended due to limited safety and efficacy data. The products are recalled. **References:** Drug Administration of Viet Nam Official documents No. 423/QĐ-QLD, 29 July 2015.

PRODUCT NAME: biperiden

C.A.S. NUMBER: 514-65-8

OTHER NAMES: Akineton

Country	Effective Date	Description of action taken
United Arab Emirates		Akineton 2 mg and Akineton Retard 4 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: biphenyl dimethyl dicarboxylate

C.A.S. NUMBER: 792-74-5

OTHER NAMES:

Country	Effective Date	Description of action taken
Viet Nam	31 March 2014	The MAH has been requested to provide more data to prove the product's characteristics of safety and efficacy, due to limited safety and efficacy data of the oral form. Meanwhile the registration of the product and importation of the ingredients/products are suspended. **References:** Drug Administration of Viet Nam Official No. 4822/QLD-DK, 31 March 2014

PRODUCT NAME: boceprevir

C.A.S. NUMBER: 394730-60-0

OTHER NAMES: Victrelis

Country	Effective Date	Description of action taken
Brazil	February 2012	Health professionals were informed about drug interactions in patients co-infected with chronic hepatitis C treated with atazanavir, lopinavir and darunavir potentiated by ritonavir, with potential reduction of efficacy of these drugs when co-administered. Victrelis is not indicated for patients co-infected with HIV-1 and chronic hepatitis C. The product package leaflet has been updated. **References:**

		ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).
USA	9 February 2012	The U.S. Food and Drug Administration (FDA) notified health-care professionals and patients that drug interactions between the hepatitis C virus (HCV) protease inhibitor boceprevir and certain ritonavir-boosted human immunodeficiency virus (HIV) protease inhibitors (atazanavir, lopinavir, darunavir) can potentially reduce the effectiveness of these medicines when they are used together. A drug interaction study showed that taking bocprevir with ritonavir in combination with atazanavir or darunavir or lopinavir/ritonavir reduced the blood levels of the HIV medicines and boceprevir in the body. **References:** FDA Drug Safety Communication, US FDA, 9 February 2012 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 2, 2012.
Europe	16 February 2012	The European Medicines Agency (EMA)'s Committee for Medicinal Products for Human Use (CHMP) concluded that the lower blood levels seen in the drug interaction study with boceprevir and ritonavir-boosted HIV protease inhibitors atazanavir, darunavir, and lopinavir could mean that the medicines are less effective when given together. However, the committee acknowledged that further studies are needed to determine the clinical impact of this drug interaction. The CHMP recommends that physicians treating patients coinfected with hepatitis C and HIV should not coadminister boceprevir with ritonavir-boosted darunavir or lopinavir. However, coadministration of boceprevir with ritonavir-boosted atazanvir may be considered on a case-by-case basis if deemed necessary. **References:** Press release, EMA, 16 February 2012 (www.ema.europa.eu). WHO Pharmaceuticals Newsletter No. 2, 2012.
USA	26 April 2012	The US FDA notified health-care professionals that the drug label has been revised to state that coadministration of boceprevir along with certain ritonavir-boosted HIV protease inhibitors is not recommended. The findings of a drug-drug interaction study and clinical trial showed that coadministration increased the possibility of reducing the effectiveness of the medicines, permitting the amount of HCV or HIV virus in the blood to increase. Ritonavir-boosted HIV protease inhibitors include ritonavir-boosted atazanavir (Reyataz®), ritonavir-boosted darunavir (Prezista®), and lopinavir/ritonavir (Kaletra®). **References:** FDA Drug Safety Communication, US FDA, 26 April 2012 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 3, 2012.

PRODUCT NAME: boric acid

C.A.S. NUMBER: 10043-35-3

OTHER NAMES: Trihydrooxidoboronl, Orthoboric acid, Boracic acid, Optibor,Borofax

Country	Effective Date	Description of action taken
Azerbaijan	25 May 2012	Boric acid containing powder form medicines have been suspended due to high risk of toxicity in infants and allergic reactions in adults. **References:** Ministry of Health Pharmacology and Pharmacopeia Advisory Council, May 2012.

PRODUCT NAME: bortezomib

C.A.S. NUMBER: 179324-69-7

OTHER NAMES: Velcade

Country	Effective Date	Description of action taken
Canada	31 January 2012	Three cases of inadvertent intrathecal administration of bortezomib with fatal outcomes have been reported worldwide. Therefore, it is advised that bortezomib should only be administered via the approved intravenous (IV) route. Health-care professionals should administer chemotherapy via intrathecal route at a different time than other parenteral chemotherapy. Different connectors should be used for medicinal products administered via intrathecal or intravenous route. **References:** Advisories, Warnings and Recalls, Health Canada, 31 January 2012 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 2, 2012. WHO Pharmaceuticals Newsletter No. 5, 2015.
Brazil	February 2012	ANVISA published recommendations for Velcade not to be administered intrathecally following reports of three cases of fatal outcomes worldwide with intrathecal Velcade administration. Although there were no reports of administration in this route in Brazil, precautionary measures were recommended in order to reduce administration errors. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: brentuximab vedotin

C.A.S. NUMBER: 914088-09-8

OTHER NAMES: Adcetris

Country	Effective Date	Description of action taken
USA	13 January 2012	The U.S. Food and Drug Administration (FDA) added a new Boxed Warning to brentuximab vedotin highlighting the potential risk of developing progressive multifocal leukoencephalopathy (PML), a rare but serious brain infection that can result in death. In addition, a new contraindication was added against using brentuximab vedotin with the cancer drug bleomycin due to increased risk of pulmonary toxicity. **References:** FDA Drug Safety Communication, US FDA, 13 January 2012 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 1, 2012.

PRODUCT NAME: brimonidine tartrate

C.A.S. NUMBER: 70359-46-5

OTHER NAMES: Alphagan

Country	Effective Date	Description of action taken
United Arab Emirates		Brimonidine tartrate ophthalmic solution by Alcon Laboratories Inc. were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. Alphagan® 0.2% were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: bromocriptine

C.A.S. NUMBER: 25614-03-3

OTHER NAMES:

Country	Effective Date	Description of action taken
Chile	15 June 2015	The product label is updated to include new contraindications: Bromocriptine should not be used in women with uncontrolled hypertension, hypertensive disorders of pregnancy (eclampsia, pre-eclampsia or hypertension during pregnancy), postpartum hypertension, a history of ischemic heart disease or other serious cardiovascular diseases, nor in those with symptoms or a history of severe psychiatric pathology. The decision took into consideration similar recommendations by EMA. **References:** Instituto de Salud Publica (www.ispch.cl). EMA Referrals, 20 August 2014 (www.ema.europa.eu).

United Arab Emirates		Antiprotin 2.5 mg and Parlodel 2.5 mg were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: buclizine

C.A.S. NUMBER: 82-95-1

OTHER NAMES: Longifene

Country	Effective Date	Description of action taken
United Arab Emirates		Longifene were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: budesonide

C.A.S. NUMBER: 51333-22-3

OTHER NAMES: Pulmicort, Budecort, Entocort

Country	Effective Date	Description of action taken
United Arab Emirates		The application for Budecort respules 0.5 mg was rejected by the committee for various reasons. Other budesonide-containing products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: bufexamac

C.A.S. NUMBER: 2438-72-4

OTHER NAMES: Paraderm, Parfenac, Protozan

Country	Effective Date	Description of action taken
Madagascar	15 September 2010	The drug has been withdrawn due to the high risk of sometimes serious contact allergy. **References:** Communication from the Madagascar National Pharmacovigilance Centre July, 2012.
Azerbaijan	25 May 2012	Bufexamac containing medicines have been suspended due to high risk of developing a contact allergic reaction,

		especially in patients with pre-disposing conditions, such as certain forms of eczema. **References:** Ministry of Health Pharmacology and Pharmacopeia Advisory Council, May 2012.

PRODUCT NAME: buflomedil

C.A.S. NUMBER: 55837-25-8

OTHER NAMES: Bufedil, Loftyl

Country	Effective Date	Description of action taken
France	17 February 2011	The French Health Products Safety Agency (Afssaps) decided on the suspension of the marketing authorizations of buflomedil containing products on 11 February 2011. All batches of buflomedil-containing products were recalled in France on 17 February 2011. The action was taken following notification of serious nervous (convulsions, myoclonia and status epilepticus) and cardiac (tachycardia, hypotension, ventricular rhythm disorders and cardiac arrest) events especially in accidental overdose or voluntary overdose. **References:** Spécialités à base de Buflomédil - Retrait de produits, Afssaps, 17 February 2011 (www.afssaps.fr). WHO Pharmaceuticals Newsletter No. 2, 2011.
Madagascar	2 March 2011	The risk/benefit ratio is considered unfavorable because of its low efficacy and with regards to a risk of serious side-effects linked to neurological and cardiac misuse (non-compliance with the indication, contraindications, dosage, and monitoring of renal function) and the therapeutic range is narrow. **References:** Communication from the Madagascar National Pharmacovigilance Centre July, 2012.
Europe	20 May 2011	The European Medicines Agency (EMA) recommended that the supply of oral buflomedil containing medicines be suspended in all European Union (EU) Member States where it is currently authorized. The EMA advised that doctors should stop prescribing oral buflomedil and consider alternative treatment options, including managing underlying health problems which can increase the risk of peripheral arterial occlusive disease (PAOD), such as diabetes and high blood pressure. **References:** Press release EMA, 20 May 2011 (www.ema.europa.eu). WHO Pharmaceuticals Newsletter No. 3, 2011.
Brazil	July 2011	After the EMA decides to provisionally suspend the marketing, distribution and use of the drug Bufedil® in the form of tablets until the finalization of an ongoing review assessing the risk-benefit ratio of the use of the product,

		due to severe and sometimes fatal cardiovascular and neurological risks related to drug overdose, ANVISA made recommendations to health professionals regarding the assiduous follow-up of patients using the product and notification, through the ANVISA Electronic Notification System, of suspected adverse events with the use of Bufedil. The registration of the drug was canceled in Brazil in November 2015. **References:** ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia). Official Gazette, cancellation of registration, 04 July 2010 (Resolution-RE No. 2878).
Europe	17 November 2011	The European Medicines Agency (EMA)'s Committee for Medicinal Products for Human Use (CHMP) recommended that the marketing authorisations of all buflomedil-containing medicines be suspended in all European Union (EU) Member States where they are currently authorized. The Committee stated that the risks of these medicines, specifically the risks of severe cardiological and neurological adverse reactions, are greater than their limited benefits in the treatment of patients with chronic peripheral arterial occlusive **References:** Press release, EMA, 17 November 2011 (www.ema.europa.eu). WHO Pharmaceuticals Newsletter No. 6, 2011.
Egypt	26 January 2012	Buflomedil-containing medicines in all its pharmaceuticals forms and concentrations have been suspended. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.
Viet Nam	27 August 2012 13 September 2012	The marketing authorisation for this product is suspended due to reported adverse reactions in cardiovascular system and nervous system. The products are recalled. **References:** Drug Administration of Viet Nam Official documents No. 12792/QLD-CL, 27 August 2012, and No. 13702/QLD-DK, 13 September 2012.

PRODUCT NAME: bupropion

C.A.S. NUMBER: 34911-55-2

OTHER NAMES: Wellbutrin, Zyban

Country	Effective Date	Description of action taken
Brazil	October 2012	Considering the results of an epidemiological study that suggested a possible increased risk of congenital cardiovascular malformations, the package leaflets of

		bupropion-containing products were updated with additional information related to pregnancy. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: buserelin

C.A.S. NUMBER: 68630-75-1

OTHER NAMES: Suprefact

Country	Effective Date	Description of action taken
United Arab Emirates		Sprefact 1.05 mg/g spray were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: buspirone

C.A.S. NUMBER: 36505-84-7

OTHER NAMES: Buspar

Country	Effective Date	Description of action taken
United Arab Emirates		Buspar 5 mg, 10 mg, and 30 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: butorphanol

C.A.S. NUMBER: 42408-82-2

OTHER NAMES: Stadol

Country	Effective Date	Description of action taken
United Arab Emirates		Stadol were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cabazitaxel

C.A.S. NUMBER: 183133-96-2

OTHER NAMES: Jevtana, Cabazred, Proazitax

Country	Effective Date	Description of action taken
Brazil	November 2013	Due to cases of errors in the reconstitution of Jevtana that occurred in the European Union, which could lead to an overdose of the product, instructions for the proper preparation of Jevtana were reiterated. ANVISA issued an alert detailing the correct preparation of drugs containing cabazitaxel, emphasizing that, because it is an oncology product, its preparation should be carried out carefully by a health professional, and that any error in the dilution of the product can increase the risk of adverse reaction. **References:** ANVISA Pharmacovigilance Alert, and Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: calcipotirol

C.A.S. NUMBER: 112965-21-6

OTHER NAMES: Daivonex, Dovonex, Sorilux

Country	Effective Date	Description of action taken
United Arab Emirates		Daivonex cream and ointment were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: calcitonin

C.A.S. NUMBER: 47931-85-1

OTHER NAMES:

Country	Effective Date	Description of action taken
Oman	2013	Calcitonin-containing medicines are withdrawn from the market. The HCPs are reminded to not dispense the products. The decision took into consideration similar action in EU due to increased risk of malignancy associated with the use of calcitonin. **References:** Oman Ministry of Health Circular No. 43, 2013.
Brazil	August 2012	Following the request from EMA's CHMP to assess the risks and benefits of calcitonin, the manufacturer detected a statistically significant increase in the observed incidence of malignancies with prolonged use of calcitonin. Therefore, health professionals were informed of the updates on

		product label, with guidelines for the treatment to occur in the shortest possible period, as well as the need for careful and individualized evaluation of the risk-benefit of its use. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).
Europe	13 February 2013	The EMA's Committee for Medicinal Products for Human Use (CHMP) recommended that calcitonin-containing medicines should only be authorised for short-term use in Paget's disease, acute bone loss due to sudden immobilisation and hypercalcaemia caused by cancer. The Committee also concluded that the benefits of calcitonin-containing medicines did not outweigh their risks in the treatment of osteoporosis and that they should no longer be used for this condition. **References:** European Commission final decision (www.ema.europa.eu) WHO Pharmaceuticals Newsletter No. 4, 2012.
Chile	25 April 2013	Marketing authorisation for solutions for nebulization is suspended; while indications for injectable are restricted to the following: (a) prevention of acute loss of bone mass due to sudden immobilization, with usual treatment duration of two weeks, and maximum duration of four weeks, (b) Paget's disease, in patients who do not respond to alternative treatments or when said treatments they are not convenient, for a period of three months, or exceptionally up to 6 months and (c) hypercalcemia caused by cancer. In general, it is recommended that treatment with calcitonin should be limited to the shortest possible time period and using the minimum effective dose. **References:** Instituto de Salud Publica (www.ispch.cl)
Viet Nam	5 October 2012 31 October 2014	The marketing authorisation of calcitonin nasal spray was suspended. The use of calcitonin injection was restricted to the following indications: - Treatment of Paget's disease for patients who cannot be treated with alternative treatments - Prevention of acute bone loss due to sudden immobilisation such as in patients with recent osteoporotic fractures - Treatment of hypercalcaemia caused by cancer The benefits of calcitonin-containing medicines did not outweigh their risks of cancer in the treatment of osteoporosis (the only indication of calcitonin nasal spray). The benefit-risk balance remains positive only for certain uses of caclcitonin injection, according to EMA's decision. **References:**

		Drug Administration of Viet Nam Official Dispatch No. 15226/QLD-DK, 05 October 2012, and No. 18672/QLD-DK, 31 October 2014.

PRODUCT NAME: calcitonin-salmon

C.A.S. NUMBER: 47931-85-1

OTHER NAMES: Miacalcin®, Calcitec®

Country	Effective Date	Description of action taken
United Arab Emirates		Calcitec® was discontinued. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: calcium glubionate

C.A.S. NUMBER: 299-28-5

OTHER NAMES:

Country	Effective Date	Description of action taken
United Kingdom	August 2010	The Medicines and Healthcare products Regulatory Agency (MHRA) notified healthcare professionals that calcium gluconate injection packed in small-volume glass containers is now contraindicated for use as repeated or prolonged treatment, including an intravenous infusion, in children younger than 18 years and in patients with renal impairment. Aluminium can be leached from the glass after contact with calcium gluconate solution, leading to a risk of exposure to aluminium which might have adverse effects on bone mineralization and neurological development in children and those with renal impairment. **References:** Drug Safety Update, MHRA, Volume 4, Issue 1, August 2010 (www.mhra.gov.uk). WHO Pharmaceuticals Newsletter No. 5, 2010.
United Arab Emirates		Calcium Sandoz 10% injection were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: canagliflozin

C.A.S. NUMBER: 928672-86-0

OTHER NAMES: Invokana

Country	Effective Date	Description of action taken
Brazil	May 2016	Following the observation of a higher incidence of lower limb amputation, especially toes, in patients treated with canagliflozin from the CANVAS study (an ongoing study of cardiovascular outcomes in diabetic patients at high risk of cardiovascular events), health professionals were reminded of guidelines regarding routine preventive foot care practices , including monitoring of patients with risk factors for amputation events, amon. The medicine package leaflet has been updated. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: captopril

C.A.S. NUMBER: 62571-86-2

OTHER NAMES: Midopril

Country	Effective Date	Description of action taken
United Arab Emirates		Midopril 25 and Midopril 50 were suspended. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: carbamazepine

C.A.S. NUMBER: 298-46-4

OTHER NAMES: Tegretol, Temporol, Neurotol

Country	Effective Date	Description of action taken
India	12 May 2015	The Central Drugs Standard Control Organization (CDSCO) has requested all states/Union Territories drug controllers to instruct all manufactures licenced for carbamazepine in the country to include Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis (SJS/TEN) in prescribing information and on their official website. **References:** Letter issued by CDSCO on 12 May 2015. WHO Pharmaceuticals Newsletter No. 2, 2016. WHO Pharmaceuticals Newsletter No. 3, 2018.
United Arab Emirates		Tegretol 125 and 250 were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: carbocisteine

C.A.S. NUMBER: 638-23-3

OTHER NAMES: Mucofront, Pectox

Country	Effective Date	Description of action taken
United Arab Emirates		Mucofront syrup and capsules, and Pectox syrup were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: carboplatin

C.A.S. NUMBER: 41575-94-4

OTHER NAMES: Paraplatin

Country	Effective Date	Description of action taken
United Arab Emirates		Paraplatin injections were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: carvedilol

C.A.S. NUMBER: 72956-09-3

OTHER NAMES: Dilatrend, Carvetrend, Coryol, Milenol

Country	Effective Date	Description of action taken
Montenegro	13 February 2015	In accordance with Law on medicines, the Agency for Medicines and Medical Devices of Montenegro (CALIMS) has sent DHPC to relevant HCPs to inform them of the perceived increased risk of serious skin reactions (Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis [SJS/TEN]). The summary of product characteristics (SmPC) and patient information leaflet (PIL) are updated accordingly to new safety findings generated from Roche safety database. **References:** CALIMS, Direct healthcare professional communications.

PRODUCT NAME: cefaclor

C.A.S. NUMBER: 53994-73-3

OTHER NAMES: Tabiclor, Biocef, Ceclor, Vercef

Country	Effective Date	Description of action taken
United Arab Emirates		Vercef 250 mg capsules, and various Tabiclor products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cefadroxil

C.A.S. NUMBER: 66592-87-8

OTHER NAMES: Duricef,

Country	Effective Date	Description of action taken
United Arab Emirates		Duricef 500 mg and 1 g were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cefalexin (cephalexin)

C.A.S. NUMBER: 15686-71-2

OTHER NAMES: Ospexin, Ultrasporin, Midaflex, Cephalex, Pharmexin

Country	Effective Date	Description of action taken
United Arab Emirates	2010	Cefalexin-containing products (Ospexin, Ultrasporin, Cephalex, certain Pharmexin products) were withdrawn by the MAH before getting approval. In addition Pharmexin 1g tablets, 125 mg/5 ml and 250 mg/5 ml suspension, Midaflex suspensions and Midaflex 500 mg capsule were suspended. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cefatrizine

C.A.S. NUMBER: 51627-14-6

OTHER NAMES: Zanitrin

Country	Effective Date	Description of action taken
United Arab Emirates		Zantitrin capsules and suspensions were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cefazolin

C.A.S. NUMBER: 25953-19-9

OTHER NAMES: Pan-Cefazoline, Totacef

Country	Effective Date	Description of action taken
United Arab Emirates		Pan-Cerazoline 1 g (IM) products were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. Totacef 250 mg, 500 mg and 1 g injection products were withdrawn by the MAH before the product getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: Cefepime

C.A.S. NUMBER: 123171-59-5

OTHER NAMES: Pozineg, Maxipime

Country	Effective Date	Description of action taken
United Arab Emirates		Pozineg 2000 and Maxipime 500 mg injection products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cefetamet

C.A.S. NUMBER: 65052-63-3

OTHER NAMES:

Country	Effective Date	Description of action taken
Viet Nam	28 March 2014 29 July 2015	In March 2014, the MAH was requested to provide more data to prove the product's characteristic of safety and efficacy. At the same time registration and importing of the product/ingredients was suspended. In July 2015, the marketing authorisation of the product was revoked, and the products recalled, due to limited safety and efficacy data. **References:** Drug Administration of Viet Nam Official Official documents No. 4810/QLD-DK, 28 March 2014, and No. 423/QD-QLD, 29 July 2015.

PRODUCT NAME: cefixime

C.A.S. NUMBER: 79350-37-1

OTHER NAMES: Suprax Solutab

Country	Effective Date	Description of action taken
Armenia	2018	After an assessment by the Scientific Centre of Drug and Medical Technology Expertise after Academician E. Gabrielyan (SCDMTE), the product information of Suprax Solutab was updated to include information on posology and administration for reducing risk of fatal mechanical asphyxia due to inappropriate use of the medicine and ingestion of a whole tablet without prior dissolution in water. As a risk minimization measure a DHPC was circulated. **References:** Communication from Armenian National Pharmacovigilance Centre, 2018.

PRODUCT NAME: cefmetazole

C.A.S. NUMBER: 56796-20-4

OTHER NAMES:

Country	Effective Date	Description of action taken
Viet Nam	13 July 2018	The use of cefmetazole is restricted to treat infections caused by susceptible organisms: cystitis, nephritis, pyelonephritis, peritonitis, cholecystitis, cholangitis, Bartholin's abscess and adnexitis, endometritis, conjunctivitis, osteonecrosis of the jaw. The restrictions are based on evidence from clinicals. **References:** Drug Administration of Viet Nam Official Dispatch No. 13398/QLD-DK, 13 July 2018.

PRODUCT NAME: cefotaxime

C.A.S. NUMBER: 63527-52-6

OTHER NAMES: Taxime

Country	Effective Date	Description of action taken
United Arab Emirates		Taxime injection products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cefoxitin

C.A.S. NUMBER: 35607-66-0

OTHER NAMES: Mefoxin

Country	Effective Date	Description of action taken
United Arab Emirates		Foxitin 1 g, Mefoxin 1 g and 2 g injection products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cefpodoxime

C.A.S. NUMBER: 80210-62-4

OTHER NAMES: Auropodox

Country	Effective Date	Description of action taken
United Arab Emirates		Auropodox 100 products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cefradine

C.A.S. NUMBER: 38821-53-3

OTHER NAMES: Intracef, Velosef, Vepesid

Country	Effective Date	Description of action taken
United Arab Emirates		Vepesid 50 mg and 100 mg capsules, Velocef products in various forms and strengths were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: Ceftazidime

C.A.S. NUMBER: 78439-06-2

OTHER NAMES: Fortum

Country	Effective Date	Description of action taken
United Arab Emirates		Fortum 250 mg and 2 g injection products were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: ceftriaxone

C.A.S. NUMBER: 73384-59-5

OTHER NAMES: Mesporin, Roxcef, Rocephin, Axone

Country	Effective Date	Description of action taken
New Zealand	September 2011	Ceftriaxone is contraindicated in neonates if they require (or are expected to require) treatment with calcium containing intravenous solutions due to the risk of calcium precipitation. In addition, ceftriaxone must not be administered simultaneously with calcium-containing intravenous solutions, including continuous calcium containing infusions via a Y site, because calcium precipitation can occur. **References:** Prescriber Update Vol. 32 No. 3, September 2011 (www.medsafe.govt.nz). WHO Pharmaceuticals Newsletter No. 5, 2011.
United Arab Emirates		Axone 500 mg and 1 g IV injection products were suspended. Mesporin and Roxcef IM/IV products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cefuroxime

C.A.S. NUMBER: 56238-63-2; 64544-07-6

OTHER NAMES: Xorim, Cefutil, Zinoximor, Zinoxime

Country	Effective Date	Description of action taken
United Arab Emirates		Xorim and Zinoxime 1.5 g injection products, Cefutil 125 mg and Zinoximor 125 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: celecoxib

C.A.S. NUMBER: 169590-42-5

OTHER NAMES: Celebrex, Celebra

Country	Effective Date	Description of action taken
Europe	20 May 2011	The EMA concluded that existing evidence of safety and efficacy does not support the use of celecoxib in familial adenomatous polyposis (FAP) patients.

		References: Press release, EMA, 20 May 2011 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 3, 2011.
Egypt	16 June 2011	It was decided that the following indication for celecoxib is not approved anymore: "Familial adenomatous polyposis (FAP)" **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.

PRODUCT NAME: cephapirin

C.A.S. NUMBER: 21593-23-7

OTHER NAMES: Cefatrexyl

Country	Effective Date	Description of action taken
United Arab Emirates		Cefatrexyl 500 mg and 1 g were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cerivastatin sodium

C.A.S. NUMBER: 145599-86-6

OTHER NAMES: Baycol, Lipobay

Country	Effective Date	Description of action taken
United Arab Emirates		Lipobay 0.1 mg, 0.2 mg, and 0.3 mg products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cetirizine dihydrochloride

C.A.S. NUMBER: 83881-52-1

OTHER NAMES: Finallerg, Histatin

Country	Effective Date	Description of action taken
United Arab Emirates		Finallerg 10 mg/ml drops and Histasin 10 mg tablet (Iceland registration only) were suspended. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cetrorelix

C.A.S. NUMBER: 120287-85-6

OTHER NAMES: Cetrotide

Country	Effective Date	Description of action taken
United Arab Emirates		The products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cetuximab

C.A.S. NUMBER: 205923-56-4

OTHER NAMES: Erbitux

Country	Effective Date	Description of action taken
Brazil	December 2014	Health professionals were informed of changes in the product package leaflet, approved by the European Union and in Brazil, regarding its indication for the treatment of patients with non-mutated RAS metastatic colorectal cancer and with epidermal growth factor receptor (EGFR) expression. Additionally, the combination of Erbitux® with oxaliplatin-containing chemotherapy is contraindicated in patients with metastatic colorectal cancer (CCRm) RAS mutated based on available tests or whose RAS status is unknown. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: chlorhexidine gluconate

C.A.S. NUMBER: 55-56-1

OTHER NAMES: Septivon

Country	Effective Date	Description of action taken
Togo	12 April 2018	The MAH voluntarily withdrew the marketing authorisation of chlorhexidine gluconate (Septivon Care) in the form of cutaneous spray solution. **References:**

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: chloroquine

C.A.S. NUMBER: ; 132-73-0

OTHER NAMES: Malarivon, Avloclor, Malarex

Country	Effective Date	Description of action taken
United Arab Emirates		Chloroquine phosphate containing products Avloclor 250 mg, Malarex 250 mg, and Malarex 75 mg/5 ml were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. Malarivon 50 mg/5 ml was withdrawn by the MAH before getting approval. In addition, Nivaquine 200 mg/5 ml (chloroquine sulphate) solution for injection was withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: chlorphenamine maleate

C.A.S. NUMBER: 113-92-8

OTHER NAMES: chlorpheniramine, Phensedyl

Country	Effective Date	Description of action taken
United Arab Emirates		Chlorpheniramine 2 mg/5 ml was voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. Phensedyl syrup were withdrawn by the MAH before the product getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: chlorpromazine

C.A.S. NUMBER: 50-53-3

OTHER NAMES: Amplictil, Largactil, Thorazine, Diabinese

Country	Effective Date	Description of action taken
Brazil	September 2012	Healthcare professionals were informed of the updated information on adverse reactions within the package leaflet of Amplictil regarding gastrointestinal disorders characterized by ischemic colitis, intestinal obstruction, gastrointestinal necrosis, necrotizing colitis (sometimes fatal) and intestinal perforation (sometimes fatal). **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).
United Arab Emirates		Largactil products and Diabinese 250 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: chlortalidone

C.A.S. NUMBER: 77-36-1

OTHER NAMES: Hygroton

Country	Effective Date	Description of action taken
United Arab Emirates		Hygroton 50 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cholecalciferol

C.A.S. NUMBER:

OTHER NAMES: ITRO-D3

Country	Effective Date	Description of action taken
United Arab Emirates		The application for Itro-D3® 22.400 I.U. was rejected by the committee for various reasons. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cholestyramine

C.A.S. NUMBER: 11041-12-6

OTHER NAMES: Questran, Cholybar, Olestyr

Country	Effective Date	Description of action taken
United Arab Emirates		Questran powder were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: chymotrypsin

C.A.S. NUMBER: 9004-07-03

OTHER NAMES: alpha-chymotrypsin

Country	Effective Date	Description of action taken
Viet Nam	26 December 2017	The use of alpha-chymotrypsin is restricted to treat oedema after trauma, surgery, burns. The restrictions intend to conclude the indication of oral and sublingual alpha-

		chymotrypsin according to Viet Nam National Formulary and last SmPC approved in France. **References:** Drug Administration of Viet Nam Official Dispatch No. 22098/QLD-DK, 26 December 2017.

PRODUCT NAME: ciclopirox

C.A.S. NUMBER: 29342-05-0

OTHER NAMES: Mycoster

Country	Effective Date	Description of action taken
United Arab Emirates		Mycoster 1% solution and powder were withdrawn by the MAH before getting approval. Mycoster 1% cream and 8% powder were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cilazapril

C.A.S. NUMBER: 92077-78-6

OTHER NAMES: Inhibace

Country	Effective Date	Description of action taken
United Arab Emirates		Inhibace 0.5 mg and 1 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cilostazol

C.A.S. NUMBER: 73963-72-1

OTHER NAMES: Pletal, Ekistol

Country	Effective Date	Description of action taken
Europe	22 March 2013	The EMA's Committee for Medicinal Products for Human Use (CHMP) recommended that cilostazol should only be used in patients whose symptoms have not improved despite prior lifestyle changes such as exercise, healthy diet and stopping smoking. In addition, cilostazol-containing medicines should not be used in patients who have suffered severe tachyarrhythmia, or recent unstable angina, heart attack or bypass surgery, or who take two or more antiplatelet or anticoagulant medicines such as aspirin and clopidogrel.

		The recommendations followed a review of current evidence, which indicated that the modest benefits of these medicines are only greater than their risks in a limited subgroup of patients. **References:** European Commission final decision (www.ema.europa.eu) WHO Pharmaceuticals Newsletter No. 3, 2013.
Chile	4 June 2013	The indications for cilostazol is restricted to: the relief of intermittent claudication and other symptoms related to chronic occlusive arterial disease, in patients who have not responded adequately to changes in lifestyle (including quitting smoking and exercise programs) alone. New contraindications are added to contraindicated in patients with unstable angina or those who have had myocardial infarction or coronary intervention in the last six months, patients with a history of severe tachyarrhythmia, and patients who use two or more antiplatelet agents or anticoagulants. **References:** Instituto de Salud Publica (www.ispch.cl)
United Arab Emirates		Platel 50 mg and 100 mg were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cimetidine

C.A.S. NUMBER:

OTHER NAMES: Citius

Country	Effective Date	Description of action taken
United Arab Emirates		Citius 200 mg and 400 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cinacalcet

C.A.S. NUMBER: 364782-34-3

OTHER NAMES: Mimpara, Sensipar

Country	Effective Date	Description of action taken
Brazil	February 2013	ANVISA warned about the occurrence of a fatal case involving a patient who developed severe hypocalcemia while receiving Mimpara in a pediatric clinical study. It was

		believed that the drug has not been approved for use in pediatric patients. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: cinnarizine

C.A.S. NUMBER: 298-57-7

OTHER NAMES: Stugeron

Country	Effective Date	Description of action taken
United Arab Emirates		Stugeron Forte 75 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ciprofloxacin

C.A.S. NUMBER: 85721-33-1

OTHER NAMES: Ciprox

Country	Effective Date	Description of action taken
United Arab Emirates		Marketing authorisation for Ciprox 0.2% w/v infusion products were suspended. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cisapride

C.A.S. NUMBER: 81098-60-4

OTHER NAMES: Prepulsid, Propulsid, Prokinate

Country	Effective Date	Description of action taken
India	10 February 2011	Cisapride and its formulations for human use are prohibited in India. **References:** The Gazette of India, No. 71, New Delhi 10 February 2011.
Montenegro	3 February 2012	Based on EMA referral and in accordance with Law on medicines, the Agency for Medicines and Medical Devices of Montenegro (CALIMS) has sent DHPC to relevant HCPs to inform them of the perceived increased risk of serious arrhythmias related to the use of cisapride. **References:** CALIMS, Direct healthcare professional communications.

Bhutan	22 July 2015	All forms of cisapride-containing medicines are banned due to reports about cardiac arrhythmias with highest strength cisapride. All patients require ECG and renal functions test before and during the treatment. The decision considered similar actions in other countries. Pharmacies have been notified of the restrictions in the importation and sales of cisapride. **References:** Bhutan Drug Regulatory Authority, List of Banned Drugs (www.dra.gov.bt).
United Arab Emirates		The application for Prokinate products (tablets and suspension) was rejected by the committee for various reasons. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cisatracurium besilate

C.A.S. NUMBER:
96946-42-8
OTHER NAMES: Nimbex Forte

Country	Effective Date	Description of action taken
United Arab Emirates		Nimbex Forte 5 mg/ml were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cisplatin

C.A.S. NUMBER: 15663-27-1
OTHER NAMES: Platinol, Platinex

Country	Effective Date	Description of action taken
United Arab Emirates		Platinex 10 mg, 25 mg, and 50 mg injection products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: citalopram

C.A.S. NUMBER: 59729-32-7

OTHER NAMES: Cipramil, Celapram, Denyl, Celexa

Country	Effective Date	Description of action taken
USA	24 August 2011	The US FDA notified healthcare professionals and patients that the antidepressant citalopram hydrobromide should no longer be used at doses greater than 40 mg per day, because it can cause abnormal changes in the electrical activity of the heart (prolongation of the QT interval of the electrocardiogram [ECG]). According to the US FDA, studies did not show a benefit in the treatment of depression at doses higher than 40 mg per day. **References:** FDA Drug Safety Communication, US FDA, 24 August 2011 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 5, 2011.
Ireland	27 October 2011	Citalopram may cause QT prolongation and the product information will be updated, in particular to reduce the maximum daily dose to 40mg/day in adults and 20 mg/day in the elderly and in patients with impaired liver function. **References:** European Medicines Agency Science Medicines Health, Monthly Report, No. 1110, 27 October 2011 (http://www.dohc.ie/).
Egypt	24 November 2011	It was decided to amend the products SPC according to the following: Dose restriction: - Remove the dose recommendation of 60mg/day. - Citalopram should no longer be prescribed at doses greater than 40 mg per day. - 20 mg per day is the maximum recommended dose for patients with hepatic impairment, who are greater than 60 years of age, who are CYP 2C19 poor metabolizers, or who are taking concomitant cimetidine (Tagamet®), because these drug factors lead to increased blood levels of citalopram thereby increasing the risk of QT interval prolongation and Torsade de Pointes. -Citalopram is contraindicated in patients with congenital long QT syndrome. Warning & precaution: -Patients with congestive heart failure, bradyarrhythmias, myocardial infarction or predisposition to hypokalemia or hypomagnesaemia because of concomitant illness or drugs, are at higher risk of developing Torsade de Pointes. -Health Care Professionals should consider more frequent electrocardiogram (ECG) monitoring in patients with congestive heart failure, bradyarrhythmias. -Hypokalemia and hypomagnesaemia should be corrected before administering citalopram. Electrolytes should be monitored as clinically indicated.

		-Patients should contact a healthcare professional immediately if they experience signs and symptoms of an abnormal heart rate or rhythm while taking citalopram. -Patients should be advised not to stop taking citalopram or change or reduce the dose without first consulting their healthcare professional, as withdrawal symptoms may occur when citalopram treatment is discontinued, particularly if this is abrupt. Contraindications: -Do not use citalopram with other medicinal products known to prolong the QT interval. -Citalopram is contraindicated in patients with congenital long QT syndrome. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.
United Kingdom	December 2011	The MHRA advised that citalopram and escitalopram are associated with dose-dependent QT interval prolongation and should not be used in those with congenital long QT syndrome, preexisting QT interval prolongation, or in combination with other medicines that prolong the QT interval. The agency also revised the maximum daily dose for citalopram to 40 mg for adults, 20 mg for patients old than 65, and 20 mg for those with hepatic impairment. For escitalopram the maximum daily dose for patients older than 65 is reduced to 10 mg; other doses remain unchanged. **References:** Drug Safety Update, December 2011, Volume 5, issue 5, A1, MHRA, (www.mhra.gov.uk). WHO Pharmaceuticals Newsletter No. 1, 2012. WHO Pharmaceuticals Newsletter No. 4, 2016.
Switzerland	2 December 2011	Citalopram has been associated with a dose dependent QT prolongation. **References:** Communication from Swissmedic, July 2012.
Egypt	29 December 2011	Withdrawal of products containing citalopram 60 mg. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.
Canada	30 January 2012	Citalopram hydrobromide should no longer be used at doses greater than 40 mg per day due to study results indicating a dose dependent potential for QT prolongation. The maximum recommended dose is 20 mg per day for patients with hepatic impairment, patients who are 65 years or age or older, patients who are CYP2C19 poor metabolizers, or patients who are taking concomitant cimetidine or another CYP2C19 inhibitor. Citalopram hydrobromide is contraindicated in patients with congenital long QT syndrome or known QT interval prolongation. Patients

		should contact their health-care professional immediately if they experience signs and symptoms of an abnormal heart rate or rhythm while taking citalopram hydrobromide. **References:** Advisories, Warnings and Recalls, Health Canada, 30 January 2012 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 6, 2011. WHO Pharmaceuticals Newsletter No. 2, 2012.
Australia	February 2012	The Therapeutic Goods Administration (TGA) has reduced the maximum daily dose of citalopram to 40 mg following a study which showed dose-dependent QT prolongation with the medicine. In people over the age of 65, those with hepatic dysfunction, those takin **References:** Medicines Safety Update Vol 3, No. 1, February 2012 (www.tga.gov.au). WHO Pharmaceuticals Newsletter No. 2, 2012.
USA	28 March 2012	The labeling recommendation for patients with congenital long QT syndrome has been changed from “contraindicated” to “not recommended,” because it is recognized that there may be some patients with this condition who could benefit from a low dose of citalopram and who lack viable alternatives. The maximum recommended dose of citalopram is 20 mg per day for patients older than 60 years of age. **References:** FDA Drug Safety Communication, US FDA, 28 March 2012 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 3, 2012.
Brazil	2011 2012 2013	In September 2011, ANVISA warned that citalopram should no longer be used at doses greater than 40 mg/day because it may cause abnormal changes in cardiac electrical activity. Studies have not shown a benefit in the treatment of depression at doses greater than 40 mg/day. A letter to HCPs was published with this warning. In October 2011, ANVISA warned of the risk of prolongation of the QT and Torsade de Pointes interval associated with high doses of the drug. Considering that USFDA planned to update the product label in 2012, ANVISA decided to evaluate the new information available on the safety of citalopram-contain medicines. Subsequently, in February 2013, a new alert was published informing about the package leaflet update requested by ANVISA for all citalopram-containing products registered in Brazil. In June and September 2012, as well as February and April 2013, safety warnings about drugs containing citalopram and escitalopram oxalate have been communicated with health professionals, according to updates published in some clinical and consolidated studies by the UK MHRA and US FDA. The main topics concern the association with dose-dependent prolongation of the QT interval and

		recommended maximum daily doses. The package leaflets of the medications were updated. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: citicoline

C.A.S. NUMBER: 987-78-0

OTHER NAMES:

Country	Effective Date	Description of action taken
Viet Nam	13 November 2017 6 April 2018	The use of injectable citicoline was restricted to treat acute phase of cranial-cerebral trauma with impaired alertness in adults. The decision took into consideration the SmPC approved in France. For oral form citicoline, more data is requested to prove the product's characteristics of safety and efficacy, due to current limited safety and efficacy data of this form in Alzheimer, stroke and cardiovascular diseases. **References:** Drug Administration of Viet Nam Official Dispatch No. 18583/QLD-DK, 13 November 2017, and Official No. 6964/QLD-DK, 06 April 2018.

PRODUCT NAME: clarithromycin

C.A.S. NUMBER: 81103-11-9

OTHER NAMES: Biaxin, Maxilin

Country	Effective Date	Description of action taken
United Arab Emirates		The application for Maxilin® IV was rejected by the committee for various reasons. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: clemastine

C.A.S. NUMBER: 15686-51-8

OTHER NAMES: meclastin, Tavegyl

Country	Effective Date	Description of action taken
United Arab Emirates		Tavegyl 1 mg products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

United Arab Emirates		Tavegyl 0.1 mg/ml syrup and 1 mg/ml injection products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: clindamycin

C.A.S. NUMBER: 18323-44-9

OTHER NAMES: Cleocin, Clinacin, Dalacin-C, Clinium

Country	Effective Date	Description of action taken
United Arab Emirates		Clinium tablets and Dalacin-C 75 mg/5 ml solution were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: clodronate disodium

C.A.S. NUMBER: 22560-50-5

OTHER NAMES: Ostac

Country	Effective Date	Description of action taken
United Arab Emirates		Ostac 300 mg/10 ml infusion and 400 mg capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: clonazepam

C.A.S. NUMBER: 1622-61-3

OTHER NAMES: Klonopin, Rivotril

Country	Effective Date	Description of action taken
United Arab Emirates		Rivotril 1 mg/ml were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: clopidogrel

C.A.S. NUMBER: 113665-84-3

OTHER NAMES: Plavix

Country	Effective Date	Description of action taken
Egypt	17 September 2009	Proton pumb inhibitors should not be taken routinly in patients receiving clopidogrel. Only when necessary patients receiving clopidogrel may use proton pumb inhibitors with caution. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012. WHO Pharmaceuticals Newsletter No. 6, 2014.
Canada	22 September 2011	Proton pump inhibitors (PPIs) known to strongly or moderately reduce clopidogrel effectiveness should be avoided. Omeprazole is one of these. If a PPI must be used in a patient taking clopidogrel, consider a PPI that does not interact as strongly. Pantoprazole is one of these. **References:** Advisories, Warnings and Recalls, Health Canada, 22 September 2011 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 5, 2011.

PRODUCT NAME: clotrimazole

C.A.S. NUMBER: 23593-75-1

OTHER NAMES: Canesten

Country	Effective Date	Description of action taken
United Arab Emirates		Canesten 1% powder were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cobimetinib

C.A.S. NUMBER: 934660-93-2

OTHER NAMES: Cotellic

Country	Effective Date	Description of action taken
Brazil	December 2016	Health professionals were advised to exercise caution when prescribing cobimetinib in patients with additional risk factors for bleeding, such as brain metastases and/or use of concomitant medications that increase the risk of bleeding. This came after identification of additional adverse events of severe bleeding, including intracranial and gastrointestinal tract bleeding, in patients receiving Cotellic, in post-marketing safety reports and ongoing clinical studies. **References:**

		ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: colchicine

C.A.S. NUMBER: 64-86-8

OTHER NAMES: Colcrys

Country	Effective Date	Description of action taken
New Zealand	March 2011	Medsafe advised that the lowest effective dose of colchicine should be used and must not exceed 6 mg over four days. Colchicine should not be used in patients with hepatic or renal impairment who are also taking CYP3A4 and P-glycoprotein inhibitors. **References:** Prescriber Update Vol. 32, No.1 March 2011, (www.medsafe.govt.nz). WHO Pharmaceuticals Newsletter No. 2, 2011.

PRODUCT NAME: colestipol

C.A.S. NUMBER: 37296-80-3

OTHER NAMES: Colestid

Country	Effective Date	Description of action taken
United Arab Emirates		Colestid granules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: crizotinib

C.A.S. NUMBER: 877399-52-5

OTHER NAMES: Xalkori

Country	Effective Date	Description of action taken
Montenegro	11 December 2015	The Agency for Medicines and Medical Devices of Montenegro (CALIMS) has sent DHPC to relevant HCPs to inform them of the perceived increased risk of serious cardiovascular reactions (heart failure). The summary of product characteristics (SmPC) and patient information leaflet (PIL) are updated accordingly to new safety findings generated from clinical trials and postmarketing experience. **References:** CALIMS, Direct healthcare professional communications.

PRODUCT NAME: cyclophosphamide

C.A.S. NUMBER: 50-18-0

OTHER NAMES: Endoxan, Cytoxan, Neosar, Procytox, Revimmune, Cycloblastin

Country	Effective Date	Description of action taken
United Arab Emirates		Endoxan 50 mg tablets, Endoxan 200 mg, 500 mg and 1 g injection products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cyclosporine

C.A.S. NUMBER:

59865-13-3

OTHER NAMES: Neoral, Sandimmune, ciclosporin A, cicloimmune

Country	Effective Date	Description of action taken
United Arab Emirates		The application for Cicloimmune 25, 50 and 100 was rejected by the committee for various reasons. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: cyproterone acetate

C.A.S. NUMBER: 427-51-0

OTHER NAMES: Androcur, Cyprostat

Country	Effective Date	Description of action taken
Egypt	24 June 2010	Cyproterone acetate is contraindicated in patients with meningioma or a history of meningioma. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.
United Arab Emirates		Androcur 10 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: dabigatran

C.A.S. NUMBER: 211914-51-1

OTHER NAMES: Pradaxa, Pradax, Prazaxa

Country	Effective Date	Description of action taken
Australia	December 2011	The Therapeutic Goods Administration (TGA) urged clinicians to give careful consideration to the suitability of their patients for dabigatran particularly with regard to recognized risks of bleeding. **References:** Medicines Safety Update Vol 2, No. 6, December 2011 (www.tga.gov.au). WHO Pharmaceuticals Newsletter No. 1, 2012.
United Kingdom	December 2011	The Medicines and Healthcare products Regulatory Agency (MHRA) advised health-care professionals that renal function should be assessed in all patients before starting dabigatran and at least once a year in patients older than 75 years or those with a suspected decline in renal function. Dabigatran is contraindicated in patients with severe renal impairment (creatinine clearance <30 mL/min). The MHRA also advised health-care professionals to check for signs of bleeding or anaemia and stop treatment if severe bleeding occurs. **References:** Drug Safety Update, December 2011, Volume 5, issue 5, A2, MHRA, (www.mhra.gov.uk). WHO Pharmaceuticals Newsletter No. 1, 2012.
Canada	16 March 2012	Boehringer Ingelheim (Canada) Ltd., in consultation with Health Canada, informed health-care professionals of important new recommendations for dabigatran etexilate regarding renal function assessment and use in patients with severe valvular disease or prosthetic heart valves. Prior to initiation of treatment with dabigatran etexilate, renal function should be assessed in all patients by calculating the creatinine clearance (CrCl) to exclude patients with severe renal impairment (i.e. CrCl < 30 mL/min). While on treatment with dabigatran etexilate, renal function should be assessed in clinical situations when it is suspected that renal function could decline or deteriorate rapidly, such as hypovolemia, dehydration, and with certain co-medications. These clinical situations may result in an increase of dabigatran exposure. In the elderly (> 75 years), or in patients with moderate renal impairment (CrCl 30-50 mL/min), renal function should be assessed routinely by calculating the creatinine clearance at least once a year. **References:** Advisories, Warnings and Recalls, Health Canada, 16 March 2012 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 3, 2012. WHO Pharmaceuticals Newsletter No. 2, 2015. WHO Pharmaceuticals Newsletter No. 3, 2018.
Saudi Arabia	23 May 2012	The Saudi Food and Drug Authority (SFDA) shared important safety information with healthcare professionals about an increased number of spontaneous reports of fatal cases resulting from bleeding episodes in patients treated with dabigatran etexilate. In Saudi Arabia, the drug is only

		approved for prevention of venous thromboembolism (VTE) in patients following hip or knee replacement surgery. Based on that, the SFDA advised concerned physicians to consider the following recommendations when initiating dabigatran etexilate therapy: 1. Dabigatran etexilate is contraindicated in patients with severe renal impairment (CrCl<30 ml/min); 2. Renal function should be assessed by calculating the creatinine clearance (CrCl) in all patients prior to initiating the therapy; 3. While on treatment, renal function should be assessed in clinical situations where a decline in renal function is suspected, such as hypovolemia, dehydration, and with certain co-medications, etc.; 4. In elderly patients (>75 years) or in patients with renal impairment the renal function should be assessed at least once a year. **References:** Communication from National Pharmacovigilance and Drug Safety Centre, SFDA, 23 May 2012. WHO Pharmaceuticals Newsletter No. 3, 2012.
Viet Nam	12 September 2013	The product information was updated with a new contraindication for those with mechanical heart valves. **References:** Drug Administration of Viet Nam Official Dispatch No. 15115/QLD-DK, 12eptember 2013.
Brazil	2011 2012 2013	In November 2011, new recommendations were added for evaluation of renal function in potential patients or who are already being treated with Pradaxa after reports of fatal hemorrhage cases in Japan: evaluation of renal function in all patients before starting therapy, contraindication in patients with severe renal failure; need for renal function assessment while the patient is undergoing treatment and evaluation of renal function at minimum annual frequency in elderly patients (> 75 years). In November 2012, health professionals were again informed on the risk of bleeding associated with Pradaxa treatment and recommendations to reduce it. In Januray 2013, following a phase II clinical study evaluating the use of Pradaxa® in the prevention of stroke, systemic embolism and nervous thrombosis in patients with heart valve prostheses, health professionals and patients were informed that the drug package leaflet will be updated to include a new contraindication of the drug, which cannot be used in patients with heart valve prostheses. **References:** ANVISA Pharmacovigilance Alert, and Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: darbepoetin alfa

C.A.S. NUMBER: 209810-58-2

OTHER NAMES: Aranesp

Country	Effective Date	Description of action taken
Brazil	February 2017	Healthcare professionals were informed about the risks of severe skin reactions in patients treated with Aranesp. Blistering and skin exfoliation, including multiform erythema and Stevens-Johnson syndrome (SSJ)/Toxic Epidermal Necrolysis (NET) have been reported in patients treated with Aranesp in the post-marketing period, although very rarely. Healthcare professionals were instructed to discontinue therapy immediately if a severe skin reaction such as SSJ/NET is suspected, and the switch to another Erythropoiesis Stimulating Agent is not recommended. The product package leaflet has been revised. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: dasatinib

C.A.S. NUMBER: 302962-49-8

OTHER NAMES: Sprycel, Dasanix

Country	Effective Date	Description of action taken
Brazil	August 2011	ANVISA warned about the risk of pulmonary arterial hypertension, after reassessing adverse reactions related to Sprycel. Patients are recommended to immediately report to their physician if they develop shortness of breath and fatigue after initiation of treatment with dasatinib. Healthcare professionals are advised to evaluate patients for signs and symptoms of underlying cardiopulmonary disease before starting the use of dasatinib, among other recommendations. The product package leaflet has been updated. In addition, a letter to healthcare professionals on the subject was published. **References:** ANVISA Pharmacovigilance Alert, and Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).
Switzerland	19 August 2011	Rare cases of pulmonary arterial hypertension (PAH) have been reported with dasatinib. **References:** Communication from Swissmedic, July 2012.
Canada	30 August 2011	Health Canada announced Bristol-Myers Squibb Canada's (BMS) new safety information regarding reports of serious

		pulmonary arterial hypertension (PAH) in patients treated with dasatinib. **References:** Advisories, Warnings and Recalls, Health Canada, 30 August 2011 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 5, 2011.

PRODUCT NAME: decitabine

C.A.S. NUMBER: 2353-33-5

OTHER NAMES: Dacogen

Country	Effective Date	Description of action taken
United Arab Emirates		Dacogen injection products were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: denosumab

C.A.S. NUMBER: 615258-40-7

OTHER NAMES: Prolia, Xgeva

Country	Effective Date	Description of action taken
Montenegro	11 May 2016	The Agency for Medicines and Medical Devices of Montenegro (CALIMS) has sent DHPC to relevant HCPs to inform them of the perceived increased risk of atypic fracture of femor. The summary of product characteristics (SmPC) and patient information leaflet (PIL) are updated accordingly to new safety findings approved by EMA. **References:** CALIMS, Direct healthcare professional communications.
Brazil	August 2012 January 2013 June 2015 May 2017 June 2017	In 2012, Health professionals were informed about the risk of atypical femoral fracture with the use of Prolia, after confirmation of cases in patients who were using Prolia during the open phase of a study in patients with postmenopausal osteoporosis. The package leaflet was updated with the information and a warning regarding the risk. The health professionals were reminded to alert patients of the appearance of unusual pain in the thigh, hip and groin, which should be investigated. In 2013, based on post-marketing evidence, health professionals were notified about the risk of anaphylactic reaction and hypersensitivity reactions with the use of Prolia. Updates were made to the package leaflet regarding contraindications and adverse reactions.

	In 2015, health professionals were informed of clinically significant cases of hypercalcaemia after discontinuation of Prolia treatment in growth pacientes, which occurred when the drug was used off-label (such as for osteogenesis imperfecta, fibrous dysplasia, and infant Paget's disease). It is advised that healthcare professionals monitor the development of hypercalcaemia after discontinuation of denosumab in growing patients and that Prolia not be administered for unproved indications. In May 2017, researchers participating in Xgeva® studies, on the risks of multiple vertebral fractures following treatment in individuals in patients who discontinued Xgeva, were specifically informed: After discontinuation of Xgeva® during the course of the study or after completion, the investigator should consider the individual's risk of having fractures and the risk-benefit of initiating anti-resorption therapy in accordance with local clinical guidelines for osteoporosis treatment. The reference safety information (Annex A) in the Xgeva Investigator's Brochure® has been updated. Recommendations were made so that individuals who were participating or participated in the study were informed about it. In June 2017, health professionals were informed about the risks of multiple vertebral fractures, not due to metastases, in patients who discontinued Xgeva, particularly patients with risk factors such as osteoporosis or previous fractures. Xgeva's ® package has been updated. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: desloratadine

C.A.S. NUMBER: 100643-71-8

OTHER NAMES: NeoClarityn, Claramax, Clarinex, Larinex, Aerius, Dazit, Azomyr, Deselex, Delot

Country	Effective Date	Description of action taken
Egypt	2 June 2011	Contraindicated in children less than two years. For children under 6 years it should ONLY be used under medical supervision. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.

PRODUCT NAME: desoximetasone

C.A.S. NUMBER: 382-67-2

OTHER NAMES: Topisolone, Topicort, Emcor, Desacort, Ibaril

Country	Effective Date	Description of action taken

United Arab Emirates		Ibaril 0.05% and 0.25% oitment were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: dexamethasone

C.A.S. NUMBER: 1950-02-02

OTHER NAMES: Decadron, Maxidex, Mephamesone, Dexalocal, Oradexon

Country	Effective Date	Description of action taken
United Arab Emirates		Decadron tablets and drops, Mephamesone 4 mg/ml injection, and Dexalocal 0.1% solution were withdrawn by the MAH before getting approval; while Maxidex ointment, Oradexon 0.5 mg tablet and 5 mg/mlinjection were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: dexrazoxane

C.A.S. NUMBER: 24584-09-6

OTHER NAMES: Zinecard, Cardioxane

Country	Effective Date	Description of action taken
Europe	23 June 2011	The European Medicines Agency (EMA) has recommended restricting the use of dexrazoxane to adult patients with advanced or metastatic breast cancer who have already received a minimum cumulative dose of 300 mg/m^2 of doxorubicin or 540 mg/m^2 of epirubicin to treat cancer. It also recommended that the use of dexrazoxane when used with doxorubicin should be reduced from a dose ratio of 20:1 (20 parts dexrozaxone to 1 part doxorubicin) to a ratio of 10:1. The dose ratio of dexrazoxane to epirubicin remains unchanged at 10:1. The Agency's Committee for Medicinal Products for Human Use (CHMP) also recommended contraindicating the use of this medicine in children. The restriction follows concerns that dexrazoxane could be linked to an increased risk of acute myeloid leukaemia (AML) and myelodysplastic syndrome (MDS). **References:** Press release, EMA, 23 June 2011 (www.ema.europa.eu). WHO Pharmaceuticals Newsletter No. 4, 2011.
Chile	30 December 2011	The product label is updated to include a new contraindication in children. Based on communications with the USFDA and EMA, dexrazoxane poses a greater risk of

		acute myeloid leukemia and myelodysplastic syndrome among children and teenagers; and the benefits of Dexrazoxane outweigh the risks only in adult patients with advanced or metastatic breast cancer who have received a minimum cumulative dose of 300 mg/m^2 of doxorubicin or 540 mg/m^2 of epirubicin. **References:** Instituto de Salud Publica (www.ispch.cl)

PRODUCT NAME: dextromethorphan

C.A.S. NUMBER: 125-71-3

OTHER NAMES: Mentovick, Robitussin, Delsym, DM, DexAlone, Duract

Country	Effective Date	Description of action taken
Brazil	September 2013	Following information about suspected cases of dextromethorphan poisoning among children in Paraguay, as well as potential suspected cases of intoxication detected in a Brazilian city bordering the Paraguayan city with the highest number of cases of intoxication were reported, ANVISA issued an alert informing the main symptoms of dextromethorphan intoxication, highlighting the need for immediate medical attention. It was emphasized that the drug was not registered in Brazil and that the government of Paraguay suspended the production and commercialization of the product as a monodrug in that country. I also stressed the dangers of consumin drugs that are not registered in Brazil, which puts patients' safety at risk. **References:** ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia).

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: dextropropoxyphene

C.A.S. NUMBER: 469-62-5

OTHER NAMES:

Country	Effective Date	Description of action taken
Viet Nam	14 April 2010	The marketing authorisation for dextropropoxyphene was withdrwan due to Increase the risk of serious abnormal heart rhythms that have been linked to serious adverse effects including sudden death. **References:** Drug Administration of Viet Nam Official No. 3609/QLD-DK, 14 April 2010.
United Arab Emirates		Alghaphan injection and tablets were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety.

		References: Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: diazepam

C.A.S. NUMBER: 439-14-5

OTHER NAMES: Valium, Vazepam, Valtoco

Country	Effective Date	Description of action taken
United Arab Emirates		Valium 2 mg/5 ml syrup and 2 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: dibrompropamidine isethionate

C.A.S. NUMBER: 614-87-9

OTHER NAMES: Brulidine

Country	Effective Date	Description of action taken
United Arab Emirates		Brulidine cream were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: diclofenac

C.A.S. NUMBER: 15307-86-5

OTHER NAMES: Cataflam, Voltaren, Diclorapid, Diklofen, Diklofenak, Rapten Duo, Rapten Forte, Rapten K, Dolvic-K, Rapidus, Tabiflex

Country	Effective Date	Description of action taken
United Arab Emirates	2010	Dolvik-K 50 mg were suspended; while Rapidus 25 mg and Tabiflex 25 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.
Syrian Arab Republic	8 May 2011	Based on updated drug information, the package insert is to be updated with addition of a new warning that this pharmaceutical form is not recommended in children below the age of 10 years. **References:** Circular from the Ministry of Health, 08 May 2011.

Egypt	22 September 2011	Do not use for children less than six years. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.
Montenegro	14 February 2013	Based on EMA referral and in accordance with Law on medicines, the Agency for Medicines and Medical Devices of Montenegro (CALIMS) has sent DHPC to relevant HCPs to inform them of the perceived increased risk of serious heart and circulation adverse reactions related to the use of diclofenac and new risk minimisation measures. **References:** CALIMS, Direct healthcare professional communications.
Europe	28 June 2013	The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) found that the effects of systemic diclofenac on the heart and circulation are similar to those of selective COX-2 inhibitors, another group of painkillers. This applies particularly when diclofenac is used at a high dose and for long-term treatment. The PRAC therefore recommended that the same precautions already in place to minimise the risks of blood clots in the arteries with selective COX-2 inhibitors should be applied to diclofenac. **References:** EMA Referrals (www.ema.europa.eu) WHO Pharmaceuticals Newsletter No. 5, 2013.
Singapore	27 February 2014	Taking into consideration the available scientific evidence suggesting that high doses of diclofenac used over a long duration is associated with increased cardiovascular (CV) risks, and expert opinions from local clinicians and HSA's Product Vigilance Advisory Committee as well as the regulatory developments in other international jurisdictions, the HSA recommended that the use of high dose systemic diclofenac (150mg/day) for more than four weeks be contraindicated in patients with established CV disease or uncontrolled hypertension. The product label is to be updated with the following: - The use of high dose diclofenac (150mg/day) for more than four weeks is contraindicated in patients with established cardiovascular (CV) disease or uncontrolled hypertension. - If diclofenac treatment is needed, patients with established CV disease, uncontrolled hypertension or significant CV risk factors should be treated only after careful consideration and at doses ⩽100 mg daily if the treatment is for more than 4 weeks. - As the CV risks of diclofenac may increase with dose and duration of exposure, diclofenac should always be prescribed at the lowest effective daily dose and for the shortest duration possible. **References:**

		Communication from the Health Sciences Authority, February 2014.
Indonesia	13 July 2015	The product information of all diclofenac containing products should be revised with additional information due to risk of cardiovascular events. **References:** Dear Healthcare Professional Communication SV.03.01.343.3.07.15.4239
Brazil	December 2016	ANVISA warned that intramuscular administration of the injectable form of diclofenac should be carefully evaluated due to the risk of injection site injury. To reduce the risk of injury occurring with intramuscular use of diclofenac, several recommendations were made. **References:** ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia).
Viet Nam	27 April 2017	The product information for diclofenac-containing medicines was updated with new contraindications: established congestive heart failure (NYHA II-IV), ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease. All NSAIDs were recommeded to use the lowest effective dose for the shortest duration necessary to control symptoms. The restrictions intend to minimise the cardiovascular risk. EMA's evaluation showed a consistent but small increase in the risk of cardiovascular side effects for diclofenac compared with other NSAIDs. **References:** Drug Administration of Viet Nam Official Dispatch No. 5749/QLD-DK, 27 April 2017.

PRODUCT NAME: diclofenamide

C.A.S. NUMBER: 120-97-8

OTHER NAMES: Oratrol

Country	Effective Date	Description of action taken
United Arab Emirates		Oratrol 50 mg were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: diethylamine salicylate

C.A.S. NUMBER: 4419-92-5

OTHER NAMES: Algesal

Country	Effective Date	Description of action taken
United Arab Emirates		Algesal and Algesal Suractive cream were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: difemerine

C.A.S. NUMBER: 70280-88-5

OTHER NAMES: Luostyl

Country	Effective Date	Description of action taken
United Arab Emirates		Luostyl capsules and 1 mg/ml injection products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: diflucortolone

C.A.S. NUMBER: 59198-70-8

OTHER NAMES: Temetex

Country	Effective Date	Description of action taken
United Arab Emirates		Temetex cream and ointment were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: diflunisal

C.A.S. NUMBER: 22494-42-4

OTHER NAMES: Dolobid

Country	Effective Date	Description of action taken
United Arab Emirates		Dolobid 250 mg and 500 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: digoxin

C.A.S. NUMBER: 20830-75-5

OTHER NAMES: Lanoxin

Country	Effective Date	Description of action taken
United Arab Emirates		Lanoxin PG 0.0625 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: diiodohydroxyquinoline

C.A.S. NUMBER: 83-73-8

OTHER NAMES: Diodoquin

Country	Effective Date	Description of action taken
Egypt	13 May 2010	Not used for children. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.

PRODUCT NAME: dimethicone

C.A.S. NUMBER: 9006-65-9

OTHER NAMES: polysilane

Country	Effective Date	Description of action taken
United Arab Emirates		Polysilane tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: dinoprostone

C.A.S. NUMBER:

363-24-6

OTHER NAMES: Prostin E2, Cervidil, Propess

Country	Effective Date	Description of action taken
United Arab Emirates		Prostin E2 0.5 mg tablets were withdrawn by the MAH before getting approval. **References:**

		Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: diphenhydramine

C.A.S. NUMBER: 58-73-1

OTHER NAMES: Pellit

Country	Effective Date	Description of action taken
United Arab Emirates		Pellit gel were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: dipivefrin

C.A.S. NUMBER: 52365-63-6

OTHER NAMES: Propine, Pivalephrine, Dipivefrin

Country	Effective Date	Description of action taken
United Arab Emirates		Propine 0.1% drops were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: dolasetron mesylate

C.A.S. NUMBER: 115956-13-3

OTHER NAMES: Anzemet

Country	Effective Date	Description of action taken
USA	17 December 2010	The US FDA notified health-care professionals that the injection form of dolasetron mesylate should no longer be used to prevent chemotherapy induced nausea and vomiting (CINV) in pediatric and adult patients. A contraindication against this use is being added to the product label for dolasetron mesylate injection. Dolasetron mesylate injection can increase the risk of developing torsade de pointes, which can be fatal. **References:** FDA Drug Safety Communication, US FDA, 17 December 2010 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 1, 2011.
Brazil	February 2011	The product label is updated with the removal of the indication for nausea and vomiting induced by chemotherapy, due to the potential risk of increased cardiac

		events (mainly linked to prolongation of the QT interval) related to approved dosage of 100 mg single intravenous dose. The indication for post-operative nausea and vomiting at the recommended dose of 12.5 mg remains approved on the package leaflet. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).
Canada	26 April 2011	Health Canada and Sanofi-Aventis Canada Inc. informed the withdrawal of dolasetron mesylate intravenous injection as it is no longer indicated to prevent nausea and vomiting in adults undergoing chemotherapy. Intravenous administration of the injectable form of dolasetron mesylate is associated with QTc prolongation, to an extent which may potentially result in serious arrhythmias at the doses recommended for the prevention of nausea and vomiting. **References:** Advisories, Warnings and Recalls, Health Canada, 26 April 2011 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 3, 2011.
Switzerland	29 April 2011	Withdrawal of 200 mg tablets and solution for injection due to QT-prolongation and risk of cardiac arrhythmia. **References:** Communication from Swissmedic, July 2012.

PRODUCT NAME: dolutegravir

C.A.S. NUMBER: 1051375-16-6

OTHER NAMES: Tivicay, Triumeq

Country	Effective Date	Description of action taken
Brazil	May 2018	ANVISA warned of a possible risk of developing neural tube defects due to exposure of women with HIV to the drug dolutegravir at the time of conception. In addition to recommending additional risk minimisation measures to be adopted for the use of this drug, it was reported that the safety profile of the drug has been monitored by ANVISA in conjunction with the main international regulatory agencies and the manufacturer of the drug. Letter to health professionals was issued. **References:** ANVISA Pharmacovigilance Alert, and Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: domperidone

C.A.S. NUMBER: 57808-66-9

OTHER NAMES: Gastroperidon, Tametil, Motilium

Country	Effective Date	Description of action taken
Oman	2014	The product information for domperidone was updated with new restrictions based on EMA recommendations. The suppositories of 10 mg and 60 mg are suspended. The Circular containing this information was sent to the MAH and HCPs. **References:** Oman Ministry of Health Circular No. 94, 2014.
Montenegro	14 November 2011	Based on EMA referral and in accordance with Law on medicines, the Agency for Medicines and Medical Devices of Montenegro (CALIMS) has sent DHPC to relevant HCPs to inform them of the perceived increased risk of serious ventricular arrhythmias and sudden cardiac death related to the use of domperidone. **References:** CALIMS portal (www.calims.me), 14 November 2011
Chile	30 July 2012	Condition of sale for domperidone has been modified from over-the-counter to with medical prescription. The decision is based on information from other reglators in Europe, US and Spain, as well as ADRs received involving domperidone in Chile. **References:** Instituto de Salud Publica (www.ispch.cl)
Europe	8 March 2013	The CMDh endorsed PRAC recommendations that domperidone-containing medicines should only be used to relieve symptoms of nausea and vomiting, and that doses and length of treatment should be restricted and that they should be adjusted carefully by the patient's weight where availabel for use in children. In addition, domperidone will no longer be authorised to treat other conditions such as bloating or heartburn. It must not be given to patients with moderate or severe impairment of liver function, or in those who have existing abnormalities of electrical activity in the heart or heart rhythm, or who are at increased risk of such effects. In addition, it should not be used with other medicines that have similar effects on the heart or reduce the breakdown of domperidone in the body (thus increasing the risk of side effects). The product information has been amended appropriately. Products supplying a dose of 20 mg by mouth, and suppositories of 10 or 60 mg are no longer recommended for use and should be withdrawn, as should combination products with cinnarizine where available. **References:** EMA Referrals (www.ema.europa.eu) WHO Pharmaceuticals Newsletter No. 3, 2013.
Viet Nam	25 May 2015	The use of domperidone was restricted to the symptomatic treatment of nausea and vomiting. The product information

		was also updated with a new contraindication for patients with severe hepatic impairment, conditions where cardiac conduction is, or could be, impaired or where there is underlying cardiac disease such as congestive heart failure, and when co-administered with QT-prolonging medicines or potent CYP3A4 inhibitors. **References:** Drug Administration of Viet Nam Official Dispatch No. 9234/QLD-DK, 25 May 2015.
Singapore	19 October 2016	Labelling updates: - Contraindication of use in patients with known existing prolongation of cardiac conduction intervals, particularly QTc, patients with significant electrolyte disturbances or underlying cardiac disease and when co-administrated with QT-prolonging medicines or potent CYP3A4 inhibitors. - In adults and children aged ⩾ 12 years old weighing ⩾ 35 kg, the recommended maximum oral daily dose is 30 mg, given in doses of 10 mg up to three times daily. - In children aged < 12 years old and those aged ⩾ 12 years old weighing < 35 kg, the recommended dose is 0.25 mg/kg orally up to three times daily. For rectal administration, these patients may also be given 0.75 mg/kg twice daily as suppositories. Taking into consideration findings of epidemiology studies suggesting an increased risk of ventricular arrhythmia and sudden cardiac death, the availability of alternative treatments, local safety data, expert opinion from local clinicians and international regulatory actions, the HSA concluded that the benefit-risk profile of domperidone for treatment of dyspepsia, nausea and vomiting remains favourable if additional measures are taken to mitigate the risk of cardiotoxicity, including restricting the use in high risk patients. **References:** Communication from the Health Sciences Authority, October 2016. WHO Pharmaceuticals Newsletter No. 4, 2017.
United Arab Emirates		Motilium injection and drops were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: doripenem

C.A.S. NUMBER: 364622-82-2

OTHER NAMES: Doribax

Country	Effective Date	Description of action taken

United Arab Emirates		Doribax 500 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: doxycycline

C.A.S. NUMBER: 564-25-0

OTHER NAMES: Doxy, Vibramycin, Dotur, Unidox Solutab

Country	Effective Date	Description of action taken
Armenia	2018	After an assessment by the Scientific Centre of Drug and Medical Technology Expertise after Academician E. Gabrielyan (SCDMTE), the product information of Unidox Solutab was updated to include information on posology and administration for reducing risk of fatal mechanical asphyxia due to inappropriate use of the medicine and ingestion of a whole tablet without prior dissolution in water. As a risk minimization measure a DHPC was circulated. **References:** Communication from Armenian National Pharmacovigilance Centre, 2018.
United Arab Emirates		Doxy 200 mg and Doxy Comb, Vibramycin 100 mg, and Dotur 100 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: dronedarone

C.A.S. NUMBER: 141626-36-0

OTHER NAMES: Multaq

Country	Effective Date	Description of action taken
Switzerland	11 July 2011	There is a risk of cardiovascular events in patients with permanent atrial fibrillation. **References:** Communication from Swissmedic, July 2012.
Canada	4 August 2011	Dronedarone should be prescribed only in patients with a history of, or current non-permanent atrial fibrillation (AF) to reduce the risk of cardiovascular hospitalization due to AF. Dronedarone must not be prescribed in patients with permanent AF (duration for at least six months or duration unknown), and in whom an attempt to restore sinus rhythm

		is no longer considered. Dronedarone is contraindicated in patients with severe congestive heart failure (Stage NYHA IV) and other unstable hemodynamic conditions and bradycardia < 50 bpm. Dronedarone should be used with caution in patients with moderate congestive heart failure (Stage NYHA III) and only if the benefits outweigh the risks. If heart failure develops or worsens suspension or discontinuation of dronedarone should be considered. **References:** Advisories, Warnings and Recalls, Health Canada, 4 August 2011 (www.hc-sc.gc.ca).
Europe	22 September 2011	Treatment with dronedarone should be restricted to patients with paroxysmal or persistent atrial fibrillation when sinus rhythm has been obtained. It is no longer indicated for use in patients when atrial fibrillation is still present. Dronedarone must not be used in patients with permanent atrial fibrillation, heart failure or left ventricular systolic dysfunction (impairment of the left side of the heart), or patients who have had previous liver or lung injury following treatment with amiodarone. **References:** Press release, EMA, 22 September 2011 (www.ema.europa.eu). WHO Pharmaceuticals Newsletter No. 5, 2011.
Brazil	December 2011	ANVISA warned about risks of serious cardiovascular events, including death, related to the use of Multaq, according to reviews of the benefit-risk balance of the drug by the EMA and US FDA. Recommendations were communicated with prescribers and patients. **References:** ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia).
Canada	8 December 2011	Dronedarone is now indicated for the treatment of patients with paroxysmal or persistent atrial fibrillation who are in sinus rhythm or who are intended to be cardioverted, to reduce the risk of cardiovascular hospitalization due to atrial fibrillation. Dronedarone should only be used after other treatment options have been considered and treatment with dronedarone should exclude patients with permanentatrial fibrillation of any duration, patients with a history of, or current heart failure regardless of New York Heart Association (NYHA) functional class, patients with left ventricular systolic dysfunction (LVSD), patients with certain conduction abnormalities, and patients with liver or lung toxicity related to pervious use with amiodarone. Information has been added to the “Warnings and Precautions” section of the Product Monograph regarding anticoagulation therapy as well as the use of dronedarone in the elderly, in patients with coronary artery disease and in patients who develop congestive heart failure or LVSD

		during treatment with dronedarone. New cardiovascular and renal monitoring recommendations as well as the need for pulmonary clinical evaluation have also been added to the Product Monograph. **References:** Advisories, Warnings and Recalls, Health Canada, 8 December 2011 (www.hc-sc.gc.ca).
USA	19 December 2011	A safety review showed that dronedarone increased the risk of serious cardiovascular events, including death, when used by patients in permanent atrial fibrillation (AF). Health-care professionals should not prescribe dronedarone to patients with AF who cannot or will not be converted into normal sinus rhythm because dronedarone doubles the rate of cardiovascular death, stroke, and heart failure in such patients. Patients should have their heart (cardiac) rhythm monitored by electrocardiogram (ECG) at least every three months. If the patient is in AF dronedarone should be stopped or, if clinically indicated, the patient should be cardioverted. Patients prescribed dronedarone should receive appropriate antithrombotic therapy. **References:** FDA Drug Safety Communication, US FDA, 19 December 2011.
Singapore	22 February 2012	The use of dronedarone will be restricted to patients with history of non-permanent atrial fibrillation in sinus rhythm for the maintenance of sinus rhythm after alternative treatment options have been considered. Labelling updates: - Restriction of indication to adult clinically stable patients with history of paroxysmal or persistent atrial fibrillation (AF) when sinus rhythm has been restored, for the maintenance of sinus rhythm. - Contraindication of use in patients with unstable haemodynamic conditions, history of or current heart failure or left ventricular systolic dysfunction, permanent AF, liver and lung toxicity related to the previous use of amiodarone. - Strengthening of warning on cardiac and pulmonary toxicity. **References:** Dear Healthcare Professional Letter (DHCPL), 22 February 2012. (http://www.hsa.gov.sg/).

PRODUCT NAME: droperidol

C.A.S. NUMBER: 548-73-2

OTHER NAMES: dehydrobenzperidol, Inapsine, Droleptan, Dridol, Xomolix

Country	Effective Date	Description of action taken

Canada	25 August 2010	Droperidol Injection USP is no longer indicated for use in anesthesia for sedation or tranquilization, neuroleptanalgesia, or in the management of acute stages of Meniere's disease. Droperidol Injection USP should only be used for the prevention and treatment of post-operative nausea and vomiting in patients for whom other treatments are ineffective or inappropriate. Droperidol Injection USP is contraindicated in patients with known or suspected QT prolongation. A new Boxed Warning highlights the risk of QT prolongation and measures to minimize this risk, including a recommendation for screening ECG and cardiac monitoring. **References:** Advisories, Warnings and Recalls, Health Canada, 25 August 2010 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 5, 2010.
United Arab Emirates		Dehydrobenzperidol 2.5 mg/ml solution for injection were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: drospirenone

C.A.S. NUMBER: 67392-87-4

OTHER NAMES: Lyllas, Elani, Elô

Country	Effective Date	Description of action taken
Brazil	October 2011	Following articles published in the British Medical Journal and other studies, ANVISA warned of an increased risk of blood clots forming in women taking contraceptives containing the hormone drospirenone. It is worth noting that, at this moment, the benefit-risk profile of contraceptives containing drospirenone remains favorable, provided that the drug is used under medical supervision and according to the guidelines contained in the package leaflet. Recommendations were made to prescribers and patients. **References:** ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: drotrecogin alfa (activated)

C.A.S. NUMBER: 98530-76-8

OTHER NAMES: Xigris

Country	Effective Date	Description of action taken
Oman	2011	The manufacturer withdrew Xigris due to benefit risk assessment outcome in clinical trial.

		References: Oman Ministry of Health Circular No. 116, 2011.
Brazil	October 2011	The marketing authorisation was withdran. The results of a new clinical study did not confirm the benefit of the drug in improving survival 28 days after the use of Xigris in patients with septic shock. The company reported the withdrawal of the drug from the market worldwide. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia). Official Gazette, cancellation of registration, 13 February 2012 (Resolution-RE No. 576).
Canada	25 October 2011	Health Canada informed Canadians of the withdrawal of drotrecogin alfa from the Canadian market, in light of the company's decision to withdraw the products from the market worldwide. The withdrawal is in light of a large international clinical trial, known as the PROWESSSHOCK study that showed no benefit for patients receiving drotrecogin alfa compared to patients who did not receive it. **References:** Advisories, Warnings and Recalls, Health Canada, 25 October 2011 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 6, 2011.
Switzerland	25 October 2011	Market withdrawal due to insufficient efficacy. **References:** Communication from Swissmedic, July 2012.
USA	25 October 2011	The U.S. Food and Drug Administration (US FDA) notified healthcare professionals and the public that on 25 October 2011, Eli Lilly and Company announced a worldwide voluntary market withdrawal of drotrecogin alfa (activated). In a clinical trial drotrecogin alfa (activated) failed to show a survival benefit for patients with severe sepsis and septic shock. **References:** FDA Drug Safety Communication, US FDA, 25 October 2011 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 6, 2011.
Singapore	27 October 2011	Healthcare professionals are advised to discontinue patients who are currently on Xigris® and to not initiate treatment in new patients. This comes after a worldwide voluntary recall of Xigris® [drotrecogin alfa (activated)] due to new clinical trial findings of lack of efficacy of the product. **References:** Dear Healthcare Professional Letter (DHCPL), 27 October 2011. (http://www.hsa.gov.sg/).
Chile	30 December 2011	Marketing authorisation of drotrecogin alfa (activated) is withdrawn based on similar decision by other regulators in

		Spain, US and Europe. The PROWESS-SCHOCK trial results did not demonstrate benefits in mortality reduction in experiment group. **References:** Instituto de Salud Publica (www.ispch.cl)

PRODUCT NAME: elotuzumab

C.A.S. NUMBER: 915296-00-3

OTHER NAMES: Empliciti

Country	Effective Date	Description of action taken
United Arab Emirates		Renitec IV injection products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: enalapril

C.A.S. NUMBER: 75847-73-3

OTHER NAMES: Renitec, Vasotec, Enacard

Country	Effective Date	Description of action taken
United Arab Emirates		Empliciti™ 300 mg and 400 mg injection products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: epicillin

C.A.S. NUMBER: 26774-90-3

OTHER NAMES: Dexacillin

Country	Effective Date	Description of action taken
United Arab Emirates		Dexacillin capsules and injection products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: epinephrine

C.A.S. NUMBER: 51-43-4

OTHER NAMES: Epifrin

Country	Effective Date	Description of action taken
United Arab Emirates		Epifrin 1% and 2% drops were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: epirubicin

C.A.S. NUMBER: 25316-40-9

OTHER NAMES: Epirubicin Ebewe

Country	Effective Date	Description of action taken
United Arab Emirates		Epirubicin Ebewe 100 mg/50 ml, 50 mg/25 ml, and 10 mg/5 ml solution were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: epoetin alfa

C.A.S. NUMBER: 113427-24-0

OTHER NAMES: Eprex

Country	Effective Date	Description of action taken
Singapore	2 October 2013	Labelling updates: - Subcutaneous administration of Eprex is contraindicated in patients with chronic kidney disease including patients with end stage renal disease. The HSA assessed that given the increased frequency of antibody mediated pure red cell aplasia (PRCA) locally, a contraindication of the subcutaneous route in Singapore is warranted to minimise the risk of PRCA occurring in chronic kidney disease patients. **References:** Communication from the Health Sciences Authority, October 2013.
Viet Nam	28 March 2014	The product information was updated with a new contraindication for patients who develop pure red cell aplasia (PRCA) following treatment with any erythropoietin. Also, in patients with chrnonic renal failure, administration by the intravenous route was preferable after hemodialysis and peritoneal dialysis. The subcutaneous route was also used where intravenous access was not readily. The decision was based on careful risk-benefit assessement.

		The restrictions intended to reduce the risk of PRCA, especially when the number of PRCA cases with subcutaneous administration of epoetin alfa increased in Singapore. **References:** Drug Administration of Viet Nam Official Dispatch No. 4764/QLD-DK, 28 March 2014.

PRODUCT NAME: ergoloid

C.A.S. NUMBER: 8067-24-1

OTHER NAMES: Hydergin

Country	Effective Date	Description of action taken
United Arab Emirates		Hydergin 1.5 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: erlotinib

C.A.S. NUMBER: 183321-74-6

OTHER NAMES: Tarceva

Country	Effective Date	Description of action taken
Brazil	July 2016	Based on the results of a phase 3 study, the benefit-risk ratio of Tarceva® was not considered favorable for first-line maintenance treatment in patients without activating mutation in the epidermal growth factor receptor (EGFR). The indication of the product in the package insert was updated to "the first-line and maintenance treatment of patients with locally advanced or metastatic non-small cell lung cancer (CPNPC), with EGFR activating mutations. In maintenance treatment, no clinically relevant benefit has been demonstrated in patients with NSCLC without EGFR activating mutation." **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: escitalopram

C.A.S. NUMBER: 128196-01-1

OTHER NAMES: Lexapro, Cipralex, Nexito, Anxiset-E, Seroplex, Lexamil, Lexam, Entact, Losita

Country	Effective Date	Description of action taken

United Kingdom	December 2011	The MHRA advised that citalopram and escitalopram are associated with dose-dependent QT interval prolongation and should not be used in those with congenital long QT syndrome, preexisting QT interval prolongation, or in combination with other medicines that prolong the QT interval. The agency also revised the maximum daily dose for citalopram to 40 mg for adults, 20 mg for patients old than 65, and 20 mg for those with hepatic impairment. For escitalopram the maximum daily dose for patients older than 65 is reduced to 10 mg; other doses remain unchanged. **References:** Drug Safety Update, December 2011, Volume 5, issue 5, A1, MHRA, (www.mhra.gov.uk). WHO Pharmaceuticals Newsletter No. 2, 2012.
Canada	7 May 2012	Escitalopram should not be used in patients with a heart condition known as congenital long QT syndrome, or in patients with QT interval prolongation. In addition, 10 mg per day is the maximum recommended dose for patients who are 65 and older, have heart problems, or are taking omeprazole or cimetidine which can increase the blood levels of escitalopram. **References:** Advisories, Warnings and Recalls, Health Canada, 7 May 2012 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 3, 2012.
Brazil	February 2012 June 2012 September 2012 February 2013	In February 2012, after a safety study reported a small QT-dependent dose-dependent prolongation observed on electrocardiogram, as well as the review of data from spontaneous reports involving cases of QT interval prolongation and ventricular arrhythmias, including Torsade de Pointes, associated with the use of escitalopram, the drug package leaflet was revised to include these and other information about contra-indications, warnings, precautions and interactions. Subsequently, safety warnings about drugs containing citalopram and escitalopram oxalate have been reported to health professionals, according to updates published in some clinical studies and consolidated by the Medicines and Healthcare Products Regulatory Agency (MHRA - UK). The main topics concern the association with dose-dependent prolongation of the QT interval and recommended maximum daily doses. The leaflets of the medications were updated. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: esmolol

C.A.S. NUMBER: 81161-17-3

OTHER NAMES: Brevibloc

Country	Effective Date	Description of action taken
United Arab Emirates		Brevibloc premixed 10 mg/ml solution were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: estradiol

C.A.S. NUMBER: 50-28-2

OTHER NAMES: Aerodiol

Country	Effective Date	Description of action taken
United Arab Emirates		Aerodiol nasal spray were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: etofibrate

C.A.S. NUMBER: 31637-97-5

OTHER NAMES: Lipo-Merz

Country	Effective Date	Description of action taken
United Arab Emirates		Lipo-Merz capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: etoposide phosphate

C.A.S. NUMBER: 117091-64-2

OTHER NAMES: Etopophos

Country	Effective Date	Description of action taken
United Arab Emirates		Etopophos 100 mg injection products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: everolimus

C.A.S. NUMBER: 159351-69-6

OTHER NAMES: Certican, Afinitor, Zortress

Country	Effective Date	Description of action taken
United Arab Emirates		Certican® products were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: famotidine

C.A.S. NUMBER: 76824-35-6

OTHER NAMES: Pepcidin, Pepcid

Country	Effective Date	Description of action taken
United Arab Emirates		Pepcidin 20 mg and 40 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: fenclofenac

C.A.S. NUMBER: 34645-84-6

OTHER NAMES: Flenac

Country	Effective Date	Description of action taken
United Arab Emirates		Flenac 300 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: fenofibrate

C.A.S. NUMBER: 49562-28-9; 42017-89-0

OTHER NAMES: Lipanthyl, Tricor, Fenoglide, Lipofen; Trilipix, Fibricor

Country	Effective Date	Description of action taken
USA	9 November 2011	The US FDA notified healthcare professionals that the cholesterol-lowering medicine fenofibric acid may not lower a patient's risk of having a heart attack or stroke. **References:** FDA Drug Safety Communication, US FDA, 9 November 2011 (www.fda.gov).

	WHO Pharmaceuticals Newsletter No. 6, 2011.
United Arab Emirates	Lipanthyl 160 mg were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: fentanyl

C.A.S. NUMBER: 437-38-7

OTHER NAMES: Durogesic® D-Trans, Actiq, Duragesic, Fentora, Fentavera

Country	Effective Date	Description of action taken
Brazil	October 2013	ANVISA warned of the risk of children being exposed to transdermal patches containing fentanyl, following an US FDA communication. Poisoning related to fentanyl overdose, which can occur accidentally in children (who could find discarded adhesives from the trash), can lead to death due to respiratory depression and increased levels of carbon dioxide in the bloodstream. This can occur even if the adhesive has already been used by the patient. It was recommended that users of transdermal fentanyl adhesives take various precautions regarding their storage, use and disposal. **References:** ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia).
United Arab Emirates		Fentavera patches from 12.5 mcg/h to 100 mcg/h were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ferric saccharate

C.A.S. NUMBER: 8047-67-4

OTHER NAMES: Sucrofer, Hippiron, proferrin, iviron; ironsugar, Fesin, Venofer

Country	Effective Date	Description of action taken
Brazil	August 2012 April 2013	In 2012, ANVISA informed health professionals and patients that an evaluation of the benefit-risk ratio of Sucrofer® was being carried out, following reported increase of adverse reactions potentially related to the product. Patients and health professionals were reminded of the common adverse reactionsand recommendations described in the package

		leaflet, especially the notification of suspected serious adverse reactions. In 2013, due to the observation of adverse events resulting from the administration of the drug, especially with regard to the dilution and infusion of the product, recommendations about its correct dilution were published, exclusively in sterile sodium chloride solution 0.9% w/v, with an emphasis on increasing minimum infusion time which provides a lower incidence of adverse events. **References:** ANVISA Pharmacovigilance Alert, and Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: fexofenadine

C.A.S. NUMBER: 83799-24-0

OTHER NAMES: Fexon 60

Country	Effective Date	Description of action taken
United Arab Emirates		Fexon 60 tablets were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: filgrastim

C.A.S. NUMBER: 143011-72-7

OTHER NAMES: Neupogen

Country	Effective Date	Description of action taken
Bosnia and Herzegovina	29 March 2015	The marketing authorisation for filgrastim injectin solution is withdrawn. All batches of the product are recalled from the market. **References:** Agency for Medicinal Products and Medical Devices news release (www.almbih.gov.ba).

PRODUCT NAME: finasteride

C.A.S. NUMBER: 98319-26-7

OTHER NAMES: Proscar, Propecia

Country	Effective Date	Description of action taken

Canada	4 August 2011	Health Canada is informing healthcare practitioners and patients of a labeling update for finasteride that includes information on rare reports of breast cancer in men. **References:** Advisories, Warnings and Recalls, Health Canada, 4 August 2011 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 5, 2011. WHO Pharmaceuticals Newsletter No. 1, 2016. WHO Pharmaceuticals Newsletter No. 3, 2017.

PRODUCT NAME: fingolimod

C.A.S. NUMBER: 162359-55-9

OTHER NAMES: Gilenya

Country	Effective Date	Description of action taken
Europe	20 January 2011	Following concerns over the effects of fingolimod on the heart after the first dose, the Committee for Medicinal Products for Human Use (CHMP) is advising doctors to increase their level of monitoring of patients after the first dose of the medicine. **References:** Press release, EMA, 20 January 2011 (www.ema.europa.eu). WHO Pharmaceuticals Newsletter No. 1, 2012.
Canada	27 February 2012	It is recommended that physicians obtain an ECG before the first dose of fingolimod is given. If an ECG is not available within the last six months. Patients should be observed for signs and symptoms of bradyarrhythmia and their blood pressure should be monitored regularly. Patients taking fingolimod who experience symptoms of heart problems should report them immediately. **References:** Advisories, Warnings and Recalls, Health Canada, 27 February 2012. WHO Pharmaceuticals Newsletter No. 2, 2012. WHO Pharmaceuticals Newsletter No. 5, 2015. WHO Pharmaceuticals Newsletter No. 5, 2016. WHO Pharmaceuticals Newsletter No. 6, 2017. WHO Pharmaceuticals Newsletter No. 1, 2018.
Europe	20 April 2012	The European Medicines Agency recommended new advice to health-care professionals to reduce the risk of adverse effects on the heart associated with the use of fingolimod. Following a review of the latest evidence of the safety of the medicine, the Agency's Committee for Medicinal Products for Human Use (CHMP) recommended that doctors should not prescribe fingolimod to patients with a history of cardiovascular and cerebrovascular disease or who take heart-rate lowering medication. However, when treatment with fingolimod is considered necessary in these patients, their heart activity should be monitored at least overnight following the first dose of fingolimod and doctors should seek advice from a cardiologist on appropriate monitoring.

		The CHMP also recommended that all patients starting treatment with fingolimod should have their heart activity monitored before receiving the first dose of the medicine and continuously for at least six hours after. Monitoring should be extended for at least two hours in patients whose heart rate is lowest six hours after receiving the first dose of fingolimod. In patients who develop clinically significant heart problems such as bradycardia or atrioventricular (AV) block, monitoring should continue at least overnight and until the problems have been resolved. **References:** Press release, EMA, 20 April 2012 (www.ema.europa.eu). WHO Pharmaceuticals Newsletter No. 6, 2017.
USA	14 May 2012	Data show that, although the maximum heart rate lowering effect of fingolimod usually occurs within six hours of the first dose, the maximum effect may occur as late as 20 hours after the first dose in some patients. For this reason, fingolimod is now contraindicated in patients with certain pre-existing or recent (within last six months) heart conditions or stroke, or who are taking certain antiarrhythmic medications. In addition, the US FDA is now also recommending that the time of cardiovascular monitoring be extended past six hours in patients who are at higher risk for or who may not tolerate bradycardia. Extended monitoring should include continuous ECG monitoring that continues overnight. **References:** FDA Drug Safety Communication, US FDA, 14 May 2012 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 1, 2012. WHO Pharmaceuticals Newsletter No. 3, 2012. WHO Pharmaceuticals Newsletter No. 5, 2015. WHO Pharmaceuticals Newsletter No. 6, 2018.
Chile	14 March 2013	The product label is updated to include a new contraindication in patients with cardiovascular diseases history. Based on information from the USFDA, EMA, Health Canada and AGEMED, sudden deaths following the first dose were reported among patients with history of cardiovascular diseases. **References:** Instituto de Salud Publica (www.ispch.cl)
Brazil	August 2015	ANVISA warned of the risk of severe bradycardia after administration of the first dose, either at the beginning of treatment with Gilenya or after its reintroduction after a period of discontinuation of the drug. Recommendations are made regarding the need to measure blood pressure, heart rate and electrocardiogram at established frequencies. It also communicated the US FDA's warning about the occurrence of a severe low-frequency cerebral infection (progressive multifocal leukoencephalopathy) in patients using Gilenya.

		References: ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia).
Montenegro	25 January 2016	The Agency for Medicines and Medical Devices of Montenegro (CALIMS) has sent DHPC to relevant HCPs to inform them of the perceived increased risk of serious adverse reactions due to its immunosupresive effects. **References:** European Commission final decision based on CHMP opinion and variation type II

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: flecainide

C.A.S. NUMBER: 54143-55-4

OTHER NAMES: Tambocor

Country	Effective Date	Description of action taken
United Arab Emirates		Tambocor 10 mg/ml injection products were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: fluconazole

C.A.S. NUMBER: 86386-73-4

OTHER NAMES: Candeur, Exomax, Flucand, Forcan-150, Gynosant

Country	Effective Date	Description of action taken
United Arab Emirates	2012	The application for Forcan-150 was rejected by the committee for various reasons. Exomax 2 mg/ml infusion was suspended. Candeur 150 mg were withdrawn by the MAH before getting approval. While Flucand 50 mg and 150 mg, and Gynosant 100 were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: flucytocine

C.A.S. NUMBER: 2022-85-7

OTHER NAMES: Ancobon, Ancotil, Cytoflu

Country	Effective Date	Description of action taken

United Arab Emirates		Ancotil 500 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: flumetasone

C.A.S. NUMBER: 2135-17-3

OTHER NAMES: Locacorten

Country	Effective Date	Description of action taken
United Arab Emirates		Locacorten 0.02% ointment were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: flunarizine

C.A.S. NUMBER: 52468-60-7

OTHER NAMES:

Country	Effective Date	Description of action taken
Viet Nam	21 April 2016	The use of flunarizine iss restricted to prophylaxis of migraine when other therapies are ineffective or poorly tolerated. This decision was based on the evaluation by Agence Nationale de Sécurité du Médicament et des Produits de Santé (ANSM's), which indicated the benefits of flunarizine outweighed the risks only when those were reserved for prophylaxis of migraine when other therapies are ineffective or poorly tolerated in adults and children above 12 years old. **References:** Drug Administration of Viet Nam Official Dispatch No. 6257/QLD-DK, 21 April 2016.

PRODUCT NAME: fluorouracil

C.A.S. NUMBER:

51-21-8

OTHER NAMES: Fluoro-uracil

Country	Effective Date	Description of action taken
United Arab Emirates		Fluoro-Uracil 250 mg/5 ml were withdrawn by the MAH before getting approval.

		References: Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: fluoxetine

C.A.S. NUMBER: 54910-89-3

OTHER NAMES: Linz 20, Fluneurin, Prozac, Sarafem, Adofen

Country	Effective Date	Description of action taken
United Arab Emirates		Linz 20 and Fluneurin 20 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: flupentixol

C.A.S. NUMBER: 2413-38-9

OTHER NAMES: Fluanxol

Country	Effective Date	Description of action taken
United Arab Emirates		Fluanxol 3 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: fluphenazine

C.A.S. NUMBER: 69-23-8

OTHER NAMES: Modecate, Moditen, Motival

Country	Effective Date	Description of action taken
United Arab Emirates		Moditen 2.5 mg and 5 mg tablets, Motival, and Modecate 25 mg/ml injection products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: flupirtine

C.A.S. NUMBER: 75507-68-5

OTHER NAMES: Katadolon

Country	Effective Date	Description of action taken
Europe	23 March 2018	The Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) has endorsed EMA's recommendation to withdraw the marketing authorisation for flupirtine, because of the risk of serious liver injury. **References:** European Commission final decision (www.ema.europa.eu) WHO Pharmaceuticals Newsletter No. 3, 2013. WHO Pharmaceuticals Newsletter No. 5, 2013. WHO Pharmaceuticals Newsletter No. 2, 2018.

PRODUCT NAME: formoterol fumatate

C.A.S. NUMBER: 183814-30-4

OTHER NAMES: Foradil

Country	Effective Date	Description of action taken
United Arab Emirates		Foradil 12 mcg inhaher were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: fosfestrol tetrasodium

C.A.S. NUMBER: 4719-75-9

OTHER NAMES: Honvan

Country	Effective Date	Description of action taken
United Arab Emirates		Honvan 120 mg tablets and 300 mg injection products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: fosinopril

C.A.S. NUMBER: 98048-97-6

OTHER NAMES: Staril, Monopril

Country	Effective Date	Description of action taken
United Arab Emirates		Staril 10 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: fotemustine

C.A.S. NUMBER:
92118-27-9

OTHER NAMES: Muphoran, Mustophoran

Country	Effective Date	Description of action taken
United Arab Emirates		Muphoran 208 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: framycetin

C.A.S. NUMBER: 28002-70-2

OTHER NAMES: Soframycin

Country	Effective Date	Description of action taken
United Arab Emirates		Soframycin drops, ointment, and eye ointment were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: frusemide

C.A.S. NUMBER: 54-31-9

OTHER NAMES: furosemide, Impugan, Lasix, Lasix Retard

Country	Effective Date	Description of action taken
United Arab Emirates		Lasix 500 mg tablets and Lasix Retard 60 mg capsules were withdrawn by the MAH before getting approval. Impugan 20 mg/2 ml injection and Impugan 40 mg tablets were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: furosemide

C.A.S. NUMBER: 54-31-9

OTHER NAMES: Lasix, Frusemide

Country	Effective Date	Description of action taken

India	20 April 2017	The Central Drugs Standard Control Organization (CDSCO) requested to incorporate furosemide associated dermatitis into the package inserts of suspected drugs marketed in India. **References:** Letter issued by CDSCO on 20 April 2017. WHO Pharmaceuticals Newsletter No. 2, 2017.

PRODUCT NAME: fusafungine

C.A.S. NUMBER: 1393-87-9

OTHER NAMES: Bioparox

Country	Effective Date	Description of action taken
Armenia	2016	After an assessment by the Scientific Centre of Drug and Medical Technology Expertise after Academician E. Gabrielyan (SCDMTE), the product information of Bioparox was withdrawn due to negative benefit-risk balance and increased risk of allergic reactions with fatal outcome. **References:** Communication from Armenian National Pharmacovigilance Centre, 2016. EMA press release, April 2016.
Brazil	June 2015	After periodic review of cases of post-marketing allergic reactions, health professionals were informed of new contraindications of the drug: for children under 12 years (previously contraindicated for children under 30 months); patients with allergic tendencies and bronchospasm. Fusafungine should only be used in the treatment of upper respiratory tract infections. The package leaflet was updated. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).
Europe	April 2016	The CMDh has endorsed by consensus the revocation of marketing authorisations for fusafungine sprays in the EU due to serious allergic reactions and limited evidence of benefit. **References:** European Commission final decision (www.ema.europa.eu) WHO Pharmaceuticals Newsletter No. 2, 2016.
Azerbaijan	28 June 2016	Fusafungine containing medicines have been suspended due to serious allergic reactions and limited evidence of benefit. **References:** Ministry of Health final desicion N 159-S, June 2016.
United Arab Emirates		Locabiotal solution were withdrawn by the MAH before getting approval. **References:**

		Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: fusidic acid

C.A.S. NUMBER: 6990-06-04

OTHER NAMES: Fucidin, Fucithalmic, Stafine

Country	Effective Date	Description of action taken
United Kingdom	July 2011	The Medicines and Healthcare products Regulatory Agency (MHRA) announced that product information for systemic fusidic acid is being updated to include a strict warning against concomitant use with statins because of a risk of serious and potentially fatal rhabdomyolysis. In patients for whom the use of systemic fusidic acid is essential, statin treatment should be temporarily discontinued throughout the duration of fusidic acid treatment. **References:** Drug Safety Update, July 2011, Volume 5, issue 2, A1, MHRA, (www.mhra.gov.uk). WHO Pharmaceuticals Newsletter No. 5, 2011.
United Arab Emirates		Fucidin 250 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: galactose-based ultrasound contrast agents

C.A.S. NUMBER:

OTHER NAMES: Echovist

Country	Effective Date	Description of action taken
United Arab Emirates		Echovist 200 were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: galantamine

C.A.S. NUMBER: 357-70-0

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		The application for Galantamina Azevedos (4 mg, 8 mg and 12 mg) was rejected by the committee for various reasons.

		References: Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: gallamine triethiodide

C.A.S. NUMBER: 65-29-2

OTHER NAMES: Flaxedil

Country	Effective Date	Description of action taken
United Arab Emirates		Flaxedil 4% injection products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: gatifloxacin

C.A.S. NUMBER: 112811-59-3

OTHER NAMES: Gatiflo, Tequin, Zymar, Gatispan

Country	Effective Date	Description of action taken
India	16 March 2011	Gatifloxacin formulation for systemic use in human by any route including oral and injectable is prohibited in India. **References:** The Gazette of India, No. 139, New Delhi 16 March 2011.
Azerbaijan	25 May 2012	Marketing authorization is withdrawn due to risk of serious side effects - life-threatening hypoglycemia and hyperglycemia. Gatifloxacin containing medicines have been suspended, except for 0.5% gatifloxacin solution containing eye drops. **References:** Ministry of Health Pharmacology and Pharmacopeia Advisory Council, May 2012.
Viet Nam	14 February 2015	The marketing authorisation of gatifloxacin-containing eye drops (only available form of gatifloxacin in Viet Nam) is suspended due to harmful side effects. The products are recalled. **References:** Drug Administration of Viet Nam Official documents No. 101/QĐ-QLD, 14 February 2015.
United Arab Emirates		Zymar 0.3% drops were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:**

		Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: gemtuzumab ozogamicin

C.A.S. NUMBER: 220578-59-6

OTHER NAMES: Mylotarg

Country	Effective Date	Description of action taken
USA	21 June 2010	The US Food and Drug Administration (US FDA) has announced that Pfizer Inc. will voluntarily withdraw gemtuzumab ozogamicin from the United States market. In a clinical trial it was determined that there was no improvement in clinical benefit, and a greater number of deaths occurred in the group of patients who received gemtuzumab ozogamicin compared with those receiving chemotherapy alone. The Agency also states that at initial approval, the medicine was associated with a serious liver condition called venoocclusive disease, and this rate has increased in the post market setting. **References:** News Release, US FDA, 21 June 2010 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 4, 2010.

PRODUCT NAME: gentamicin sulphate

C.A.S. NUMBER: 1405-41-0

OTHER NAMES: Prefrin, Isopto Frin, Alcomicin, Pred-G, Prefrin-A

Country	Effective Date	Description of action taken
United Arab Emirates		Alcomicin drops, Prefrin 0.12% liquifilm drops, and Isopton Frin drops, Pred-G Liquifilm, and Prefrin-A Liquifilm were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: gliclazide

C.A.S. NUMBER: 21187-98-4

OTHER NAMES: Diamicron

Country	Effective Date	Description of action taken
United Arab Emirates		Diamicron® were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: glipizide

C.A.S. NUMBER: 29094-61-9

OTHER NAMES: Glibenese, Glucotrol

Country	Effective Date	Description of action taken
United Arab Emirates		Glibenese 5 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: glyburide

C.A.S. NUMBER: 10238-21-8; 26944-48-9

OTHER NAMES: Diabeta, Flycron, Glynase, Glymide; Glutril, Micronase

Country	Effective Date	Description of action taken
United Arab Emirates		Glynase 5 mg was suspended in 2018. Micronase 5 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: goserelin

C.A.S. NUMBER: 65807-02-5

OTHER NAMES: Gosacin

Country	Effective Date	Description of action taken
United Arab Emirates		Gosacin 3.6 mg and 10.8 mg implants were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: halometasone

C.A.S. NUMBER: 50629-82-8

OTHER NAMES: Sicorten

Country	Effective Date	Description of action taken
United Arab Emirates		Sicorten 0.05% ointment were withdrawn by the MAH before getting approval. **References:**

		Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: haloperidol

C.A.S. NUMBER: 52-86-8

OTHER NAMES: Haldol, Serenace

Country	Effective Date	Description of action taken
Chile	12 April 2012	Haloperidol is contraindicated in patients with clinically significant cardiac disorders, such as acute myocardial infarction, decompensated heart failure, arrhythmias treated with class IA and III antiarrhythmics, prolongation of the QT interval of the electrocardiogram, history of ventricular arrhythmia or torsades de pointes, clinically significant bradycardia, second or third degree heart block, hypokalemia. Haloperidol should not be used with other products that prolong the QT interval of the electrocardiogram. The decision is based on USFDA warning in September 2007, which states that haloperidol administered intravenously increases the risk of patients presenting prolongation of the QT interval of the electrocardiogram and torsades de pointes, which are arrhythmias that can be fatal. **References:** Instituto de Salud Publica (www.ispch.cl)
United Arab Emirates		Haldol 0.5 mg and 5 mg tablets, Haldol 5 mg/ml, Haldol Decanoas 50 mg/ml and 100 mg/ml injection products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: halothane

C.A.S. NUMBER: 151-67-7

OTHER NAMES: Fluothane, Halothan

Country	Effective Date	Description of action taken
United Arab Emirates		Fluothane, Halothan and Halothane 10% solutions were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: heparin

C.A.S. NUMBER: 9005-49-7

OTHER NAMES: Liquemin, Hep-Lock

Country	Effective Date	Description of action taken
Sudan	31 October 2011	• Importation of the drug has been suspended. • Pharmacovigilance centre is currently performing an ongoing safety review of heparin and increasing body temperature (fever) or other adverse reactions related to the drug by gathering information from individuals' case safety reports (ICSRs), after national and worldwide regulatory authorities reviews were assessed. **References:** Communication from the Sudan National Pharmacovigilance Centre, July 2012.
United Arab Emirates		Liquemin S/C 5,000 IU/0.25ml and 25,000 IU/5ml injection solutions were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: heparin + dexpanthenol + dimethyl sulfoxide

C.A.S. NUMBER:

OTHER NAMES: Dolobene

Country	Effective Date	Description of action taken
United Arab Emirates		Dolobene was withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: human anti-D immunoglobulin

C.A.S. NUMBER:

OTHER NAMES: Rhophylac 200

Country	Effective Date	Description of action taken
United Arab Emirates		Rhophylac 200 was withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: human immunoglobulin G

C.A.S. NUMBER: 308067-58-7

OTHER NAMES: Octagam

Country	Effective Date	Description of action taken
USA	25 August 2010	Octapharma USA Inc. and the US FDA notified health-care professionals that on 23 September 2010, the company initiated a voluntary market withdrawal of all lots of Octagam. The US FDA states that the company has determined that until a root cause of the reported thromboembolic events can be determined and the problem corrected, the most prudent course of action is to suspend further administration of Octagam. **References:** Safety Information, US FDA, 24 September and 25 August 2010 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 5, 2010.
Europe	24 September 2010	The EMA has recommended the suspension of the marketing authorizations for Octagam (human normal immunoglobulin 5% and 10%) and a recall of Octagam currently on the market in Europe. This is due to increases in thrombotic events associated with Octagam. **References:** Press release, Questions and answers, EMA, 24 September 2010 (www.ema.europa.eu). WHO Pharmaceuticals Newsletter No. 5, 2010.
Brazil	October 2010	ANVISA issued a warning about the suspension of the import, distribution, trade and use of all batches of Octagam 5%. The products are also recalled from the market. The decision was based on a higher than expected risk of thromboembolic events (stroke, acute myocardial infarction, deep vein thrombosis, pulmonary embolism, among others) related to the use of the products, some of which severe. It also took into consideration similar measures already taken by the US FDA and EMA. Additional recommendations were made to health professionals. **References:** ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia).
Sudan	4 October 2010	The product has been put in the negative list for its registration following an unexpected increase in reports of thromboembolic reactions, including stroke, myocardial infarction and pulmonary embolism in patients receiving the medicine. **References:** Communication from the Sudan National Pharmacovigilance Centre, July 2012.

PRODUCT NAME: hydrocortisone butyrate

C.A.S. NUMBER: 13609-67-1

OTHER NAMES: Hydro-B

Country	Effective Date	Description of action taken
United Arab Emirates		Hydro-B were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: hydroquinone

C.A.S. NUMBER: 123-31-9

OTHER NAMES: benzene-1,4-diol, quinol

Country	Effective Date	Description of action taken
Sudan	2011	• Hydroquinone should not be used in cosmetic products as a whitening material. • Its use in medicines should not exceed concentrations greater than 2%. **References:** Communication from the Sudan National Pharmacovigilance Centre, July 2012.

PRODUCT NAME: hydroxyethyl starch (HES)

C.A.S. NUMBER: 9005-27-0

OTHER NAMES: Hespan, Voluven, Volulyte, Voluven, Tetrahes, Hestar, Istarthes, Plasmin, Plasmo-Tech 6, Plasmo-Tech 10, OslaDex

Country	Effective Date	Description of action taken
Armenia	2018	After an assessment by the Scientific Centre of Drug and Medical Technology Expertise after Academician E. Gabrielyan (SCDMTE), the product information of Plasmo-Tech 6, Plasmo-Tech 10, OslaDex was updated to include information on restrection in use of HES solutions for infusion. As a risk minimization measure a DHPC was circulated. **References:** Communication from Armenian National Pharmacovigilance Centre, 2018. EMA press release, 17 July 2018.
Oman	2018	Following EMA review that indicated serious risk of kidney injury associates with the use of HES, the marketing authorisation of the prodcut is suspended and all batches of the products are recalled from the market. **References:**

		Oman Ministry of Health Circular No. 22, 2018.
Bosnia and Herzegovina	7 March 2013	The product label for Hydroxyethyl Starch (HES) is updated based on EMA recommendations . **References:** Agency for Medicinal Products and Medical Devices news release (www.almbih.gov.ba). EMA Referrals, October 2013 (www.ema.europa.eu).
Chile	28 April 2014	The indications for hydroxyethyl starch are restricted to: the treatment of hypovolemia caused by acute hemorrhage, when the use of crystalloid solutions is not considered sufficient, for a maximum of 24 hours, in adult patients. The decision took into consideration similar actions by EMA and US FDA. **References:** Instituto de Salud Publica (www.ispch.cl). EMA Referrals, October 2013 (www.ema.europa.eu). US FDA decision, November 2013 (https://www.fda.gov/drugs).
Viet Nam	30 June 2014	The use of HES solutions was restricted in patients with hypovolaemia caused by acute blood loss, where treatment with alternative infusions solutions known as 'crystalloids' alone are not considered to be sufficient. According to EMA's assessment, there was an increased risk of mortality in patients with sepsis and increased risk of kidney injury requiring dialysis in critically ill patients. **References:** Drug Administration of Viet Nam Official Dispatch No. 11039/QLD-DK, 30 June 2014.
Indonesia	22 July 2014	The product information, in Indication, Contraindication Warning and Precaution section, has been revised for Hydroxyethyl Starch (HES). **References:** Dear Healthcare Professional Communication PW.02.03.343.3.07.14.5859
Montenegro	7 September 2018	Based on EMA referral and in accordance with Law on medicines, the Agency for Medicines and Medical Devices of Montenegro (CALIMS) has sent DHPC to relevant HCPs to inform them of further restricted use of this product (no use in patients with sepsis or burn injuries or in critically ill patients). **References:** CALIMS, Direct healthcare professional communications.
Europe	23 October 2013 17 July 2018	The CMDh has decided that hydroxyethyl starch (HES) solutions for infusion should remain on the market provided

		that a combination of additional measures to protect patients, including training, controlled access and warnings on the packaging, is implemented. The decision c resulted from considering PRAC's assessment of the serious risks in critically ill patients and patients with sepsis, the place of HES in the clinical practice of some countries, as well as the fact that previous risk minimisation measures had some effect. The CMDh also requested marketing authorisation holders to conduct studies to check that only patients who should be treated with these medicines are receiving them, in addition to ongoing studies on the benefits and risks of HES solutions in patients with trauma and those undergoing elective surgery. **References:** European Commission final decision (www.ema.europa.eu) WHO Pharmaceuticals Newsletter No. 6, 2017. WHO Pharmaceuticals Newsletter No. 2, 2018. WHO Pharmaceuticals Newsletter No. 4, 2018.
Brazil	August 2013 November 2018	In 2013, ANVISA warned of the risk of kidney damage and increased bleeding related to volume-expanding products based on HES. Recommendations were communicated with health professionals. The product leaflets were updated. The decision took into consideration similar actions from the US FDA and EMA PRAC recommendation to temporarily suspend the marketing authorization of HES-based volume expanders, prompted by clinical studies that demonstrated evidence of increased mortality, increased likelihood of kidney damage, and increased risk of bleeding in users of the product. In 2018, in line with regulatory actions adopted by foreign regulators, ANVISA warned about new safety information for solutions containing hydroxyethyl starch, especially about contraindications in patients with sepsis, renal failure or in critically ill patients. Additional risk minimisation measures are recommended to be adopted for the use of these solutions. **References:** ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: hydroxyzine

C.A.S. NUMBER: 66-88-2

OTHER NAMES: Atarax, Vistaril

Country	Effective Date	Description of action taken
Armenia	2015	After an assessment by the Scientific Centre of Drug and Medical Technology Expertise after Academician E. Gabrielyan (SCDMTE), the product information of hydroxyzine-containing medicinal product was updated in

		order to minimise exposure and reduce the risks of effects on heart rhythm. **References:** Communication from Armenian National Pharmacovigilance Centre, 2015. EMA press Release, , 13 February 2015.
Europe	13 February 2015	EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has completed a review of medicines containing the antihistamine hydroxyzine, following concerns over the risk of possible effects on heart rhythm with these medicines. The PRAC considered that hydroxyzine was associated with a small but definite risk of QT interval prolongation and torsade de pointes (alterations in the electrical activity of the heart that can lead to abnormal heart rhythms and cardiac arrest). Based on the assessed data, the risk did not differ between its various approved indications, and the Committee recommended that hydroxyzine could continue to be used provided that provided that measures to minimise the risk of problems with heart rhythm were taken. **References:** EMA press Release, , 13 February 2015. WHO Pharmaceuticals Newsletter No. 3, 2014. WHO Pharmaceuticals Newsletter No. 3, 2015.
Chile	20 May 2016	The product label is updated with new contraindications: hydroxycine is contraindicated in patients with prolongation of the known QT interval, whether congenital or acquired, and patients with known predisposing risk factors for prolongation of the QT interval including pre-existing cardiovascular disease, electrolyte balance disturbances (hypokalemia, hypomagnesemia), family history of sudden cardiac death, significant bradycardia and concomitant use of drugs with recognized potential to produce prolongation of the QT interval and / or inducing torsades de pointes. The decision took into consideration similar actions by EMA. **References:** Instituto de Salud Publica (www.ispch.cl). EMA Referrals, 27 March 2015 (www.ema.europa.eu).
Viet Nam	27 April 2017	The product information wasupdated with a new contraindication: patients with known acquired or congenital QT interval prolongation, or with a known risk factor for QT interval prolongation such as cardiovascular disease, significant electrolyte imbalance (hypokalaemia, hypomagnesaemia), family history of sudden cardiac death, significant bradycardia, or concomitant use of drugs known to prolong the QT interval and/or induce torsades de pointes. The restrictions intend to minimise the risks of effects on heart rhythm. **References:**

		Drug Administration of Viet Nam Official Dispatch No. 5750/QLD-DK, 27 April 2017.

PRODUCT NAME: hypromellose

C.A.S. NUMBER: 9004-65-3

OTHER NAMES: Artelac

Country	Effective Date	Description of action taken
United Arab Emirates		Artelac® were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ibandronate sodium

C.A.S. NUMBER: 138926-19-9

OTHER NAMES: Bonviva

Country	Effective Date	Description of action taken
Brazil	April 2012	Health professionals were informed of reports of cases of anaphylactic reactions in patients treated with intravenous sodium ibandronate, including fatal episodes. The product label of Bonviva® intravenous was updated with new safety information, as well as the inclusion of anaphylactic reactions and anaphylactic shocks in both intravenous and oral presentations. Recommendations involving appropriate medical support and measures for patient monitoring were also provided. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: ibrutinib

C.A.S. NUMBER:

936563-96-1

OTHER NAMES: Imbruvica

Country	Effective Date	Description of action taken
Brazil	September 2017	Based on a cumulative review of data from clinical studies and post-marketing reports, health professionals were informed about hepatitis B reactivation in patients treated with ibrutinib. It was recommended that patients be tested for HBV infection prior to initiation of Imbruvica treatment. In cases of hepatitis B positive serology, it was recommended to consult a specialist before starting

		treatment. Patients with hepatitis B positive serology requiring treatment with Imbruvica should be monitored and managed in accordance with local treatment standards for prevention of hepatitis reactivation. The product leaflet has been updated. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: ibuprofen

C.A.S. NUMBER: 15687-27-1

OTHER NAMES: Advil, Motrin, Nurofen, Brufen, Rapidol, Fenbid, Prof

Country	Effective Date	Description of action taken
Indonesia	5 June 2015	The product information of all ibuprofen containing products should be revised to inform the risk of cardiovascular event when it is used in high dose (>=2400 mg daily). **References:** Dear Healthcare Professional Communication PW.13.01.343.3.12.14.9295
United Arab Emirates		Balkaprofen 200 mg, Fenbid 300 mg, and Prof 100 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: idelalisib

C.A.S. NUMBER: 870281-82-6

OTHER NAMES: Zydelig

Country	Effective Date	Description of action taken
United Arab Emirates		Zydelig 100 mg and 100 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: idoxuridine

C.A.S. NUMBER: 54-42-2

OTHER NAMES: Herpidu

Country	Effective Date	Description of action taken

United Arab Emirates		Herpidu C ointment, Herpidu ointment and 0.1% drops were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ifosfamide

C.A.S. NUMBER: 3778-73-2

OTHER NAMES: Ifex, Holoxan

Country	Effective Date	Description of action taken
United Arab Emirates		Holoxan® 500 mg, 1 g and 2 g were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ilaprazole

C.A.S. NUMBER: 172152-36-2

OTHER NAMES: illatac, Noltec

Country	Effective Date	Description of action taken
United Arab Emirates		The application for illatac was rejected by the committee for various reasons. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: imatinib

C.A.S. NUMBER: 152459-95-5

OTHER NAMES: Gleevec, Glivec

Country	Effective Date	Description of action taken
Brazil	April 2016	EMA review indicated that cases of hepatitis B reactivation may occur in patients who are chronic carriers of the virus after receiving a tyrosine kinase inhibitor. Recommendations were made for to test patients for hepatitis B infection before the start of imatinib treatment, and to identify patients with chronic viruses. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

United Arab Emirates		Glivec 100 mg were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: indometacin

C.A.S. NUMBER: 53-86-1

OTHER NAMES: Confortid, Indocid, Indocin

Country	Effective Date	Description of action taken
United Arab Emirates		Indocid 25 mg capsules were withdrawn by the MAH before getting approval. Confortid 100 mg suppository were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: insulin detemir

C.A.S. NUMBER: 169148-63-4

OTHER NAMES: Levemir

Country	Effective Date	Description of action taken
Egypt	22 September 2011	It was decided to add the following to the product insert "contraindicated in children under the age of 6 years". **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.

PRODUCT NAME: insulin glargine

C.A.S. NUMBER: 160337-95-1

OTHER NAMES: Lantus OptiSet

Country	Effective Date	Description of action taken
United Arab Emirates		Lantus OptiSet 100 IU/ml were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: insulin glulisine

C.A.S. NUMBER: 207748-29-6

OTHER NAMES: Apidra

Country	Effective Date	Description of action taken
United Arab Emirates		Apidra 100 IU/ml were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: insulin human (recombinant)

C.A.S. NUMBER: 11061-68-0

OTHER NAMES: xubera

Country	Effective Date	Description of action taken
United Arab Emirates		Exubera 1 mg and 3 mg inhalers were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: interferon beta -1a

C.A.S. NUMBER: 145258-61-3

OTHER NAMES: Rebif, Avonex

Country	Effective Date	Description of action taken
United Arab Emirates		Avonex 30 mcg injection productes were withdrawn by the MAH before getting approval; while Rebif 66 mcg injection productes were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: iohexol

C.A.S. NUMBER: 66108-95-0

OTHER NAMES: Omnipaque

Country	Effective Date	Description of action taken
United Arab Emirates		Omnipaque 140 mg I/ml and 180 mg I/ml solutions for injection were withdrawn by the MAH before getting approval.

		References: Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: iopromide

C.A.S. NUMBER: 73334-07-3

OTHER NAMES: Ultravist

Country	Effective Date	Description of action taken
United Arab Emirates		Ultravist 240 solution for injection were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: iotalamate meglumine

C.A.S. NUMBER: 13087-53-1

OTHER NAMES: Conray

Country	Effective Date	Description of action taken
United Arab Emirates		Conray 280 and 325 injections were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: iotrolan

C.A.S. NUMBER: 79770-24-4

OTHER NAMES: Isovist

Country	Effective Date	Description of action taken
United Arab Emirates		Isovist 240 and 300 solutions for injection were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ipratropium bromide

C.A.S. NUMBER: 66985-17-9

OTHER NAMES: Atropulm, Atrovent, Apovent, Ipravent, Ipraxa

Country	Effective Date	Description of action taken

United Arab Emirates		Atropulm 250 mcg/ml and 500 mcg/ml solutions, and Ipravent 20 HPA inhaler were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: isoflurane

C.A.S. NUMBER: 26675-46-7

OTHER NAMES: Forane

Country	Effective Date	Description of action taken
United Arab Emirates		Forane solutions were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: isopropamide iodide

C.A.S. NUMBER: 71-81-8

OTHER NAMES: Priamide

Country	Effective Date	Description of action taken
United Arab Emirates		Priamide drops and tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: isosorbide dinitrate

C.A.S. NUMBER: 87-33-2

OTHER NAMES: Isoket Retard, Isomack, Isomack Retard

Country	Effective Date	Description of action taken
United Arab Emirates		Isomack Retard 20 mg, 40 mg and Isomack 1.25 mg spray, as well as Isoket Retard 20 were withdrawn by the MAH before getting approval. Isoket Retard 20 were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: isosorbide mononitrate

C.A.S. NUMBER: 16051-77-7

OTHER NAMES: Ismo, Neosorbide, Monomack

Country	Effective Date	Description of action taken
United Arab Emirates		Ismo 20 mg and 40 mg, Neosorbide 20 mg, 40 mg and Neosorbide-SR 30 mg and 60 mg, as well as Monomack 20 mg and 40 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: isotretinoin

C.A.S. NUMBER: 4759-48-2

OTHER NAMES: Roaccutane, Roacutan, Accutane

Country	Effective Date	Description of action taken
New Zealand	September 2011	Medsafe reminds prescribers that all patients treated with isotretinoin need to be informed of the risk of depression and/or suicidal ideation and be monitored for the development of depression during treatment. In addition, the following safety information was added to the data sheet: Side-effects may occur more commonly if leflunomide is given concomitantly with other hepatotoxic or haematotoxic medicines. Monitoring guidelines contained in the leflunomide data sheet should be carefully followed. **References:** Prescriber Update Vol. 32 No. 3, September 2011 (www.medsafe.govt.nz). WHO Pharmaceuticals Newsletter No. 5, 2011. WHO Pharmaceuticals Newsletter No. 4, 2018.
Brazil	October 2015	Health professionals were reminded about the risk of teratogenity in cases of pregnancy during or in the month following the end of treatment with Roacutan. Risk-benefit considerations and precautions are necessary when women of childbearing age are treated, taking into consideration all possible side effects. It emphasized that pregnancy is an absolute contraindication for treatment with Roacutan®. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).
United Arab Emirates		Roaccutane 2.5 mg and 5 mg were withdrawn by the MAH before getting approval. **References:**

		Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: isradipine

C.A.S. NUMBER: 75695-93-1

OTHER NAMES: Lomir

Country	Effective Date	Description of action taken
United Arab Emirates		Lomir 2.5 mg tablet and Lomir Sro 5 mg capsules were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. Lomir 0.1 mg/ml solution for injection were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: itopride

C.A.S. NUMBER: 122892-31-3

OTHER NAMES: Ganaton

Country	Effective Date	Description of action taken
United Arab Emirates		Ganaton were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ivabradine

C.A.S. NUMBER: 155974-00-8

OTHER NAMES: Procoralan, Corlanor

Country	Effective Date	Description of action taken
Brazil	January 2015	Following the results of a clinical study, new recommendations were made regarding the use of ivabradine in order to minimize risks of cardiovascular events and severe bradycardia. Recommendations include monitoring heart rate, situations where treatment should be discontinued, as well as contraindication of concomitant use with verapamil or diltiazem and warning of risk of development of atrial fibrillation. The package leaflet was updated. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: josamycin propionate

C.A.S. NUMBER: 31674-19-8

OTHER NAMES: Wilprafen Solutab

Country	Effective Date	Description of action taken
Armenia	2018	After an assessment by the Scientific Centre of Drug and Medical Technology Expertise after Academician E. Gabrielyan (SCDMTE), the product information of Wilprafen Solutab was updated to include information on posology and administration for reducing risk of fatal mechanical asphyxia due to inappropriate use of the medicine and ingestion of a whole tablet without prior dissolution in water. As a risk minimization measure a DHPC was circulated. **References:** Communication from Armenian National Pharmacovigilance Centre, 2018.

PRODUCT NAME: ketoconazole

C.A.S. NUMBER: 79156-75-5; 65277-42-1

OTHER NAMES: Nizoral, Feoris, Sebizole, Ketomed, Keton, Candoral, Zolmicol, etc.

Country	Effective Date	Description of action taken
Madagascar	15 June 2011	The product has been withdrawn because liver toxicity is more frequent and severe than with other antifungal treatments. **References:** Communication from the Madagascar National Pharmacovigilance Centre July, 2012.
Egypt	16 June 2011	Withdrawal of oral dosage forms of ketoconazole, this decision does not apply to topical ketoconazole preparations. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.
Sudan	21 July 2011	Prescribers are requested to follow the following recommendations: 1. Ketoconazole tablets should be initiated by a physician who is experienced in the management of fungal infections. 2. Use only when potential benefits are considered to outweigh potential risks, taking into consideration the availability of other effective antifungal therapy. 3. Risk of serious hepatotoxicity increases with duration of treatment

		4. Liver function must be monitored before starting treatment, at week 2 and week 4 of treatment, and then monthly. 5. Advice for healthcare professionals to report any case of hepatotoxicity. **References:** Communication from the Sudan National Pharmacovigilance Centre, July 2012.
Viet Nam	24 April 2012	The marketing authorisation for ketoconazole-containing medicinesis suspended due to reports of serious adverse drug reactions of hepatic injury. **References:** Drug Administration of Viet Nam Official documents No. 5865/QLD-DK, 24 April 2012.
Montenegro	29 July 2013	Based on EMA referral and in accordance with Law on medicines, the Agency for Medicines and Medical Devices of Montenegro (CALIMS) has sent DHPC to relevant HCPs to inform them of the perceived increased risk of liver injuries related to the use of oral ketoconazole. **References:** CALIMS, Direct healthcare professional communications.
Armenia	October 2013	After an assessment by the Scientific Centre of Drug and Medical Technology Expertise after Academician E. Gabrielyan (SCDMTE), the marketing authorisations of ketoconazole containing orally administred tablets were withdrawn due to increased risk of liver toxicity. **References:** Communication from Armenian National Pharmacovigilance Centre, October 2013. EMA press release, October 2011.
Chile	24 October 2013	The indications for ketoconazole are restricted to: the treatment of blastomycosis, coccidioidomycosis, histoplasmosis, chromomycosis, and paracoccidioidomycosis in patients for whom other treatment alternatives cannot be used. Ketoconazole tablets should not be used as first line treatment for any fungal infection, but should be reserved only for certain fungal infections, when alternative therapies are not available or they are not tolerated. The decision took in to consideration similar actions by US and European regulators, as well as ADRs received by the National Pharmacovigilance System, which consisted of at least five reports of liver involvement, related to systemic use of ketoconazole , among which one was considered serious. **References:** Instituto de Salud Publica (www.ispch.cl). EMA Referrals 29 July 2013 (www.ema.europa.eu).

		US FDA decision 26 July 26, 2013 (https://www.fda.gov/drugs).
Guatemala	July 2014	Withdrawal from the market and cancellation of registration due to elevated risk of early onset liver damage. **References:** Departamento de Regulación y Control de Productos Farmacéuticos y Afines (www.siamed.mspas.gob.gt) Guatemala, July 2014.
Indonesia	13 July 2015	product information of all ketoconazole containing oral preparation should be revised with additional information due to risk of liver injury. The information to be added include restriction use/indication, posology and box warning. **References:** Dear Healthcare Professional Communication Number SV.03.01.343.3.07.15.4237

PRODUCT NAME: Ketoconazole

C.A.S. NUMBER: 79156-75-5; 65277-42-1

OTHER NAMES: Nizoral, Feoris, Sebizole, Ketomed, Keton, Candoral, Zolmicol, etc.

Country	Effective Date	Description of action taken
Brazil	October 2012 November 2013	In 2012, Health professionals were informed of the suspension of the marketing authorisation for Nizoral® tablets and all other products containing oral ketoconazole by the Lebanese health authority, based on the decision by French regulators in July 2011. Due to the risk of severe liver toxicity of Nizoral® tablets, the production company recommended of its continued use in Brazil only in cases where the potential benefits are determined to outweigh the potential risks, considering other effective antifungal therapies. In 2013, ANVISA warned of the risks of severe liver reactions associated with oral use of the drug. The post-marketing data analyzed by ANVISA pointed to an unfavorable benefit-risk profile, in agreement with the evaluations performed by the EMA and US FDA. The package leaflet of the medicine was updated to reflect indications only for tinea capitis, Malassezia folliculitis and chronic mucocutaneous candidiasis, where oral ketoconazole should be used only if the potential benefits are considered to outweigh the potential risks. The medicine must not be used in patients with acute or chronic liver disease. **References:** ANVISA Pharmacovigilance Alert, and Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: ketoprofen

C.A.S. NUMBER: 22071-15-5

OTHER NAMES: Oruvail, Profenid, Fastum

Country	Effective Date	Description of action taken
Sudan	2010	The outer packaging and/or inner labels for ketoprofen gels have been changed to carry advisory information and directions for use such as: 1. Users should avoid direct sunlight, ultraviolet rays, and sun beds or sunlamps and exercise caution for two weeks after stopping treatment; 2. Ketoprofen should be stopped and medical attention should be sought if skin reactions develop; 3. Monitoring of registered type. Special warnings and precautions for use: 1. Hands should be washed before use and immediately after use (unless they are being treated). 2. Not for use with occlusive dressing. 3. Topical application of large amounts may result in systemic effects including hypersensitivity and asthma (renal disease has also been reported). **References:** Communication from the Sudan National Pharmacovigilance Centre, July 2012.
United Arab Emirates		Oruvail 100 mg I.M and Profenid 100 mg I.M were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ketorolac tromethamine

C.A.S. NUMBER: 74103-06-3

OTHER NAMES: Toradol, Acular, Sprix, Dolac

Country	Effective Date	Description of action taken
United Arab Emirates		The application for Dolac 30 solution for injection was rejected by the committee for various reasons; while Acular 0.5% drops were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: kinilentin

C.A.S. NUMBER: 747-45-5

OTHER NAMES: Kinidin Durules

Country	Effective Date	Description of action taken
United Arab Emirates		Kinidin Durules 200 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: lactitol

C.A.S. NUMBER: 585-86-4

OTHER NAMES: Importal

Country	Effective Date	Description of action taken
United Arab Emirates		Importal were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: lactulose

C.A.S. NUMBER: 4618-18-2

OTHER NAMES: Cholac, Generlac, Consulose, Duphalac, Lacty

Country	Effective Date	Description of action taken
United Arab Emirates	2012	Duphalac Dry powder were withdrawn by the MAH before getting approval. Lacty® were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: lapatinib

C.A.S. NUMBER: 231277-92-2

OTHER NAMES: Tykerb, Tyverb

Country	Effective Date	Description of action taken
Brazil	October 2012 July 2013	In 2012,results from comparative studies showed that in patients with metastatic HER2+ breast cancer who did not receive previous trastuzumab therapy, lapatinib-based regimens were less effective than trastuzumab-based regimens. Thus, the prescription recommendations -

		including in the package leaflet - have been updated to recommend that patients receiving lapatinib should have progressed on previous trastuzumab therapy in a metastatic context. In 2013, health professionals were informed that Tykerb should not be prescribed in combination with capecitabine unless the patient has progressed with trastuzumab in the presence of metastases. This was based on two studies that showed a statistically significant higher efficacy of trastuzumab when compared to lapatinib. The medicine package leaflet has been reviewed. **References:** ANVISA Pharmacovigilance Alert, and Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: leflunomide

C.A.S. NUMBER: 75706-12-6

OTHER NAMES: Arava, Lefumide, Arabloc, Lunava

Country	Effective Date	Description of action taken
USA	13 July 2010	The US FDA announced that information on severe liver injury is being added to the Boxed Warning of leflunomide following the Agency's review of adverse event reports. Patients with pre-existing liver disease should not receive leflunomide. In addition, patients with elevated liver enzymes (ALT greater than two times the upper limit of normal) should not receive leflunomide. **References:** FDA Drug Safety Communication, US FDA 13 July 2010 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 4, 2010.
New Zealand	June 2011	New Zealand Medicines and Medical Devices Safety Authority (Medsafe) advised that prescribers are reminded that if serious adverse reactions occur, leflunomide must be stopped and a cholestyramine or charcoal wash-out procedure initiated immediately. **References:** Prescriber Update Vol. 32 No. 2, June 2011 (www.medsafe.govt.nz). WHO Pharmaceuticals Newsletter No. 4, 2011.
Egypt	20 October 2011	Leflunomide is contraindicated in pregnant women, or those with childbearing potential who are not using reliable contraception. Male patients should be aware of the possible male-mediated fetal toxicity. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.

Brazil	April 2016	ANVISA warned about the risk of miscarriage and malformations in fetuses related to the use of leflunomide, in addition to the association with the emergence or reactivation of cases of tuberculosis and other infections during treatment with the medicine. Pregnancy should be avoided throughout treatment and up to two years after its discontinuation, due to the long period of effect of the drug in the body. Recommendations were made about its safe use. **References:** ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: lenalidomide

C.A.S. NUMBER: 75706-12-6

OTHER NAMES: Revlimid

Country	Effective Date	Description of action taken
United Kingdom	May 2011	The Medicines and Healthcare products Regulatory Agency (MHRA) warned that the use of lenalidomide in patients with newly diagnosed multiple myeloma or other unlicensed indications is not recommended. **References:** Drug Safety Update, May 2011, Volume 4, Issue 10, A2, MHRA (www.mhra.gov.uk). WHO Pharmaceuticals Newsletter No. 2, 2011. WHO Pharmaceuticals Newsletter No. 3, 2011.
United Kingdom	November 2011	The (MHRA) advised that there may be a small increased risk development of second primary malignancy in patients treated with lenalidomide. **References:** Drug Safety Update, November 2011, Vo.5, issue 4, A1, MHRA, (www.mhra.gov.uk). WHO Pharmaceuticals Newsletter No. 6, 2011. WHO Pharmaceuticals Newsletter No. 2, 2013.
Canada	May 2012	Lenalidomide is only available through a controlled distribution program called RevAid®. Under this program, only prescribers and pharmacists registered with the program are able to prescribe and dispense the product. In addition, lenalidomide can only be dispensed to patients who are registered and agree to comply with the requirements of the RevAid® program. **References:** Advisories, Warnings and Recalls, Health Canada, 1 May 2012 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 3, 2012. WHO Pharmaceuticals Newsletter No. 1, 2014.
USA	7 May 2012	The US FDA notified the public of an increased risk of second primary malignancies in patients with newly-diagnosed multiple myeloma who received lenalidomide. Clinical trials

		conducted after the drug was approved showed that newly-diagnosed patients treated with the drug had an increased risk of developing second primary malignancies compared to similar patients who received a placebo. Specifically, these trials showed there was an increased risk of developing acute myelogenous leukemia, myelodysplastic syndromes, and Hodgkin lymphoma. This safety information has been added to the Warnings and Precautions section of the drug label. **References:** FDA Drug Safety Communication, US FDA, 7 May 2012 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 3, 2012.
Montenegro	17 October 2016	The Agency for Medicines and Medical Devices of Montenegro (CALIMS) has sent DHPC to relevant HCPs to inform them of important new aspects of Revlimid clinical use - Pregnancy Prevention Programme. The summary of product characteristics (SmPC) and patient information leaflet (PIL) are updated accordingly to new safety findings approved by EMA. **References:** CALIMS, Direct healthcare professional communications.

PRODUCT NAME: levetiracetam

C.A.S. NUMBER: 102767-28-2

OTHER NAMES: Keppra

Country	Effective Date	Description of action taken
Montenegro	2 February 2017	Following CHMP advice that only the syringe provided with the package should be used to measure the dose of Keppra, the Agency for Medicines and Medical Devices of Montenegro (CALIMS) has sent DHPC to relevant HCPs to inform them of the potential risk of medication errors and overdosing. **References:** EMA Press Release, 14 October 2016 WHO Pharmaceuticals Newsletter No. 3, 2012.

PRODUCT NAME: levobunolol

C.A.S. NUMBER: 47141-42-4

OTHER NAMES: Betagan

Country	Effective Date	Description of action taken
United Arab Emirates		Betagan 0.25% and 0.5% solutions were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: levodropropizine

C.A.S. NUMBER: 17692-31-8

OTHER NAMES: Levopront

Country	Effective Date	Description of action taken
United Arab Emirates		Levopront 60 mg/10 ml syrup were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: lidocaine

C.A.S. NUMBER: 137-58-6; 73-78-9

OTHER NAMES: Xylocaine, Xylozan

Country	Effective Date	Description of action taken
United Arab Emirates		The application for Xylozan 20 mg/ml solution for injection was rejected by the committee for various reasons. Xylocaine 4% solution were withdrawn by the MAH before getting approval. Xylocaine 5% ointment and 2% jelly were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: lincomycin

C.A.S. NUMBER: 154-21-2

OTHER NAMES: Biocine, Cillimycin

Country	Effective Date	Description of action taken
United Arab Emirates		Cillimycin 500 mg capsules and Cillimycin 600 mg/2 ml solution for injection were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: lindane

C.A.S. NUMBER: 58-89-9

OTHER NAMES: gamma-hexachlorocyclohexane, gammaxene, Gammallin

Country	Effective Date	Description of action taken
Chile	12 March 2012	The market authorisation of the product is withdrawn, due to its toxic effects on environment and human health. **References:** Instituto de Salud Publica (www.ispch.cl)

PRODUCT NAME: liraglutide

C.A.S. NUMBER: 204656-20-2

OTHER NAMES: Victoza, Saxenda

Country	Effective Date	Description of action taken
Brazil	September 2011	After identification of off-label use of Victoza® for the treatment of obesity, ANVISA conducted a survey on the safety of the drug in its databases and among the main international regulatory agencies. Consequently an alert was issued emphasizing that the only currently approved indication for the drug in Brazil is as an antidiabetic agent, and there are no studies that prove the efficacy and safety of the use of liraglutide for weight reduction and treatment of obesity. The use of the product for any purpose other than as an antidiabetic poses a risk to the health of the population. **References:** ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: lisinopril

C.A.S. NUMBER: 83915-83-7

OTHER NAMES: Linopril, Prinivil, Zestril

Country	Effective Date	Description of action taken
United Arab Emirates		Linopril 5 mg, 10 mg, and 20 mg were suspended. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: lisuride hydrogen maleate

C.A.S. NUMBER: 18016-80-3

OTHER NAMES: Dopergin, Proclacam, Revanil

Country	Effective Date	Description of action taken
United Arab Emirates		Dopergin 0.2 mg were withdrawn by the MAH before getting approval.

		References: Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: lithium carbonate

C.A.S. NUMBER: 554-13-2

OTHER NAMES: Camcolit, Hypnorex

Country	Effective Date	Description of action taken
India	17 March 2017	The Central Drugs Standard Control Organization (CDSCO) requested to incorporate lithium carbonate associated drug reaction with eosinophilia and systemic symptoms (DRESS) into the package inserts of the suspected drug marketed in India. **References:** Letter issued by CDSCO on 17 March 2017. WHO Pharmaceuticals Newsletter No. 2, 2017.

PRODUCT NAME: lomefloxacin

C.A.S. NUMBER: 98079-51-7

OTHER NAMES: Maxaquin, Okacyn, Okacin, Uniquin

Country	Effective Date	Description of action taken
United Arab Emirates		Okacin 0.3% were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: loperamide

C.A.S. NUMBER: 53179-11-6

OTHER NAMES: Imodium

Country	Effective Date	Description of action taken
United Arab Emirates		Imodium suspension were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: loratadine

C.A.S. NUMBER: 79794-75-5

OTHER NAMES: Claritin, Claratyne, Clarityn, Lorano

Country	Effective Date	Description of action taken
United Arab Emirates		Lorano 10 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: lornoxicam

C.A.S. NUMBER: 70374-39-9

OTHER NAMES: Xefo

Country	Effective Date	Description of action taken
United Arab Emirates		Xefo 4 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: lynestrenol

C.A.S. NUMBER: 52-76-6

OTHER NAMES: Orgametril, Exluton, Ministat, Linestrenol, Lynenol

Country	Effective Date	Description of action taken
United Arab Emirates		Orgametril 5 mg were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: lysine acetylsalicylate

C.A.S. NUMBER: 62952-06-1

OTHER NAMES: Aspegic

Country	Effective Date	Description of action taken
United Arab Emirates		Aspegic 0.5 g solution for injection, Aspegic 100 mg, 500 mg, and 1,000 mg powder were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: lysozyme

C.A.S. NUMBER: 9001-63-2

OTHER NAMES: muramidase

Country	Effective Date	Description of action taken
Viet Nam	3 November 2014	The marketing authorisation is withdrawn due to unfavorable risk-benefit profile. **References:** Drug Administration of Viet Nam Official No. 627/QĐ-QLD, 03 November 2014.

PRODUCT NAME: maprotiline

C.A.S. NUMBER: 10262-69-8

OTHER NAMES: ludiomil

Country	Effective Date	Description of action taken
United Arab Emirates		Ludiomil 10 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: mebendazole

C.A.S. NUMBER: 31431-39-7

OTHER NAMES: Vermox, Mezol, Wormazole

Country	Effective Date	Description of action taken
United Arab Emirates	2018	Mebzol 100 mg tablets was suspended. Wormazol 100 mg tablets and 100 mg/5 ml suspension were were withdrawn by the MAH before getting approval. Mebzol 100 mg/5 ml suspension were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.
United Arab Emirates		Combantrin 125 mg tablets and 250 mg/5 ml suspension were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: mebeverine

C.A.S. NUMBER: 2753-45-9

OTHER NAMES: Duspatalin

Country	Effective Date	Description of action taken
United Arab Emirates		Dehydrobenzperidol 2.5 mg/ml solution for injection were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: medazepam

C.A.S. NUMBER:

OTHER NAMES: Nobrium, Rudotel, Azepamid

Country	Effective Date	Description of action taken
United Arab Emirates		Nobrium 10 mg capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: medroxyprogesterone acetate

C.A.S. NUMBER: 520-85-4

OTHER NAMES: Provera, Progestin; Progestogen

Country	Effective Date	Description of action taken
United Arab Emirates		Provera 10 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: mefenamic acid

C.A.S. NUMBER: 61-68-7

OTHER NAMES: Ponstel, Ponstan

Country	Effective Date	Description of action taken
Egypt	14 April 2011	Mefenamic acid is contraindicated in the third trimester of pregnancy because of risk of premature closure of the ductus arteriosus and prolonged parturition. It is also contraindicated in children and adolescents less than 14 years of age. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.

PRODUCT NAME: megestrol acetate

C.A.S. NUMBER: 3562-63-8

OTHER NAMES: Megace

Country	Effective Date	Description of action taken
United Arab Emirates		Megace 160 mg tablets and 40 mg/ml suspension were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: meloxicam

C.A.S. NUMBER: 71125-38-7

OTHER NAMES: Melocam, Mobic, Metacam, Anjeso

Country	Effective Date	Description of action taken
United Arab Emirates		Melocam 15 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: mephenesin

C.A.S. NUMBER: 59-47-2

OTHER NAMES: Decontractyl

Country	Effective Date	Description of action taken
United Arab Emirates		Decontractyl ointment were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: mepyramine maleate

C.A.S. NUMBER: 59-33-6

OTHER NAMES: Anthisan

Country	Effective Date	Description of action taken
United Arab Emirates		Anthisan 2% cream were withdrawn by the MAH before getting approval. **References:**

		Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: mesna

C.A.S. NUMBER: 19767-45-4

OTHER NAMES: Mesnex, Uromitexan

Country	Effective Date	Description of action taken
United Arab Emirates		Uromitexan 400 mg and 600 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: methocarbamol

C.A.S. NUMBER: 532-03-6

OTHER NAMES: Robaxin, Marbaxin

Country	Effective Date	Description of action taken
United Arab Emirates		Robaxin solution for injection, and Robaxin 500 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: methotrexate

C.A.S. NUMBER: 133073-73-1

OTHER NAMES: Methotrexate "Ebewe"

Country	Effective Date	Description of action taken
United Arab Emirates		Methotrexate "Ebewe" solutions for injection 5000 mg/50 ml, 500 mg/5 ml, and 50 mg/ 5 ml were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: methylergomethrine

C.A.S. NUMBER: 113-42-8

OTHER NAMES: methylergobasine, methylergobrevin, methylergonovine, Methergine

Country	Effective Date	Description of action taken

Brazil	November 2011	ANVISA informed HCPs of medication errors related to the use of oral solution in newborns reported in Italy. Although this pharmaceutical form is not available in Brazil, attention was drawn to the correct use of the approved forms in the country - injectable solution and tablets. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).
Switzerland	17 November 2011	Suspension of deliveries for drops (oral formulation) 0.25 mg/ml. **References:** Communication from Swissmedic, July 2012.
United Arab Emirates		Methergin® 0.125 mg were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: methylphenidate

C.A.S. NUMBER: 113-45--1

OTHER NAMES: Ritalin

Country	Effective Date	Description of action taken
New Zealand	2 June 2010	The data sheets of methylphenidate have been updated to include the following contraindications: diagnosis or history of severe depression, anorexic disorders, suicidal tendencies, psychotic symptoms, severe mood disorders, mania, schizophrenia, psychopathic/borderline personality disorder; pre-existing cardiovascular disorders; pre-existing cerebrovascular disorders. **References:** Prescriber Update Vol. 31 No. 2 June 2010 (www.medsafe.govt.nz). WHO Pharmaceuticals Newsletter No. 4, 2010.

PRODUCT NAME: methylprednisolone

C.A.S. NUMBER: 83-43-2

OTHER NAMES: Medrol, Depo-Medrol, Solu-Medrol, Urbason

Country	Effective Date	Description of action taken
Montenegro	13 September 2017	Following PRAC recommendation that methylprednisolone injections must not be used in patients with a known or suspected allergy to proteins in cow's milk, the Agency for Medicines and Medical Devices of Montenegro (CALIMS) has sent DHPC to relevant HCPs to inform them of new

	contraindication of these lactose-containing medicines in patients allegic to cow's milk due to potential risk of serious allergic reactions. **References:** EMA Press Release, 01 August 2017
United Arab Emirates	Urbason tablets and solutions for injection at various strengths were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: methylthioninium chloride

C.A.S. NUMBER: 61-73-4

OTHER NAMES: methylene blue

Country	Effective Date	Description of action taken
USA	26 July 2011	The US FDA announced that the Agency has received reports of CNS reactions when the drug methylene blue is given to patients taking psychiatric medications that work through the serotonin system of the brain (serotonergic psychiatric medications). Methylene blue is a potent, reversible MAOI. It is believed that when methylene blue is given to patients taking serotonergic psychiatric medications, high levels of serotonin can build up in the brain, causing toxicity (Serotonin Syndrome). **References:** FDA Drug Safety Communication, US FDA 26 July 2011 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 4, 2011. WHO Pharmaceuticals Newsletter No. 6, 2011.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: metoclopramide

C.A.S. NUMBER: 364-62-5

OTHER NAMES: Metagliz, Primperan, Reglan, Pylomid, Maxolon, Plasil

Country	Effective Date	Description of action taken
Canada	20 July 2011	Health Canada informed health professionals and consumers that the labeling information for the drug metoclopramide is updated to include stronger warnings on the risk of a movement disorder known as "tardive dyskinesia." The risk increases with longer treatment and is higher in the elderly, especially elderly women. **References:** Advisories, Warnings and Recalls, Health Canada, 20 July 2011 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 4, 2011.

		WHO Pharmaceuticals Newsletter No. 1, 2015.
Switzerland	23 November 2011	Metoclopramide is contraindicated for children below 1 year with a withdrawal of paediatric formulations. **References:** Communication from Swissmedic, July 2012.
Egypt	16 February 2012	1.Withdrawal of dosage forms intended only for paediatric use (oral drops & oral solution). 2.Dosage forms used for "Adults & paediatrics": (10 mg tablets & 20 mg suppositories & 10 mg/2ml injectable solution) are contraindicated in children less than 18 years. Chronic use of metoclopramide has been linked to tardive dyskinesia, which may include involuntary and repetitive movements of the body, even after the drugs are no longer taken. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.
Syrian Arab Republic	3 July 2012	The package insert to be updated with addition of the following warnings: The elderly, especially elderly women are at increased risk of developing tardive dyskinesia. The risk to develop tardive dyskinesia increases with treatment length. Tardive yskinesia is irreversible with long-term treatment (over 12 weeks). Less frequently, tardive dyskinesia can develop with short term treatment at low doses; in these cases, the symptoms are more likely to disappear either partially or completely once treatment has been stopped. Metoclopramide treatment beyond 12 weeks should be avoided, unless the benefit is judged to outweigh the risks. **References:** Circular from the Ministry of Health No. 15657/4, 2012
Brazil	May 2013	The product leaflet was updated according to European guidelines in pediatrics, highlighting the contra-indication of metoclopramide for children under one year of age; non-recommendation for use in children and adolescents aged 1 to 18 years. The use of Plasil solution for injection was restricted to only hospitals. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).
Chile	12 December 2013	The indications for metoclopramide are restricted to adults in: • Symptomatic treatment of nausea and vomiting. Short-term treatment of documented gastroesophageal reflux that does not respond to conventional therapy. • Relief of symptoms of diabetic gastroparesis (gastric stasis due to diabetes).

		• Prevention and treatment of post-operative nausea and emesis and / or that caused by radiotherapy and antineoplastic chemotherapy. • Intubation of the small intestine. • Preparation of digestive tract explorations. Metoclopramide is not indicated as a usual treatment of non-complex gastrointestinal functional alterations, such as non-diabetic gastroparesis, dyspepsia or gastroesophageal reflux. In children under 18 years and older than 1 year its use is limited as second-line therapy in the treatment of post-operative nausea and vomiting and prevention of delayed nausea and vomiting after chemotherapy. The decision took into cosideration similar actions by regulators in Europe and the US, as well as 66 notifications of adverse effects involving metoclopramide received by the Pharmacovigilance Subdepartment as of August 2013. Of those 20 cases correspond to alterations in movement and muscle tone; three of them were considered serious. **References:** Instituto de Salud Publica (www.ispch.cl). EMA Referrals 26 July 2013 (www.ema.europa.eu). US FDA datasheet (https://www.fda.gov/drugs).
Viet Nam	29 September 2014	The marketing authorisation of oral liquid forms (> 1 mg/ml), injection forms (> 5 mg/ml) and suppositories 20 mg was suspended. Oral liquid forms (< 1 mg/ml), injection forms (< 5 mg/ml) and suppositories < 20 mg of metoclopramide are restricted to short-term use (up to 5 days) only. In children over 1 year of age, it can only be used as a second-choice treatment for the prevention of delayed nausea and vomiting after chemotherapy and for the treatment of post-operative nausea and vomiting; In adults, the use of metoclopramide was authorized for the prevention and treatment of nausea and vomiting associated with chemotherapy, radiotherapy, surgery and in the management of migraine. The product information was also changed to include contraindications in children below 1 year of age, in chronic conditions such as gastroparesis, dyspepsia and gastro-oesophageal reflux disease. The rstrictions intend to reduce the risk of acute neurological effects (such as extrapyramidal disorders) in children, especially when this risk was increased at high doses or with long-term treatment. **References:** Drug Administration of Viet Nam Official Dispatch No. 16752/QLD-DK, 29 September 2014.
Eritrea	July 2015	The National Medicines and Therapeutics Committee, in collaboration with Eritrea Medicines and Food Administration, has restricted all dosage forms of the

		product to be used in hospitals and higher health facilites only. This decision, taken in light of several reports of cases of extrapyramidal reactions, aims to minimize the risk of overprescription. **References:** Ministry of Health - National List of Medicines. 6th Ed. June 2015.
Singapore	23 July 2015	Taking into consideration the available evidence on the risk of neurological and other dose-related adverse reactions (ADRs) with metoclopramide, the local incidence of ADRs, the input from local clinical experts and international regulatory actions, the HSA recommended restrictions on the indication, dose and duration of use of metoclopramide. Specific labelling updates: - Indications for use in adults are restricted to short-term prevention and treatment of nausea and vomiting, including that associated with chemotherapy, radiography, surgery and migraine, with the recommended maximum daily dose of 30mg. - Indications for use in children are restricted to the second-line treatment of established post-operative nausea and vomiting (only via the intravenous route), with the maximum daily dose of 0.5 mg/kg. - Contraindicated for use in infants less than one year of age. - Treatment should be kept as short as possible, in accordance to one's clinical judgement. **References:** Communication from the Health Sciences Authority, July 2015. WHO Pharmaceuticals Newsletter No. 5, 2016.
Europe	26 July 2013 20 December 2013	EMA's Committee on Medicinal Products for Human Use (CHMP) confirmed previously recommended changes to the use of metoclopramide-containing medicines in EU, including restricting the dose and duration of use of these medicines to minimise the known risks of potentially serious neurological (brain and nerve) side effects. This followed a re-examination of the opinion originally given by the Committee on 26 July 2013. The review confirmed the well-known risks of neurological effects such as short-term extrapyramidal disorders, a group of involuntary movement disorders that may include muscle spasms (often involving the head and neck) and tardive dyskinesia (uncontrollable movements such as grimacing and twitching). The risk of acute (short-term) neurological effects is higher in children, although tardive dyskinesia is reported more often in the elderly, and the risk is increased at high doses or with long-term treatment. The evidence indicated that these risks outweighed the benefits of metoclopramide in conditions requiring long-term treatment. There have also been very rare cases of serious

		effects on the heart or circulation, particularly after injection. **References:** European Commission final decision, 26 July 2013 and 20 December 2013. WHO Pharmaceuticals Newsletter No. 5, 2013.
United Arab Emirates		Metagliz 10 mg/5 ml solution, Primperan 0.1 mg drops and 5 mg/5 ml syrup, and Clopram drops were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: metoprolol

C.A.S. NUMBER: 37350-58-6

OTHER NAMES: Lopressor, Metolar XR, Toprol XL

Country	Effective Date	Description of action taken
United Arab Emirates		Lopressor Retard 200 mg were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: metronidazole

C.A.S. NUMBER: 443-48-1

OTHER NAMES: Elyzol, Flagyl, Mirazol

Country	Effective Date	Description of action taken
United Arab Emirates		Elyzol 500 mg and 1 g suppository were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. Flagyl 500 mg/ml infusion and Mirazol 125 mg/5 ml suspension were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: miconazole

C.A.S. NUMBER: 22916-47-8

OTHER NAMES: Daktarin

Country	Effective Date	Description of action taken

United Arab Emirates		Daktarin solution for injection and 250 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: midodrine

C.A.S. NUMBER: 133163-28-7

OTHER NAMES: Amatine, ProAmatine, Gutron

Country	Effective Date	Description of action taken
USA	16 August 2010	The US FDA proposed to withdraw approval of midodrine hydrochloride, which is used to treat the low blood pressure condition orthostatic hypotension, because companies failed to provide evidence of clinical benefit of midodrine hydrochloride. **References:** FDA News Release, US FDA, 16 August 2010 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 5, 2010.

PRODUCT NAME: mirtazapine

C.A.S. NUMBER: 61337-67-5

OTHER NAMES: Mirtazapina Azevedos

Country	Effective Date	Description of action taken
United Arab Emirates		The application for Mirtazapina Azevedos 15 mg and 30 mg was rejected by the committee for various reasons. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: mivacurium chloride

C.A.S. NUMBER: 106791-40-6

OTHER NAMES: Mivacron

Country	Effective Date	Description of action taken
United Arab Emirates		Mivacron 20 mg/10 ml were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: modafinil

C.A.S. NUMBER: 68693-11-8

OTHER NAMES: Stavigile, Provigil, Alertec, Modavigil

Country	Effective Date	Description of action taken
Europe	22 July 2010	The European Medicines Agency (EMA) has recommended that modafinil-containing medicines should only be used to treat narcolepsy and that doctors and patients should no longer use the medicine for the treatment of idiopathic hypersomnia, obstructive sleep apnea and chronic shift work sleep disorder. **References:** Press release, Questions and answers, EMA, 22 July 2010 (www.ema.europa.eu). WHO Pharmaceuticals Newsletter No. 5, 2010.
United Kingdom	March 2011	Modafinil is no longer indicated for shift worker sleep disorder and obstructive sleep apnea. Modafinil should not be used in the following groups: those with uncontrolled hypertension or cardiac arrhythmias; children up to 18 years old; women who are pregnant or breastfeeding. Modafinil should be discontinued and not restarted in cases of: serious skin or hypersensitivity reactions; psychiatric disorders such as suicidal ideation. **References:** Drug Safety Update, March 2011, Volume 4, Issue 8, A1, MHRA (www.mhra.gov.uk). WHO Pharmaceuticals Newsletter No. 2, 2011.
Switzerland	11 July 2011	Modafinil is no longer indicated for obstructive sleep-apnoea syndrome. **References:** Communication from Swissmedic, July 2012.
Australia	October 2011	The indication to treat excessive sleepiness associated with moderate- to severe chronic shift work sleep disorder should be revised to include only patients where non-pharmacological interventions (e.g. planned napping) are unsuccessful or inappropriate. The Therapeutic Goods Administration (TGA) recommended that modafinil should only be used as an adjunct to CPAP when used to improve wakefulness in patients with obstructive sleep apnoea/hypopnea syndrome, because modafinil can improve the symptom of excessive sleepiness but does not treat the underlying cause. **References:** Medicines Safety Update Vol. 2, No. 5, October 2011 (www.tga.gov.au).

		WHO Pharmaceuticals Newsletter No. 6, 2011.
Brazil	March 2012	Changes in the text of the medicine package leaflet, in compliance with ANVISA recommendations, were communicated to health professionals. It regards the exclusion of indications for the treatment of idiopathic hypersomnia, excessive sleepiness associated with obstructive apnea and sleep disorder associated with shift work, because the benefits do not outweigh the risks. The medicine was contraindicated for patients with uncontrolled moderate to severe hypertension, patients with cardiac arrhythmias and for children under 18 years of age. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: molgramostim

C.A.S. NUMBER: 99283-10-0

OTHER NAMES: Leucomax

Country	Effective Date	Description of action taken
United Arab Emirates		Leucomax 0.15 mg, 0.3 mg, and 0.4 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: monobenzone

C.A.S. NUMBER: 103-16-2

OTHER NAMES: Benoquin

Country	Effective Date	Description of action taken
United Arab Emirates		Benoquin 20% ointment were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: montelukast

C.A.S. NUMBER: 151767-02-1

OTHER NAMES:

Country	Effective Date	Description of action taken

United Arab Emirates		Montelukast sodium were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: moxifloxacin

C.A.S. NUMBER: 186826-86-8

OTHER NAMES: Mo-Floren

Country	Effective Date	Description of action taken
United Arab Emirates		The application for Mo-Floren was rejected by the committee for various reasons. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: moxonidine

C.A.S. NUMBER: 75438-57-2

OTHER NAMES: Physiotens

Country	Effective Date	Description of action taken
United Arab Emirates		Physiotens 0.3 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: mycophenolate

C.A.S. NUMBER: 128794-94-5

OTHER NAMES: CellCept, Myfortic

Country	Effective Date	Description of action taken
Brazil	December 2015	Considering that mycophenolate is a potent human teratogenic, increasing the risk of miscarriages and congenital malformations, ANVISA highlighted its contraindications and new advice on pregnancy prevention for women and men undergoing CellCept treatment. The medicine package leaflet has been updated. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).
Chile	11 August 2016	The product label is updated with new contraindications:

		- This medication should not be used in pregnancy unless adequate alternative treatment is available to prevent rejection of the transplant. - This medicine should not be used in women of childbearing age who do not use highly effective contraceptive methods. - Do not start treatment with this drug in women of childbearing age without the result of a pregnancy test that discards it, in order to prevent accidental use during pregnancy. This decision took into consideration of similar actions by the AGEMED, MHRA, the USFDA and information from pharmaceutical companies indicating teratogenic risk of mycophenolate mofetil associated with the use of mycophenolate. **References:** Instituto de Salud Publica (www.ispch.cl). Spanish Agency for Medicines and Health Products (AGMED) information note, 23 October , 2015. Medicines and Healthcare products Regulatory Agency (MHRA) statement, 15 December 2015. US FDA information released, M

PRODUCT NAME: nadolol

C.A.S. NUMBER: 42200-33-9

OTHER NAMES: Corgard

Country	Effective Date	Description of action taken
United Arab Emirates		Corgard 80 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: naphazoline

C.A.S. NUMBER: 835-31-4

OTHER NAMES: Naphcon, Albalon

Country	Effective Date	Description of action taken
United Arab Emirates		Naphcon drops and Albalon Liquifilm solution were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: naproxen

C.A.S. NUMBER: 22204-53-1

OTHER NAMES: Miranax, Aleve, Naprosyn

Country	Effective Date	Description of action taken
United Arab Emirates		Miranax® tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: natalizumab

C.A.S. NUMBER: 189261-10-7

OTHER NAMES: Tysabri, Antegren

Country	Effective Date	Description of action taken
USA	5 February 2010	The US FDA has alerted health-care professionals and patients that the risk of developing progressive multifocal leukoencephalopathy (PML) increases with the number of natalizumab infusions. **References:** Safety Information, US FDA 5 February 2010 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 2, 2010. WHO Pharmaceuticals Newsletter No. 3, 2011.
United Kingdom	March 2010	The Medicines and Healthcare products Regulatory Agency (MHRA) has warned that the risk of developing progressive multifocal leukoencephalopathy (PML) with natalizumab increases after two years of therapy. Natalizumab should be promptly discontinued if PML is suspected, with subsequent appropriate evaluation including a standardised MRI scan and lumbar puncture. **References:** Drug Safety Update, MHRA Volume 3, Issue 8, March 2010 (www.mhra.gov.uk). WHO Pharmaceuticals Newsletter No. 2, 2010.
Canada	17 May 2010	Health-care professionals have been advised that the risk of developing progressive multifocal leukoencephalopathy (PML) increases with increasing duration of natalizumab (TYSABRI) treatment, and that after 24 infusions, the risks and benefits of continuing natalizumab therapy should be re-discussed with the patient. **References:** Advisories, Warnings and Recalls, Health Canada 17 May 2010 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 3, 2010. WHO Pharmaceuticals Newsletter No. 4, 2016. WHO Pharmaceuticals Newsletter No. 3, 2017.
USA	20 January 2012	The US FDA notified health-care professionals that testing positive for anti-JC virus (JCV) antibodies has been identified

		as a risk factor for PML, a rare but serious brain infection associated with use of natalizumab. **References:** FDA Drug Safety Communication, US FDA, 20 January 2012 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 1, 2012.

PRODUCT NAME: nefazodone

C.A.S. NUMBER: 82752-99-6

OTHER NAMES: Serzone

Country	Effective Date	Description of action taken
United Arab Emirates		Serzone 50 mg to 250 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: nelfinavir

C.A.S. NUMBER: 159989-64-7

OTHER NAMES: Viracept

Country	Effective Date	Description of action taken
United Arab Emirates		Viracept 250 mg tablets and 20 mg/g powder were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: neostigmine bromide

C.A.S. NUMBER: 114-80-7

OTHER NAMES: Prostigmine

Country	Effective Date	Description of action taken
United Arab Emirates		Prostigmine tablets and solution for injection were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: nesiritide

C.A.S. NUMBER: 124584-08-3

OTHER NAMES: Natrecor, Noratak

Country	Effective Date	Description of action taken
Switzerland	8 December 2011	Nesiritide was withdrawn from the market. **References:** Communication from Swissmedic, July 2012.

PRODUCT NAME: nevirapine

C.A.S. NUMBER: 129618-40-2

OTHER NAMES: Viramune

Country	Effective Date	Description of action taken
United Arab Emirates		Viramune 200 mg were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: niclosamide

C.A.S. NUMBER: 50-65-7

OTHER NAMES: Yomesan, Niclocide, Fenasal, Phenasal

Country	Effective Date	Description of action taken
United Arab Emirates		Yomesan were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: nicobrevin

C.A.S. NUMBER: 132338-74-0

OTHER NAMES:

Country	Effective Date	Description of action taken
United Kingdom	May 2011	The Commission on Human Medicines and its Pharmacovigilance Expert Advisory Group advised that the risks of Nicobrevin outweigh any benefits, and use of an unproven antismoking preparation could delay or deter patients from seeking effective smoking-cessation treatments. Therefore, Nicobrevin has been withdrawn from the UK market. The product licence was cancelled on Jan 31, 2011. **References:**

		Drug Safety Update, volume 4, issue 10, May 2011. (www.mhra.gov.uk).

PRODUCT NAME: nifedipine

C.A.S. NUMBER: 21829-25-4

OTHER NAMES: Adalat, Procardia

Country	Effective Date	Description of action taken
United Arab Emirates		Adalat 10 mg capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: niflumic acid

C.A.S. NUMBER: 4394-00-7

OTHER NAMES: Nifluril

Country	Effective Date	Description of action taken
United Arab Emirates		Nifluril ointment, Nifluril (Adult) and Nifluril (Paediatric) suppository were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: nifluroxazide

C.A.S. NUMBER: 965-52-6

OTHER NAMES: Ambatrol, Antinal, Bacifurane, Diafuryl, Pérabacticel, Antinal, Diax, Nifrozid, Ercefuryl, Erfuzide (Thailand), Endiex (Slovakia), Pentofuryl, Topron, Enterovid, Eskapar

Country	Effective Date	Description of action taken
United Arab Emirates		Ercefuryl 218 mg/5 ml suspension were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: nilotinib

C.A.S. NUMBER: 641571-10-0

OTHER NAMES: Tasigna

Country	Effective Date	Description of action taken
Sudan	2012	Nilotinib is the last choice for treatment after therapeutic failure of all 1st & 2nd line options. Prescribers should send full details about patients and send weekly reports about any ADRs or complications that appear. **References:** Communication from the Sudan National Pharmacovigilance Centre, July 2012.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: nimesulide

C.A.S. NUMBER: 51803-78-2

OTHER NAMES:

Country	Effective Date	Description of action taken
India	10 February 2011	Nimesulide formulations for human use in children below 12 years of age is prohibited in India. **References:** The Gazette of India, No. 71, New Delhi 10 February 2011.
Europe	23 June 2011	The Committee for Medicinal Products for Human Use (CHMP) has concluded that the benefits of systemic nimesulide-containing medicines continue to outweigh their risks in the treatment of patients with acute pain and primary dysmenorrhoea. However, these medicines should no longer be used for the symptomatic treatment of osteoarthritis. The CHMP concluded that nimesulide was associated with an increased risk of liver toxicity compared with other anti-inflammatory treatments. **References:** Press release, EMA, 23 June 2011 (www.ema.europa.eu). WHO Pharmaceuticals Newsletter No. 4, 2011.
Bhutan	22 July 2015	All forms of nimesulide-containing medicines are banned due to the risk of hepatoxicity and neonatal renal failure. Pharmacies have been notified of the restrictions in their importation and sales. **References:** Bhutan Drug Regulatory Authority, List of Banned Drugs (www.dra.gov.bt).
Chile	20 June 2017	The market authorisation of the product is suspended. The decision took into consideration the recommendation by the Network of Drug Information Centers of Latin America and the Caribbean (RedCIMLAC) of its withdrawal from the Latin American market, due to its associated risk of severe hepatotoxicity. The decision was based on the evaluation of nimesulide by the working group on evaluation of medicines (GEM), which reported that in Latin America 75 cases of hepatotoxicity have been documented, of which 10 ended in death of the patient. In Chile, seven suspicions of

		ADR related to liver problems associated with nimesulide have been reported to the National Pharmacovigilance Center, of which six have been considered serious. **References:** Instituto de Salud Publica (www.ispch.cl).

PRODUCT NAME: nimodipine

C.A.S. NUMBER: 66085-59-4

OTHER NAMES: Nimotop, Nymalize

Country	Effective Date	Description of action taken
United Arab Emirates		Nimotop infusion and tablets were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: nintedanib

C.A.S. NUMBER: 656247-18-6

OTHER NAMES: Ofev, Vargatef

Country	Effective Date	Description of action taken
Brazil	March 2018	ANVISA informed that severe and non-severe cases of drug-induced liver injury (LHID) were reported during the post-marketing period, including one case associated with fatal outcome. Thus, the product package leaflet was updated to reflect the increased severity of LHID observed and to provide additional guidance on the timeliness of performing liver laboratory tests. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: nitroglycerin

C.A.S. NUMBER: 55-63-0

OTHER NAMES: Nitroderm, Nitromack

Country	Effective Date	Description of action taken
United Arab Emirates		Nitroderm TTS 10 and 15 patch, and Nitromack Retard 2.5 mg capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: noradrenaline

C.A.S. NUMBER: 108341-18-0

OTHER NAMES: norepinephrine, Levophed

Country	Effective Date	Description of action taken
United Arab Emirates		The application for Levophed 1 mg/ml solution for injection was rejected by the committee for various reasons. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: norethisterone

C.A.S. NUMBER: 68-22-4

OTHER NAMES: Primolut

Country	Effective Date	Description of action taken
United Arab Emirates		Primolut Depot 500 mg solution for injection were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: norpseudoephedrine

C.A.S. NUMBER: 37577-07-4

OTHER NAMES: Mirapront

Country	Effective Date	Description of action taken
United Arab Emirates		Mirapront-N capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: nusinersen

C.A.S. NUMBER: 1258984-36-9

OTHER NAMES: Spinraza

Country	Effective Date	Description of action taken
Brazil	September 2018	Health professionals were informed of report of non-communicating hydrocephalus related to meningitis or

		bleeding, which has been reported in patients (including children) with Spinal Muscular Atrophy (EBF) treated with Spinraza®. Physicians involved in the treatment of patients with EBF (such as neurologists and neuropediatricians) were advised to assess hydrocephalus in patients displaying associated signs and symptoms, as well as to discuss this potential risk and its signs and symptoms with patients/caregivers. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: nystatin

C.A.S. NUMBER: 1400-61-9

OTHER NAMES: Mycostatin, Nystop

Country	Effective Date	Description of action taken
United Arab Emirates		Mycostatin 100,000 IU/ml suspension, Mycostatin 100,000 units/g ointment and Mycostatin Baby ointment were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: octreotide

C.A.S. NUMBER: 79517-01-4

OTHER NAMES: Sandostatin, Bynfezia Pen, Mycapssa

Country	Effective Date	Description of action taken
United Arab Emirates		Sandostatin 0.2 mg/ml and 0.5 mg/ml injection products were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ofatumumab

C.A.S. NUMBER: 679818-59-8

OTHER NAMES: Arzerra

Country	Effective Date	Description of action taken
United Arab Emirates		Arzerra™ 100mg and 1000 mg infusion were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:**

		Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: olsalazine

C.A.S. NUMBER: 6054-98-4

OTHER NAMES: Dipentum

Country	Effective Date	Description of action taken
United Arab Emirates		Dipentum 250 mg capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: omeprazole

C.A.S. NUMBER: 73590-58-6

OTHER NAMES: Losec, Prilosec, Zegerid, Omiz, Neoprazole

Country	Effective Date	Description of action taken
United Arab Emirates		Losec Mups 40 mg tablets were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. Omiz 10 and Neoprazole 10 mg capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ondansetron

C.A.S. NUMBER: 99614-02-5

OTHER NAMES: Zofran

Country	Effective Date	Description of action taken
Brazil	August 2012	Healthcare professionals were informed of the reduction in maximum daily intravenous dose from 32 mg to 16 mg, due to the results from a study that demonstrated that Zofran caused prolongation, dependent dose, of the corrected QT interval, which may result in Torsade de Points and life-threatening outcomes. The package leaflet was updated with the new guidelines. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: orciprenaline sulphate

C.A.S. NUMBER: 586-06-1

OTHER NAMES: Alupent

Country	Effective Date	Description of action taken
United Kingdom	July 2010	Orciprenaline sulphate is to be withdrawn from the UK market on Sept 30, 2010. A comprehensive analysis of the available literature was completed last year, which showed that it was significantly less efficacious than other more-specific β2 agonists and was associated with a higher incidence of side effects. **References:** Drug Safety Update, July 2010, Volume 3, issue 12, (www.mhra.gov.uk).

PRODUCT NAME: orlistat

C.A.S. NUMBER: 96829-58-2

OTHER NAMES: tetrahydrolipstatin, Xenical, Alli

Country	Effective Date	Description of action taken
Syrian Arab Republic	14 February 2011	Updates in the package insert to add a new warning that rare but serious cases of liver injurey including hepatic necrosis and acute hepatic failure were reported. Signs for hepatic failure should be recognized; If hepatic injurey is suspected, treatment should be stopped and liver function sould be assessed. **References:** Circular from the Ministry of Health No. 47340/20/1, 2011.

PRODUCT NAME: ornidazole

C.A.S. NUMBER: 16773-42-5

OTHER NAMES: Tiberal

Country	Effective Date	Description of action taken
United Arab Emirates		Tiberal solution for injection, Tiberal 125 mg, 500 mg and Tiberal Combi 500 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: oxacillin

C.A.S. NUMBER: 66-79-5

OTHER NAMES: Bactocill

Country	Effective Date	Description of action taken
Madagascar	8 June 2011	The concentration level of antibiotic necessary to be effective in the treatment of infections caused by staphylococci and/or streptococci have not been obtained at the doses recommended by the SPC for oxicillin 250 mg/5 ml powder for syrup, 500 mg capsule, or 1 g/5 ml IM injection. **References:** Communication from the Madagascar National Pharmacovigilance Centre July, 2012.

PRODUCT NAME: oxiconazole

C.A.S. NUMBER: 64211-46-7

OTHER NAMES: Oceral, Oxistat, Oxizole

Country	Effective Date	Description of action taken
United Arab Emirates		Oceral cream were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: oxyphenbutazone

C.A.S. NUMBER: 129-20-4

OTHER NAMES: Tanderil

Country	Effective Date	Description of action taken
United Arab Emirates		Tanderil ointment were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: oxytetracycline

C.A.S. NUMBER: 79-57-2

OTHER NAMES: Terramycin

Country	Effective Date	Description of action taken
United Arab Emirates		Terramycin ointment and 250 mg capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: paclitaxel

C.A.S. NUMBER: 33069-62-4

OTHER NAMES: Taxol

Country	Effective Date	Description of action taken
United Arab Emirates		Taxol infusion 100 mg/16.7 ml, 300 mg/50 ml and 30 mg/5 ml were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: paclitaxel, nanoparticle albumin–bound

C.A.S. NUMBER: 33069-62-4

OTHER NAMES: Abraxane

Country	Effective Date	Description of action taken
Brazil	March 2018	ANVISA advised that the product Abraxane® should not be replaced by other formulations of paclitaxel, since Abraxane is a solvent-free medicine with paclitaxel nanoparticles linked to albumin, which has substantially different functional properties compared to those of paclitaxel formulations in solution. The approved indication and dosage for the product are different from other formulations containing paclitaxel. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: pamidronate

C.A.S. NUMBER: 40391-99-9

OTHER NAMES: Aredia, Pamimed

Country	Effective Date	Description of action taken
United Arab Emirates		Aredia 15 mg, 30 mg and 90 mg infusion products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: panamycin

C.A.S. NUMBER: 100905-89-3

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		Panamycin 250 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: panitumumab

C.A.S. NUMBER: 339177-26-4

OTHER NAMES: Vectibix

Country	Effective Date	Description of action taken
Switzerland	12 July 2011	Rare cases of serious keratitis and ulcerative keratitis have been reported. **References:** Communication from Swissmedic, July 2012.
Brazil	July 2013	Safety information was published specific to the use of Vectibix in combination with oxaliplatin-based chemotherapy: Vectibix should not be used in combination with oxaliplatin-based chemotherapy in patients presenting with mCRC with mutant RAS (exons 2,3,4 or KRAS and NRAS) or for whom RAS status is unknown due to retrospective anasia of a phase 3 study. The package leaflet was updated. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: pantoprazole

C.A.S. NUMBER: 102625-70-7

OTHER NAMES: Panets

Country	Effective Date	Description of action taken
United Arab Emirates		Panets tablets and 120 mg/5 ml syrup were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: paracetamol

C.A.S. NUMBER: 103-90-4

OTHER NAMES: Tylenol, Tylalgin, Adol, Dafalgan, Crocin, Efferalgan, xxxx Enelfa, Panadrex, Panadol, Neomol, Tempra

Country	Effective Date	Description of action taken
New Zealand	June 2011	Medsafe reported that reports over the last 12 months describing serious adverse reactions in children due to paracetamol toxicity highlight the importance of using this medicine appropriately. **References:** Prescriber Update Vol. 32 No. 2, June 2011 (www.medsafe.govt.nz). WHO Pharmaceuticals Newsletter No. 4, 2011.
United Kingdom	July 2011	The MHRA revised the dosing for liquid paracetamol products for children to one that is based on narrower age bands with a single dosing option per band. **References:** Drug Safety Update, July 2011, Volume 4, issue 12, A2, MHRA (www.mhra.gov.uk). WHO Pharmaceuticals Newsletter No. 4, 2011. WHO Pharmaceuticals Newsletter No. 5, 2012.
Brazil	August 2013	Following an US FDA Drug Safety Communicaiton, ANVISA warned that paracetamol may cause infrequent but extremely severe hypersensitivity skin reactions. Clarifications were made about these severe diseases, their symptoms and complications, highlighting that patients who have already had some skin reaction after using paracetamol should not use this medication again; recommendations were given that in case of development of skin reactions, its use should be stopped immediately and medical helpsought. **References:** ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia).
United Arab Emirates		Adol tablets, Panadres IV infusion and Neomol Forte 650 mg tablets were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. Adol 120 mg sachet for suspension, Dafalgan 600 mg suppository, Efferalgan 150 mg/5 ml solution, xxxx Enfelfa 500 mg tablets, Tempra syrup and drops were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: paricalcitol

C.A.S. NUMBER: 131918-61-1

OTHER NAMES: Zemplar

Country	Effective Date	Description of action taken
United Arab Emirates		Zemplar 1 mcg capsules were voluntarily withdrawn by the MAH either for commercial reasons or any reason other

		than safety. Zemplar 4 mcg capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: pazopanib

C.A.S. NUMBER: 635702-64-6

OTHER NAMES: Votrient

Country	Effective Date	Description of action taken
Brazil	February 2013	Safety update in Votriet package leaflet is reported: the frequency of serum monitoring of hepatic function for hepatotoxicity should be increased due to periodic review of safety data from clinical trials with Votrient. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: pefloxacin

C.A.S. NUMBER: 70458-92-3

OTHER NAMES: Peflacine

Country	Effective Date	Description of action taken
United Arab Emirates		Peflacine 400 mg injection were withdrawn by the MAH before getting approval. Peflacine 400 mg tablets were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: pembrolizumab

C.A.S. NUMBER: 1374853-91-4

OTHER NAMES: Keytruda

Country	Effective Date	Description of action taken
Brazil	November 2018	Based on preliminary data from an ongoing clinical study, the indication of Keytruda as monotherapy was revised to: "treatment of locally advanced or metastatic urothelial carcinoma in adults who are not eligible for cisplatin-containing chemotherapy and whose tumors express PD-L1 with a combined positive score (CPS)>= 10." The package leaflet of the drug has been updated. **References:**

		ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: penciclovir

C.A.S. NUMBER: 39809-25-1

OTHER NAMES: Vectavir

Country	Effective Date	Description of action taken
United Arab Emirates		Vectavir 1% cream were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: pentoxyverine

C.A.S. NUMBER: 1045-21-2

OTHER NAMES: Toclase

Country	Effective Date	Description of action taken
United Arab Emirates		Toclase 15 mg/5 ml syrup were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: pergolide

C.A.S. NUMBER: 66104-22-2

OTHER NAMES: Permax, Pergotoliderived

Country	Effective Date	Description of action taken
Egypt	23 April 2009	Withdrawal of all registered products containing pergolide. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.
Switzerland	30 May 2011	Voluntary withdrawal of registration approval by MAH per 30.9.2011 (supply shortfall). **References:** Communication from Swissmedic, July 2012.

PRODUCT NAME: perindopril

C.A.S. NUMBER: 107133-36-8

OTHER NAMES: Coversyl

Country	Effective Date	Description of action taken
United Arab Emirates		Coversyl 2 mg, 4 mg and 8 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: Phenobarbital Sodium

C.A.S. NUMBER: 57-30-7

OTHER NAMES: Gardenal

Country	Effective Date	Description of action taken
United Arab Emirates		Gardenal (200mg/ml) solution for injection were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: phenoxymethylpenicillin

C.A.S. NUMBER: 132-98-9

OTHER NAMES: Arcasin, Cliacil, Ospen, penicillin V (PcV), penicillin VK

Country	Effective Date	Description of action taken
United Arab Emirates		Arcasin 60000IU/ml syrup, Arcasin Mio tablets, Cliacil suspension, Ospen 200 suspension, Cliacil 0.6 and 1.2 M.U tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: phenylephrine

C.A.S. NUMBER: 61-76-7

OTHER NAMES: Prefrin, Isopto Frin

Country	Effective Date	Description of action taken
United Arab Emirates		Prefrin 0.12% Liquifilm drops were withdrawn by the MAH before getting approval. Isopto Frin drops were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: phenylpropranolamine

C.A.S. NUMBER: 14838-15-5

OTHER NAMES: Accutrim

Country	Effective Date	Description of action taken
India	10 February 2011	Phenylpropanolamine and its formulations for human use are prohibited in India. **References:** The Gazette of India, No. 71, New Delhi 10 February 2011.
Bhutan	22 July 2015	All forms of phenylpropranolamine-containing medicines are banned due to the risk of hemorrhagic stroke. Pharmacies have been notified of the restrictions in their importation and sales. **References:** Bhutan Drug Regulatory Authority, List of Banned Drugs (www.dra.gov.bt).

PRODUCT NAME: phenytoin

C.A.S. NUMBER: 57-41-0

OTHER NAMES: Dilantin

Country	Effective Date	Description of action taken
India	17 March 2017	The Central Drugs Standard Control Organization (CDSCO) requested to incorporate phenytoin associated acute generalized exanthematous pustulosis (AGEP) into the package inserts of suspected drugs marketed in India. **References:** Letter issued by CDSCO on 17 March 2017.

PRODUCT NAME: phytomenadione

C.A.S. NUMBER: 84-80-0

OTHER NAMES: Konakion, Vitamin K1, phylloquinone

Country	Effective Date	Description of action taken
United Arab Emirates		Konakion 2% drops were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: pilocarpine

C.A.S. NUMBER: 92-13-7

OTHER NAMES: P.V. Carpine

Country	Effective Date	Description of action taken
United Arab Emirates		P.V. Carpine 2% and 4% drops were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.
United Arab Emirates		Isopto Carbachol 1.5% and 3% drops were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: pimozide

C.A.S. NUMBER: 2062-78-4

OTHER NAMES: Orap

Country	Effective Date	Description of action taken
United Arab Emirates		Orap 1 mg and Orap Forte 4 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: pindolol

C.A.S. NUMBER: 13523-86-9

OTHER NAMES: Visken

Country	Effective Date	Description of action taken
United Arab Emirates		Visken 5 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: pioglitazone

C.A.S. NUMBER: 111025-46-8; 112529-15-10

OTHER NAMES: Actos, Pioglit, Stanglit, Glustin, Glizone, Pioz, Zactos

Country	Effective Date	Description of action taken

France	June 2011	The French Health Products Safety Agency (Afssaps) decided to suspend the use in France of medicines containing pioglitazone. According to Afssaps, available pharmacovigilance data and the new study results of the Caisse Nationale d'Assurance Maladie (CNAMTS) confirmed low risk of occurrence of bladder cancer during the use of pioglitazone. **References:** Suspension de l'utilisation en France des médicaments contenant de la pioglitazone, Afssaps, 9 June 2011 (www.afssaps.fr). WHO Pharmaceuticals Newsletter No. 4, 2011.
USA	15 June 2011	According to the U.S. Food and Drug Administration (US FDA), pioglitazone should not be used in patients with active bladder cancer. **References:** FDA Drug Safety Communication, US FDA, 15 June 2011 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 1, 2017.
Switzerland	20 June 2011	Higher incidence of bladder carcinoma has been reported with pioglitazone. **References:** Communication from Swissmedic, July 2012.
Europe	21 July 2011	The EMA announced that the CHMP confirmed that anti-diabetic pioglitazone-containing medicines remain a valid treatment option for certain patients with type 2 diabetes but that there is a small increased risk of bladder cancer in patients taking these medicines. **References:** Press release, EMA, 21 July 2011 (www.ema.europa.eu). WHO Pharmaceuticals Newsletter No. 4, 2011.
Egypt	18 August 2011	1. Do not use pioglitazone in patients with active bladder cancer. 2. Use pioglitazone with caution in patients with prior history of bladder cancer. The benefits of glycemic control versus unknown risks for cancer recurrence with pioglitazone should be considered in patients with a prior history of bladder cancer. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.
Sudan	28 September 2011	Prescribers are requested to follow the following recommendations: • Do not use pioglitazone in patients with active bladder cancer. • Report any case of bladder cancer during pioglitazone use. **References:** Communication from the Sudan National Pharmacovigilance Centre, July 2012.

Australia	October 2011	The Therapeutic Goods Administration (TGA) advised health professionals to avoid using pioglitzone in patients with bladder cancer or a history of bladder cancer due to a possible increased risk of bladder cancer with pioglitazone use. **References:** Medicines Safety Update Vol. 2, No. 5, October 2011 (www.tga.gov.au). WHO Pharmaceuticals Newsletter No. 6, 2011. WHO Pharmaceuticals Newsletter No. 1, 2014.
Indonesia	20 March 2012	The product information of all pioglitazone-containing agents should be revised to contra-indicate the use of this product in patients with current and history of bladder cancer; and also to provide warning and precaution on risk of urinary bladder cancer. **References:** Dear Healthcare Professional Communication PN.01.02.1.31.03.12.1845
Canada	16 April 2012	Takeda Canada Inc., in collaboration with Health Canada, informed health-care professionals of important safety information regarding a potential risk of bladder cancer in patients treated with pioglitazone hydrochloride. Pioglitazone hydrochloride is now contraindicated in patients with active bladder cancer, a history of bladder cancer or uninvestigated macroscopic haematuria and any macroscopic haematuria should be investigated before starting pioglitazone therapy. **References:** Advisories, Warnings and Recalls, Health Canada, 16 April 2012 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 3, 2012.
Viet Nam	13 September 2012	The marketing authorisation for pioglitazone-containing products is suspended due to unfavorable risk-benefit profile. **References:** Drug Administration of Viet Nam Official documents No. 13702/QLD-DK, 13 September 2012.
Switzerland	19 December 2012	New contraindications and precautions have been added related to increased risk of bladder cancer. **References:** Communication from Swissmedic, July 2012.
Brazil	June 2011 September 2011	In June 2011, ANVISA warned about the possible association of risk of bladder cancer with the use of pioglitazone. An evaluation of the benefit/risk ratio of this drug was carried out. In September 2011, In the meantime, it was estimated that the benefits of pioglitazone outweighed its risks when it is used according to the recommendations provided in the package leaflet.

		In September 2011, epidemiological studies indicated an increased relative risk of developing bladder cancer in patients treated with pioglitazone. The product label of the drug has been updated accordingly. The HCPs were informed through the Letter from ANVISA. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: pipoxolan

C.A.S. NUMBER: 23744-24-3

OTHER NAMES: Rowapraxin

Country	Effective Date	Description of action taken
United Arab Emirates		Rowapraxin tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: piracetam

C.A.S. NUMBER: 7491-74-9

OTHER NAMES: Nootropil

Country	Effective Date	Description of action taken
United Arab Emirates		Nootropil400 mg capsules were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: piroxicam

C.A.S. NUMBER: 36322-90-5

OTHER NAMES: Feldene, Dolonex, Fasden, Orthocam, Piroksikam, piroxikam

Country	Effective Date	Description of action taken
Egypt	4 March 2010	Piroxicam should not be used in cases of short-term pain and inflamations. Its use should be restricted to treatment of the symptoms of osteoarthritis rheumatoid arthritis& ankylosing spondylitis. The risks outweigh the benefits when used in cases of short-term pain and inflamations. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.

United Arab Emirates		Feldene 0.5% gel, Orthocam 10 mg and 20 mg capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: podophyllotoxin

C.A.S. NUMBER: 518-28-5

OTHER NAMES: Condyline

Country	Effective Date	Description of action taken
United Arab Emirates		Condyline 5 mg/ml solution were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: policresulen

C.A.S. NUMBER:

OTHER NAMES: Albothyl, Polilen

Country	Effective Date	Description of action taken
Indonesia	15 February 2018	The Indonesian National Agency of Drug and Food Control (NADFC) suspended policresulen concentrate containing external liquid preparation due to risk of noma like lession. **References:** Head of NADFC Press Release 15 February 2018

PRODUCT NAME: polygeline

C.A.S. NUMBER: 9015-56-9

OTHER NAMES: Haemaccel

Country	Effective Date	Description of action taken
United Arab Emirates		Haemaccel infusion products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: polysorbate 80

C.A.S. NUMBER: 9005-65-6

OTHER NAMES: Alkest, Canarcel, Tween

Country	Effective Date	Description of action taken
Egypt	12 April 2012	Polysorbate 80 should not be used for children less than 4 years of age. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.

PRODUCT NAME: polyvinylpyrrolidone (PVP)

C.A.S. NUMBER: 9003-39-8

OTHER NAMES:

Country	Effective Date	Description of action taken
Azerbaijan	25 May 2012	Polyvinylpyrrolidone 12600±2700 Da containing infusions have been suspended due to lower elimination rate from kidneys, which is the leading high-risk of toxicity. **References:** Ministry of Health Pharmacology and Pharmacopeia Advisory Council, May 2012.

PRODUCT NAME: pramipexole

C.A.S. NUMBER: 191217-81-9

OTHER NAMES: Sifrol

Country	Effective Date	Description of action taken
United Arab Emirates		Sifrol 3 mg extended release tablets were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: pravastatin

C.A.S. NUMBER: 81131-70-6

OTHER NAMES: Lipostat

Country	Effective Date	Description of action taken
United Arab Emirates		Lipostat 10 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: prazosin

C.A.S. NUMBER: 19216-56-9

OTHER NAMES: Minipress, Vasoflex, Lentopres

Country	Effective Date	Description of action taken
United Arab Emirates		Minipress 1 mg, 2 mg, and 5 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: pregabalin

C.A.S. NUMBER: 148553-50-8

OTHER NAMES: Lyrica

Country	Effective Date	Description of action taken
Syrian Arab Republic	14 October 2014	Pregabalin is classified as a controlled substance. Pharmaceutical distributors should handle pregabalin as a controlled substabce. **References:** Circular from the Ministry of Health No. 26177/20/1, 2014.
Syrian Arab Republic	28 January 2015	The package insert to be updated to inform patients that: Pregabalin is contraindicated in patients with hypersensitivity to pregabalin or any of the excipients of the finished products. Cases of hypersensitivity reactions and angioedema have been seen in patients treated with pregabalin. Men treated with pregabalin should be informed about the potential risk of fetal abnormalities: in the preclinical studies, administration of pregabalin to rats was linked to increased risk of fetal abnormalities. **References:** Circular from the Ministry of Health No. 1635/20/1, 2015.
Oman		Pregabalin is classified under controlled non psychotrobic drug category to prevent misuse. HCPs should observe restriction pregabalin prescription according to rules for controlled non psychotrobic drugs. **References:** Oman Ministry of Health Circular No. 143, 2013.
United Arab Emirates		The application for Prex 50 mg, 75 mg, and 150 mg capsules was rejected by the committee for various reasons. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: prenylamine

C.A.S. NUMBER: 390-64-7

OTHER NAMES: Segontin

Country	Effective Date	Description of action taken
United Arab Emirates		Segontin 60 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: procainamide

C.A.S. NUMBER: 1951-06-09

OTHER NAMES: Pronestyl, Procan, Procanbid

Country	Effective Date	Description of action taken
United Arab Emirates		Pronestyl 100 mg/ml solution for injection were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: procaine benzylpenicillin

C.A.S. NUMBER: 6130-64-9

OTHER NAMES: Hostacillin, procaine penicillin G

Country	Effective Date	Description of action taken
United Arab Emirates		Hostacillin "Aqu" 2,000,000 IU and 4,000,000 IU solution for injection were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: prochlorperazine maleate

C.A.S. NUMBER: 1984-02-06

OTHER NAMES: Stemetil

Country	Effective Date	Description of action taken
United Arab Emirates		Stemetil syrup were withdrawn by the MAH before getting approval.

		References: Ministry of Health and Prevention Ministerial Decree No. 366.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: promethazine

C.A.S. NUMBER: 58-33-3; 60-87-7

OTHER NAMES: Phenergan, Avomine, Promethegan, Romergan, Fargan, Farganesse, Prothiazine, Atosil, Receptozine, Lergiganm, Sominex

Country	Effective Date	Description of action taken
Canada	26 April 2010	Health Canada informed health-care professionals and the public of changes to the prescribing information, including the addition of a boxed warning, for promethazine hydrochloride injection. Promethazine is not to be used in children under the age of two years due to the potentially fatal risk of respiratory depression. Caution should be used when administering promethazine in children aged two and up: health care professionals are recommended to use the lowest effective dose, and the use of other drugs that may also slow breathing should be avoided. Promethazine is not to be injected subcutaneously due to the risk of serious tissue injury. The preferred route of administration for promethazine is deep intramuscular injection. Other routes of injection, particularly into arteries or veins, have been associated with serious tissue injury. **References:** Advisories, Warnings and Recalls, Health Canada 26 April 2010 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 3, 2010.
United Arab Emirates		Avomine 25 mg tablets, Phenergan 25 mg/ml and 50 mg/2 ml injection, and Phenergan Compound were withdrawn by the MAH before the product getting approval. Phenergan 10 mg and 25 mg tablets were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: propacetamol

C.A.S. NUMBER: 66532-85-2

OTHER NAMES: Pro-Dafalgan

Country	Effective Date	Description of action taken
United Arab Emirates		Pro-Dafalgan 1 g and 2 g solution for injection were withdrawn by the MAH before getting approval. **References:**

		Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: propofol

C.A.S. NUMBER: 2078-54-8

OTHER NAMES: Diprivan

Country	Effective Date	Description of action taken
United Arab Emirates		Diprivan 2% infusion were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: propoxyphene

C.A.S. NUMBER: 469-62-5

OTHER NAMES: dextropropoxyphene, Algafan, Darvon, Darvocet-N, Di-Gesic

Country	Effective Date	Description of action taken
New Zealand	26 March 2010	The New Zealand Medicines and Medical Devices Safety Authority (Medsafe) announced that the consents to distribute medicines containing dextropropoxyphene in New Zealand will be revoked on 1 August 2010. This decision follows a review by the Medicines Adverse Reactions Committee (MARC), which concluded that the risks of these medicines outweigh their benefits. **References:** Media Releases, Medsafe 26 March 2010 Prescriber Update Vol. 31 No. 2 June 2010 (www.medsafe.govt.nz). WHO Pharmaceuticals Newsletter No. 4, 2010.
Egypt	21 October 2010	Withdrawal of registered medicinal products containing this active ingredient. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.
USA	19 November 2010	The US FDA has recommended against continued use of propoxyphene after receiving new data that indicate the risk of cardiac toxicity. **References:** MedWatch, Safety Information, US FDA, 19 November 2010 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 6, 2010.
Canada	December 2010	Health Canada and Paladin Labs Inc announced that the company has decided to voluntarily recall and withdraw dextropropoxyphene on the Canadian market and discontinue the sale of the product. The results of a new

		study show that, even at therapeutic doses, dextropropoxyphene can significantly prolong the PR interval, widen the QRS complex, prolong the QT interval and therefore increase the risk of serious abnormal heart rhythms. **References:** Advisories, Warnings and Recalls, Health Canada, 1 December 2010 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 6, 2010.
Sudan	18 December 2010	The mentioned drug has been put in negative list for its registration because new data show that the drug can cause serious toxicity to the heart, even when used at therapeutic doses. **References:** Communication from the Sudan National Pharmacovigilance Centre, July 2012.
Guatemala	June 2014	Withdrawal from the market and cancellation of registration due to elevated risk of cardiac toxicity. **References:** Departamento de Regulación y Control de Productos Farmacéuticos y Afines (www.siamed.mspas.gob.gt) Guatemala, June 2014.

PRODUCT NAME: propranolol

C.A.S. NUMBER: 525-66-6

OTHER NAMES: Inderal

Country	Effective Date	Description of action taken
United Arab Emirates		Inderal L.A 80 mg and 160 mg capsules were withdrawn by the MAH before getting approval. Inderal 10 mg tablets were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: propylene glycol

C.A.S. NUMBER: 57-55-6

OTHER NAMES:

Country	Effective Date	Description of action taken
Egypt	12 April 2012	Propylene glycol should not be used for children less than 4 years of age. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: pseudoephedrine

C.A.S. NUMBER: 90-82-4

OTHER NAMES: Genaphed, Robidrine, Sudafed , Otrinol

Country	Effective Date	Description of action taken
United Arab Emirates		Otrinol 120 mg Retard were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366. WHO Pharmaceuticals Newsletter No. 3, 2012.

PRODUCT NAME: pyridostigmine bromide

C.A.S. NUMBER: 101-26-8

OTHER NAMES: Metinon

Country	Effective Date	Description of action taken
United Arab Emirates		Mestinon 10 mg tablets and 1 mg solution for injection were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: pyridoxine

C.A.S. NUMBER: 58-56-0

OTHER NAMES: Benadon

Country	Effective Date	Description of action taken
United Arab Emirates		Benadon 100 mg and 300 mg injections and Benadon 40 mg and 300 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: pyritinol

C.A.S. NUMBER: 1098-97-1

OTHER NAMES: Encephabol

Country	Effective Date	Description of action taken
United Arab Emirates		Encephabol 80.5 mg/5 ml syrup were withdrawn by the MAH before getting approval.

		References: Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: quinagolide

C.A.S. NUMBER: 87056-78-8

OTHER NAMES: Norprolac

Country	Effective Date	Description of action taken
United Arab Emirates		Norprolac 150 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: quinine

C.A.S. NUMBER: 130-95-0

OTHER NAMES: Qualaquin

Country	Effective Date	Description of action taken
United Kingdom	June 2010	The Medicines and Healthcare products Regulatory Agency (MHRA) has warned that quinine should not be considered a routine treatment for nocturnal leg cramps, and should only be considered when cramps cause regular disruption of sleep. Quinine should only be considered: when cramps are very painful or frequent; when other treatable causes of cramps have been ruled out; and when non-pharmacological measures have not worked. **References:** Drug Safety Update, MHRA Volume 3, Issue 11, June 2010 (www.mhra.gov.uk). WHO Pharmaceuticals Newsletter No. 4, 2010. WHO Pharmaceuticals Newsletter No. 1, 2018.
USA	8 July 2010	The US FDA has announced that it has approved a Risk Evaluation and Mitigation Strategy (REMS) to warn against the use of quinine sulfate for night time leg cramps. Quinine sulfate is only approved for the treatment of uncomplicated malaria caused by the parasite Plasmodium falciparum. Quinine sulfate is not approved for the treatment or prevention of night time leg cramps. The Agency warns that the use of quinine sulfate may result in serious and life-threatening hematological reactions, including serious bleeding due to thrombocytopenia and hemolytic-uremic syndrome/thrombotic thrombocytopenic purpura, which in some cases may result in permanent kidney damage. In some patients, adverse reactions result in hospitalization and death.

		References: Safety Information, US FDA 8 July 2010 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 4, 2010.
New Zealand	December 2010	The New Zealand Medicines and Medical Devices Safety Authority (Medsafe) has reminded prescribers that quinine is no longer indicated for the treatment of leg cramps in New Zealand, after CARM continues to receive reports of adverse events associated with the use of quinine for leg cramps. **References:** Prescriber Update Vol. 31, No.4 December 2010 (www.medsafe.govt.nz). WHO Pharmaceuticals Newsletter No. 1, 2011.
Australia	August 2011	The Therapeutic Goods Administration (TGA) reported that the TGA continues to receive reports of thrombocytopenia in people taking quinine to treat muscle cramps. The TGA reminded healthcare professionals that quinine is not approved for the treatment of nocturnal cramps because of its low efficacy and the risk of thrombocytopenia. **References:** Medicines Safety Update Vol 2, No 4, August 2011 (www.tga.gov.au). WHO Pharmaceuticals Newsletter No. 5, 2011.

PRODUCT NAME: rabeprazole

C.A.S. NUMBER: 117976-90-6

OTHER NAMES: Pariet

Country	Effective Date	Description of action taken
United Arab Emirates		Pariet 10 mg tablets were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: radium-223 dichloride (Xofigo)

C.A.S. NUMBER: 444811-40-9

OTHER NAMES: Xofigo

Country	Effective Date	Description of action taken
Brazil	December 2017	Health professionals were informed of preliminary data from a study that identified an increase in the incidence of deaths and fractures in patients with metastatic castration-resistant prostate cancer (CPRCm), without previous use of chemotherapy, receiving radio chloride (223 Ra) in combination with abiraterone acetate and prednisone/prednisolone. Patients with this type of cancer

		should not be treated with radio chloride (223 Ra) in combination with abiraterone acetate and prednisone/prednisolone. Continuous monitoring of fractures should be considered in patients who have been previously treated with this combination. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).
Europe	28 September 2018	EMA recommended restricting the use of Xofigo (radium-223 dichloride) to patients who have had two previous treatments for metastatic prostate cancer (prostate cancer that has spread to the bone) or who cannot receive other treatments. Xofigo must also not be used with Zytiga (abiraterone acetate) and the corticosteroid prednisone or prednisolone. Xofigo should not be used with other systemic cancer therapies, except for treatments to maintain reduced levels of male hormones). The medicine should also not be used in patients who have no symptoms, in line with the current indication; in addition, the use of Xofigo is not recommended in patients with a low number of bone metastases. **References:** European Commissin final decision, 28 September 2018. WHO Pharmaceuticals Newsletter No. 2, 2018.

PRODUCT NAME: ranitidine

C.A.S. NUMBER: 66357-59-3

OTHER NAMES: Ranid, Antagonin

Country	Effective Date	Description of action taken
United Arab Emirates		Ranid 300 mg and Antagonin 300 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: raubasine

C.A.S. NUMBER: 483-04-5

OTHER NAMES:

Country	Effective Date	Description of action taken
Viet Nam	27 November 2012	The marketing authorisation for this product is suspended due to limited safety and efficacy data. **References:** Drug Administration of Viet Nam Official documents No. 18428/QLD-DK, 27 November 2012.

PRODUCT NAME: reboxetina

C.A.S. NUMBER: 71620-89-8

OTHER NAMES: Prolift

Country	Effective Date	Description of action taken
Brazil	November 2010 May 2013	In 2010, ANVISA issued an alert about reassessing the benefit-risk profile of the drug reboxetin, based on the findings of the article published in the British Medical Journal, which indicated possible ineffectivity of the drug. It is recommended that health professionals be aware of the effectiveness of reboxetin treatment and suspected adverse reactions, which should be reported through the ANVISA Electronic Notification System. In 2013, ANVISA issued a new alert, following a statement regarding Prolift by Swissmedic in February 2013. New restrictions were introduced for Prolift: the product is approved only for patients with severe depression and a minimum age of 18 years; the prescription should be carried out by physicians experienced in the treatment of depression. The product label was updated with the alerts and precautions related to limited experience in elderly patients older than 65 years. Health professionals were informed. **References:** ANVISA Pharmacovigilance Alert, and Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: retigabine

C.A.S. NUMBER: 150812-12-7

OTHER NAMES: Trobalt

Country	Effective Date	Description of action taken
United Arab Emirates		Trobalt 50 mg to 300 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: rifabutin

C.A.S. NUMBER: 72559-06-9

OTHER NAMES: Mycobutin

Country	Effective Date	Description of action taken

United Arab Emirates		Mycobutin 150 mg capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: rifampicin

C.A.S. NUMBER: 13292-46-1

OTHER NAMES: Rifacin, Rifadin, Rimactane

Country	Effective Date	Description of action taken
United Arab Emirates		Rifacin 150 and 300 capsules, Rimactane 200 mg/ml syrup, and Rimactane 150 mg and 400 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: riociguat

C.A.S. NUMBER: 625115-55-1

OTHER NAMES: Adempas

Country	Effective Date	Description of action taken
Brazil	September 2016	Health professionals were informed that the drug Adempas is contraindicated for patients with pulmonary hypertension associated with idiopathic interstitial pneumonia (HP-PII), considering preliminary results of a study that revealed the increased risk of mortality and serious adverse events in patients with symptomatic HP-PII treated with Adempas compared to those treated with placebo. The medicine package leaflet has been updated. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: risperidone

C.A.S. NUMBER: 106266-06-2

OTHER NAMES: Risperdal, Risperidon

Country	Effective Date	Description of action taken
Chile	27 November 2015	The product label is updated with new indication restrictions. The approved indications are: - The acute and maintenance treatment of schizophrenia. - As monotherapy for the short-term treatment of acute mania or mixed episodes associated with bipolar disorder

		and as adjuvant therapy to mood stabilizers in the management of acute or mixed manic episodes in bipolar disorder. - Short-term treatment (up to 6 weeks) of the persistent aggression that may occur in patients with moderate to severe Alzheimer's dementia who do not respond to other non-pharmacological measures and when there is a risk of harm to themselves or others ; no effect has been demonstrated on other behavioral alterations in these patients or on the very state of Alzheimer's disease. - In the short-term symptomatic treatment (up to 6 weeks) of persistent aggression in behavioral disorders in children 5 years of age and older and adolescents with below-average intellectual functioning or mental retardation diagnosed according to criteria DSM-IV, in which the severity of the aggression or other disturbing behaviors require pharmacological treatment. In this case, pharmacotherapy should be part of a more comprehensive therapeutic program, with educational and psychosocial measures; At the same time, its prescription is recommended by a specialist in child neurology and psychiatry for children and adolescents or by doctors familiar with the treatment of behavioral disorders in children and adolescents. The decision took into consideration similar actions by Health Canada, EMA, and US FDA. **References:** Instituto de Salud Publica (www.ispch.cl). Health Canada Summary Safety Review, 18 February 2015. EMA Referrals, 07 October 2008 (www.ema.europa.eu). US FDA datasheet (https://www.fda.gov/drugs).
Singapore	16 June 2016	Taking into consideration current availabel scientific evidence suggesting an increased risk of cerebrovascular adverse events (CVAE) associated with risperidone use in mixed or vascular dementia (MD/VD), inputs from local clinicians, safety data submitted by product registrant, local adverse drug reaction reports and the actions taken by other drug regulatory agencies, the HSA, in consultation with its Medicine Advisory Committee, concluded that the benefit-risk profile for use of risperidone in treatment of aggression in dementia remains favorable when it is restricted for the short-term treatment of AD. **References:** Communication from the Health Sciences Authority, June 2016. WHO Pharmaceuticals Newsletter No. 1, 2017.
Brazil	March 2012 March 2015	In 2012, health professionals were informed about the occurrence of decoupling (connection failure) of the risperdal® Consta (long-release suspension for intramuscular injection) observed in needles for application in the gluteus and deltoid, before, during, and after the injection of the medicine. In order to reduce the incidence of the problem,

		the manufacturer updated the "Instructions for use" on the product package leaflet. In 2015, ANVISA recommended that physicians evaluate the risks and benefits regarding the use of risperidone for individual elderly patients, considering the risk factors for stroke and other cardiovascular comorbidities. The recommendation followed an alert issued by Health Canada, which decided to limit the indication of the use of risperidone, in the case of elderly people with dementia, to those with Dementia of the Alzheimer type. The product label was updated in terms of restriction of indication to patients with Alzheimer's dementia. **References:** ANVISA Pharmacovigilance Alert, and Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).
United Arab Emirates		Respidon solution were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: rituximab

C.A.S. NUMBER: 174722-31-8

OTHER NAMES: Mabthera, Rituxan, MabThera

Country	Effective Date	Description of action taken
Switzerland	8 August 2011	There has been a risk of severe infusion reactions related to rituximab. **References:** Communication from Swissmedic, July 2012.
Brazil	May 2011 February 2013 July 2013	In May 2011, ANVISA warned HCPs to be aware of signs of hypersensitivity or anaphylaxis in patients during or after rituximab administration. It suggested that premedication containing analgesic-antipyretic, antihistamine and glucocorticoid should be performed to reduce the frequency and severity of infusion reactions; and patients with pre-existing heart disease and history of cardiopulmonary adverse reactions should be carefully monitored. The product package leaflet has been updated accordingly. In Feb 2013, the product label of MabThera® was updated for patients with autoimmune diseases regarding severe skin reactions such as Toxic Epidermal Necrolysis and Stevens-Johnson Syndrome (TEN/SJS) with fatal outcome. In oncological or autoimmune indications, in the event of severe skin reactions, MabThera® should be discontinued.

		In July 2013, ANVISA recommended that HCPs should screen patients for hepatitis B before the start of treatment with Mabthera, due to the risk of hepatitis B reactivation. Therefore, patients with active hepatitis B should not be treated with MabThera and patients with positive serology should consult an expert in liver diseases prior to initiation of treatment and should be monitored and treated according to the local treatment standards to avoid hepatitis B reactivation. The product label has been updated accordingly. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: rivastigmine

C.A.S. NUMBER: 129101-54-8

OTHER NAMES: Exelon

Country	Effective Date	Description of action taken
United Arab Emirates		Exelon 1.5 mg to 6 mg capsules were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: rofecoxib

C.A.S. NUMBER: 162011-90-7

OTHER NAMES: Vioxx, Ceoxx, Ceeoxx

Country	Effective Date	Description of action taken
Bhutan	22 July 2015	All forms of rofecoxib are banned because trial study showed that Rofecoxib may cause an increased risk in cardiovascular events such as heart attack and strokes especially when used for long duration. Therefore, DRA believes that the risks of using Rofecoxib outweigh the benefits and recommend that consumers no longer use such products. Pharmacies have been notified of the restrictions in their importation and sales. **References:** Bhutan Drug Regulatory Authority, List of Banned Drugs (www.dra.gov.bt).

PRODUCT NAME: roflumilast

C.A.S. NUMBER: 162401-32-3

OTHER NAMES: Daxas, Daliresp

Country	Effective Date	Description of action taken
Brazil	January 2013	ANVISA emphasised to health professionals on the need for attention on suicidal ideation and behavior, especially in patients with psychiatric diseases. The information was updated on the package leaflet under sections 'Precautions and Warnings' and 'Adverse Reactions'. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: rolitetracycline

C.A.S. NUMBER: 751-97-3

OTHER NAMES: Reverin

Country	Effective Date	Description of action taken
United Arab Emirates		Reverin 150 mg, 275 mg and 350 mg solutions for injection were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ropinirole

C.A.S. NUMBER: 91374-21-9

OTHER NAMES: Requip, Repreve, Ronirol

Country	Effective Date	Description of action taken
United Arab Emirates		Requip 0.25 mg to 5 mg tablets were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: rosiglitazone

C.A.S. NUMBER: 122320-73-4

OTHER NAMES: Avandia, Avandaryl, Avandamet

Country	Effective Date	Description of action taken
Armenia	2010	Marketing authorisations of rosiglitazone containing medicinal products were withdrawn, after an assessment by Scientific Centre of Drug and Medical Technology Expertise

		after Academician E. Gabrielyan (SCDMTE) under the under the Ministry of Health determined the increased cardiovascular risk outweighs its benefits. **References:** Communication from Armenian National Pharmacovigilance Centre, 2010. EMA press release, September 2010.
Europe	2010	The EMA recommended the suspension of the marketing authorizations for the rosiglitazone-containing anti-diabetes medicines. The EMA states that overall, the accumulated data support an increased cardiovascular risk of rosiglitazone. **References:** WHO Pharmaceuticals Newsletter No. 5, 2010.
Oman	2010	The marketing authorisation of rosiglitazone-containing medicines is suspended following similar regulatory actions by EMA and US FDA. **References:** Oman Ministry of Health Circular No. 115, 2010.
USA	2010	The US FDA announced that it will significantly restrict the use of rosiglitazone. These new restrictions are in response to data that suggest an elevated risk of cardiovascular events, such as heart attack and stroke, in patients treated with rosiglitazone. **References:** WHO Pharmaceuticals Newsletter No. 5, 2010.
Brazil	September 2010	ANVISA issued an alert regarding the suspension of the marketing authorisation of rosiglitazone-containing drugs due to unfavorable benefit/risk ratio, following findings of meta-analysis studies and systematic reviews which indicated a high probability of occurrence of ischemic diseases, such as myocardial infarction, heart failure, cardiac arrest and other cardiac disorders. Additionally, recommendations to prescribers and patients are made. **References:** ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia). Official Gazette, cancellation of registration, 29 September 2010 (Resolution-RE No. 4466).
Guatemala	September 2010	Withdrawal from the market and cancellation of registration due to elevated risk of cardiovascular events. **References:** Departamento de Regulación y Control de Productos Farmacéuticos y Afines (www.siamed.mspas.gob.gt) Guatemala, September 2010.

Egypt	25 September 2010	Withdrawal of registered products containing this active ingredient due to its cardiovascular risk. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.
Indonesia	26 September 2010	The Indonesian National Agency of Drug and Food Control (NADFC) suspended rosiglitazone-containing (single and combination) antidiabetic agents due to cardiovascular risks. **References:** Head of NADFC Press Release HM.04.01.1.23.09.10.9076
Madagascar	8 October 2010	The drug has been withdrawn because the risks outweigh the benefits. **References:** Communication from the Madagascar National Pharmacovigilance Centre July, 2012.
India	12 November 2010	Rosiglitazone and its formulations for human use are prohibited in India. **References:** The Gazette of India, No. 628, New Delhi 12 November 2010.
Canada	18 November 2010	The rosiglitazone-containing products are now indicated only in patients with type 2 diabetes mellitus for whom all other oral antidiabetic agents, in monotherapy or in combination, do not result in adequate glycemic control or are inappropriate due to contraindications or intolerance. **References:** Advisories, Warnings and Recalls, Health Canada, 18 November 2010 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 6, 2010.
New Zealand	March 2011	Medsafe (New Zealand Medicines and Medical Devices Safety Authority) announced that the consent to distribute rosiglitazone containing medicines will be suspended in New Zealand from 29 April 2011. Data from meta-analyses and observational studies have demonstrated an increased risk of myocardial infarction with rosiglitazone use. **References:** Prescriber Update Vol. 32, No.1 March 2011, (www.medsafe.govt.nz). WHO Pharmaceuticals Newsletter No. 2, 2011.
Viet Nam	22 March 2011	The marketing authorisation of rosiglitazone-containing medicines is suspended due to increase the risk of heart attack. **References:** Drug Administration of Viet Nam Official documents No. 3886/QLD-DK, 22 March 2011.

USA	18 May 2011	The US FDA notified health-care professionals and the public of new restrictions to the prescribing and use of rosiglitazone-containing medicines. Health-care providers and patients must enroll in a special program in order to prescribe and receive these drugs. **References:** FDA Drug Safety Communication, US FDA, 18 May 2011 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 3, 2011.
Singapore	24 May 2011	Labelling updates: - Restriction of indication to third-line use in mono-, dual- or triple oral hypoglycemic therapy. - Contraindication of use in patients with ischaemic heart disease. - Contraindication of use in patients with acute coronary syndrome and all classes of heart failure. - Not for use in patients with peripheral arterial disease. Restricted access programme: The prescription of rosiglitazone is restricted to selected patients who have been assessed by their doctors to be suitable for treatment with rosiglitazone. These patients should also be clearly informed of the benefits and risks associated with their medication. The Health Sciences Authority (HSA) assessed that a possible increased risk of myocardial ischaemic events associated with rosiglitazone cannot be excluded. However, for a group of patients who cannot effectively control their blood sugar using alternative medications, the benefits of rosiglitazone may exceed these risks. Additional contraindications and restrictions on the use of rosiglitazone are implemented to significantly limit its use to the group of patients mentioned above, in order to minimise any possible cardiovascular risks associated with the use of this drug. **References:** Communication from the Health Sciences Authority, May 2011.
Azerbaijan	November 2011	Rosiglitazone containing medicines have been suspended due to risk of acute myocardial infarction, stroke and heart failure. **References:** Ministry of Health Pharmacology and Pharmacopeia Advisory Council, November 2011.
USA	4 November 2011	The US FDA announced that healthcare providers must enroll in the Avandia-Rosiglitazone Medicines Access Program if they wish to prescribe rosiglitazone medicines to outpatients or patients in long-term care facilities after 18 November 2011.

		References: FDA Drug Safety Communication, US FDA, 4 November 2011 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 6, 2011. WHO Pharmaceuticals Newsletter No. 1, 2014. WHO Pharmaceuticals Newsletter No. 1, 2016.
United Arab Emirates		Avandia 2 mg, 4 mg and 8 mg tablets were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: salbutamol

C.A.S. NUMBER: 18559-94-9

OTHER NAMES: Ventolin, Proventil, ProAir, albuterol, Ventamol

Country	Effective Date	Description of action taken
United Arab Emirates		Ventamol 4 mg tablets, Ventolin 2 mg and 4 mg tablets were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.
United Arab Emirates		Salbuvent 0.5 mg/ml product for injection and 100 mcg/dose inhaler were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: saxagliptin

C.A.S. NUMBER: 361442-04-8

OTHER NAMES: Onglyza

Country	Effective Date	Description of action taken
Brazil	January 2012 June 2016	In 2012, the package leaflet of Onglyz was update and the information communicated to health professionals, about the risk of acute pancreatitis, identified during the analysis of post-marketing reports. Patients should be informed about the need to read the package leaflet, the characteristic symptoms of acute pancreatitis, and immediate discontinuation of the drug is recommended if such was suspected. In 2016, the product label was updated with information on increased risk of of hospitalization for heart failure in

		patients treated with saxagliptin compared to placebo, as reported by a clinical study. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: sibutramine

C.A.S. NUMBER: 106650-56-0

OTHER NAMES: Reductil, Sibutril, Meridia, Medaria Sibutrex, Maxislim, Redufast, Slimact, Redusco, Decaslim, Reduxade, Ectiva, Slenfig

Country	Effective Date	Description of action taken
Oman	2010	The markting authorisation of sibutramine-containing products is suspended due to risk of non fatal heart attack and stroke. The decision took into consideration EMA recommendations. **References:** Oman Ministry of Health Circular No. 23, 2010.
Montenegro	22 January 2010	Due to EMA recommendation to suspend marketing authorisation for medicines containing sibutramin across the EU, and in accordance with Law on medicines, the Agency for Medicines and Medical Devices of Montenegro (CALIMS) proposed to the competent authority – Health Inspection to withdraw Reductil from the market. CALIMS also informed health care professionals of the increased risk of serious, non-fatal cardiovascular events related to the product. **References:** CALIMS portal (www.calims.me), 25 Janurary 2010
Canada	October 2010	Health Canada has informed the public of voluntary withdrawal of sibutramine by Abbott Laboratories and Apotex Inc. The decision was made based on data from the SCOUT trial. **References:** Advisories, Warnings and Recalls, Health Canada, 18 October, 13 October and 8 October 2010 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 6, 2010.
Australia	8 October 2010	Therapeutic Goods Administration (TGA) has announced that Abbott Australasia will cease supply of sibutramine in Australia from 9 October 2010. This follows an analysis of the results of the Sibutramine Cardiovascular OUTcomes (SCOUT) study, which showed a higher rate of cardiovascular events in obese and overweight patients using sibutramine than in patients managing their weight through exercise and diet alone. **References:** Safety information, Alerts/advisories, TGA, 8 October 2010 (www.tga.gov.au).

USA	8 October 2010	The US FDA and Abbott Laboratories notified health-care professionals and patients about the voluntary withdrawal of sibutramine from the United States market because of clinical trial data indicating an increased risk of heart attack and stroke. **References:** FDA Drug Safety Communication, US FDA, 8 October 2010 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 6, 2010.
Egypt	9 October 2010	Withdrawal of registered products containing this active ingredient due to the increased risk of heart attack and stroke. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.
Chile	10 October 2010	The product is withdrawn from the market following similar decisions by Spanish Agency of Medicines and Medical Devices (AGEMED), USFDA and EMA, because its cadiovascular risks outweigh its benefits. The decision is based on USFDA and EMA information. **References:** Instituto de Salud Publica (www.ispch.cl).
Singapore	13 October 2010	Abbott Laboratories (S) Pte Ltd is informing healthcare professionals of the suspension of sales of Reductil®, Ectiva® and Reduxade® from the Singapore market at the request of Health Sciences Authority (HSA). HSA's decision to suspend sibutramine took into consideration the results of the SCOUT (Sibutramine Cardiovascular Outcomes) study. Patients treated with sibutramine experienced a 16% increased risk of a primary outcome event of non-fatal myocardial infarction, non-fatal stroke, resuscitated cardiac arrest, or cardiovascular death compared with placebo-treated patients. This result was attributed to an increased risk of non-fatal myocardial infarction and stroke. HSA concluded that the benefit-risk profile of dronedarone remains favourable in a limited group of patients with non-permanent AF and the availability of dronedarone as a treatment option for AF is clinically important. The drug would continue to be available on the market with revision of the product label to restrict its clinical use to patients with history of non-permanent AF in sinus rhythm for the maintenance of sinus rhythm after alternative treatment options have been considered and to strengthen the information on contraindications and warnings. **References:** Dear Healthcare Professional Letter (DHCPL), 13 October 2010. (http://www.hsa.gov.sg/).

Indonesia	14 October 2010	All products contaning sibutramine have been withdrawn due to increase of risk of cardivascular events in patients with history of cardiovascular disease. **References:** Head of NADFC Press Release PN.01.04.1.31.10.10.9829
New Zealand	1 December 2010	The consent to distribute sibutramine containing medicines was revoked in New Zealand on 14 October 2010, following a review on preliminary results of the Sibutramine Cardiovascular Outcome Trial (SCOUT). The SCOUT study suggests that subjects treated with sibutramine had an increased risk of non-fatal myocardial infarction and non-fatal stroke compared to those given placebo. Medsafe has advised patients to stop taking sibutramine and to talk to a health-care professional about alternative weight loss measures and maintenance programs. **References:** Prescriber Update Vol. 31, No.4 December 2010, (www.medsafe.govt.nz). WHO Pharmaceuticals Newsletter No. 1, 2011.
India	10 February 2011	Sibutramine and R-Sibutramine and its formulations for human use are prohibited in India. **References:** The Gazette of India, No. 71, New Delhi 10 February 2011.
Viet Nam	14 April 2011	The marketing authorisation for sibutramine-containing medicines is suspended due to risk of cardiovascular disorders. The products are recalled. **References:** Drug Administration of Viet Nam Official documents No. 5149/QLD-CL, 14 Apirl 2011.
Guatemala	July 2011	Withdrawal from the market and cancellation of registration due to elevated risk of cardiotoxicity. **References:** Departamento de Regulación y Control de Productos Farmacéuticos y Afines (www.siamed.mspas.gob.gt) Guatemala, July 2011.
Azerbaijan	November 2011	Sibutramine containing medicines have been suspended due to an increased risk of serious cardiovascular events in patients with a history of cardiovascular disease. **References:** Ministry of Health Pharmacology and Pharmacopeia Advisory Council, November 2011.
Chile	15 May 2013	The market authorisation of the product is withdrawn, following similar decision by other regulators such as AGEMED, USFDA and EMA. **References:** Instituto de Salud Publica (www.ispch.cl)

Europe	6 August 2020	The European Medicines Agency (EMA)'s review of the safety and effectiveness of sibutramine, through its Committee for Medicinal Products for Human Use (CHMP), has concluded that the benefits of sibutramine do not outweigh its risks, and that all marketing authorisations for medicines containing sibutramine should be suspended throughout Europe. **References:** European Commission final decision (www.ema.europa.eu)
United Arab Emirates		Reductil 10 mg and 15 mg capsules were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: sildenafil

C.A.S. NUMBER: 139755-83-2

OTHER NAMES: Viagra, Revatio

Country	Effective Date	Description of action taken
Switzerland	December 2011	There has been an increased risk of mortality in paediatric patients with pulmonary arterial hypertension (PAH). **References:** Communication from Swissmedic, July 2012.

PRODUCT NAME: simeprevir

C.A.S. NUMBER: 923604-59-5

OTHER NAMES: Olysio, Sovriad, Galexos

Country	Effective Date	Description of action taken
United Arab Emirates		Olysio 150 mg capsules were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: simvastatin

C.A.S. NUMBER: 79902-63-10

OTHER NAMES: Zocor

Country	Effective Date	Description of action taken

USA	8 June 2011	The US FDA is requiring changes to the simvastatin label to add new contraindications (should not be used with certain medications) and dose limitations for using simvastatin with certain medicines. Simvastatin 80 mg should be used only in patients who have been taking this dose for 12 months or more without evidence of muscle injury (myopathy). **References:** FDA Drug Safety Communication, US FDA 8 June 2011 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 4, 2011. WHO Pharmaceuticals Newsletter No. 1, 2012.
Egypt	21 July 2011	- Patients taking amiodarone, verapamil, or diltiazem : The dose of simvastatin should not exceed 10 mg/day. - Patients taking amlodipine or ranolazine: The dose of simvastatin should not exceed 20 mg/day. - Simvastatin therapy should be discontinued immediately if myopathy is diagnosed or suspected. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.
Brazil	August 2011	ANVISA warned of the risk of dose-dependent myopathy associated with the use of simvastin, based on study outcome that pointed to an increased risk of myopathy for patients taking simvastatin 80 mg per day. The package leaflet of the drug has been updated to include new contraindications and dose limitations for the use of simvastatin with certain medications. **References:** ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: sirolimus

C.A.S. NUMBER: 53123-88-9

OTHER NAMES: Rapamune, Rapamycin

Country	Effective Date	Description of action taken
United Arab Emirates		Rapamune 2 mg tablets and 1 mg/ml solution were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: sitaxentan

C.A.S. NUMBER: 184036-34-8

OTHER NAMES: Thelin

Country	Effective Date	Description of action taken
Europe	December 2010	The EMA has been informed of Pfizer's decision to voluntarily withdraw sitaxentan from worldwide markets and to discontinue all ongoing clinical trials, in response to new information on fatal liver injury. **References:** Press releases, EMA, 16 and 10 December 2010 (www.ema.europa.eu). WHO Pharmaceuticals Newsletter No. 1, 2011.
Australia	10 December 2010	he Therapeutic Goods Administration (TGA) notified the public that the supply of sitaxentan will be suspended in Australia, following Pfizer's announcement that it will withdraw sitaxentan from the market globally. The TGA states that this action has been taken in response to a review of safety data in clinical trials being undertaken overseas that showed patients were at risk of acute liver failure that in some cases was not reversible. **References:** Safety information, Alerts/advisories, TGA,10 December 2010 (www.tga.gov.au). WHO Pharmaceuticals Newsletter No. 1, 2011.
Canada	20 December 2010	Pfizer Canada and Health Canada informed healthcare professionals and the public that sitaxentan sodium tablets will be withdrawn from the Canadian market due to concerns about hepatotoxicity. **References:** Advisories, Warnings and Recalls, Health Canada, 20 December 2010 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 1, 2011.
United Kingdom	January 2011	On 10 December 2010, the license holder for sitaxentan announced its decision to withdraw the product from all markets worldwide and to discontinue all ongoing clinical trials. This decision was made after a review of fatal cases associated with hepatic injury, including a reported case from the UK (in 2009) and two cases from clinical trials in India and the Ukraine, which occurred in 2010. **References:** Drug Safety Update, January 2011, Volume 4, Issue 6, (www.mhra.gov.uk).
Europe	22 March 2011	The European Medicines Agency (EMA) announced the withdrawal of the marketing authorization of sitaxentan in the interest of patient safety in response to new information on two cases of fatal liver injury. **References:** Press releases, EMA, 22 March 2011 (www.ema.europa.eu). WHO Pharmaceuticals Newsletter No. 2, 2011.

PRODUCT NAME: sodium bicarbonate

C.A.S. NUMBER: 144-55-8

OTHER NAMES:

Country	Effective Date	Description of action taken
Viet Nam	13 September 2012	New resistration and registration renewal for sodium bicarbonate-containing medicines are suspended due to unfavorable risk-benefit profile. **References:** Drug Administration of Viet Nam Official documents No. 13702/QLD-DK, 13 September 2012.

PRODUCT NAME: sodium chloride

C.A.S. NUMBER: 7440-23-5

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		Sodium chloride 0.45% and 0.9% w/v BP 1988, 3% and 10% w/v BP 2003 infusion, and sodium chloride irrigation solution USP XXVII were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. Sodium chloride 0.9% (Vifor) infusion were withdrawn by the MAH before the product getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: sodium clodronate

C.A.S. NUMBER: 22560-50-5

OTHER NAMES: Bonefos

Country	Effective Date	Description of action taken
United Arab Emirates		Bonefos infusion and 400 mg capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: sodium cromoglycate

C.A.S. NUMBER: 16110-51-3

OTHER NAMES: Apicrom

Country	Effective Date	Description of action taken
United Arab Emirates		Apicrom 4% drops were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety.

		References: Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: sodium fluoride

C.A.S. NUMBER: 7681-49-4

OTHER NAMES: Zymafluor

Country	Effective Date	Description of action taken
United Arab Emirates		Zymafluor 0.25 mg and 1 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: sodium lactate

C.A.S. NUMBER: 72-17-3

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		Sodium lactate 1/6 M injection USP XXII were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: sodium picosulfate

C.A.S. NUMBER: 10040-45-6

OTHER NAMES: Skilax

Country	Effective Date	Description of action taken
United Arab Emirates		Skilax drops were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: somatotropin/somatropin

C.A.S. NUMBER: 9002-72-6; 12629-01-5

OTHER NAMES: Boostin-250 Injection, bST, Somagrebove, Somavubove, Sometribove, Somidobove, Saizen

Country	Effective Date	Description of action taken
Pakistan	6 January 2018	The marketing authorisations for Boostin-250 Injection, Boostin S Injection, and Somatech Pre Filled Syringe are suspended by the Registration Board. A country wide recall of the products was ordered. **References:** Minutes for 252nd Registration Board meeting held on 07-08th September, 2015
United Arab Emirates		Saizen 8 mg/ml (2.5 ml cartridge) injection were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: spiramycin

C.A.S. NUMBER: 8025-81-8

OTHER NAMES: Rovamycine

Country	Effective Date	Description of action taken
Madagascar	17 December 2010	The drug has been withdrawn due to increased rate of total impurity in the product life. **References:** Communication from the Madagascar National Pharmacovigilance Centre July, 2012.

PRODUCT NAME: stavudine

C.A.S. NUMBER: 3056-17-6

OTHER NAMES: Zerit

Country	Effective Date	Description of action taken
United Kingdom	April 2011	The MHRA has advised that stavudine should only be used when there are no appropriate alternatives, and for the shortest possible time, because of an increased risk of potentially severe adverse effects in patients receiving stavudine compared with alternative HIV treatments. **References:** Drug Safety Update, April 2011, Volume 4, Issue 9, A2, MHRA (www.mhra.gov.uk). WHO Pharmaceuticals Newsletter No. 3, 2011.
United Arab Emirates		Zerit 15 mg to 40 mg capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: streptomycin

C.A.S. NUMBER: 3810-74-0

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		Streptomycin sulphate 1 g solution for in jection were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: strontium ranelate

C.A.S. NUMBER: 135459-87-9

OTHER NAMES: Protelos, Protos, Bivalos

Country	Effective Date	Description of action taken
Armenia	2014	After an assessment by the Scientific Centre of Drug and Medical Technology Expertise after Academician E. Gabrielyan (SCDMTE), the product information of Bivalos was updated to include information on high risk of heart attack. As a risk minimization mesure a DHPC was circulated among healthcare proffessionals. **References:** Communication from Armenian National Pharmacovigilance Centre, 2014. EMA press release, April 2014.
Europe	16 March 2012	The risk of venous thromboembolism (VTE) is higher in patients with a history of VTE and patients who are temporarily or permanently immobilized. There is also a low risk of serious skin reactions. Patients should stop treatment immediately if symptoms of severe allergic reaction occur and treatment should not be re-started. **References:** Press release, EMA, 16 March 2012 (www.ema.europa.eu). WHO Pharmaceuticals Newsletter No. 2, 2012. WHO Pharmaceuticals Newsletter No. 4, 2013. WHO Pharmaceuticals Newsletter No. 1, 2014.
Viet Nam	22 October 2013	The product information was added the following contraindications: - Current or previous venous thromboembolic events - Temporary or permanent immobilisation - Established, current or past history of ischaemic heart disease, peripheral arterial disease and/or cerebrovascular disease - Uncontrolled hypertension

		The restrictions intended to reduce the risk of venous thromboembolic events and the cardiovascular risk, based on EMA's decision. **References:** Drug Administration of Viet Nam Official Dispatch No. 13705/QLD-DK, 13 September 2012, and Dispatch No. 17559/QLD-DK, 22 October 2013.
Europe	26 April 2014	The European Medicines Agency's (EMA's) Committee for Medicinal Products for Human Use (CHMP) has recommended a restriction in the use of the osteoporosis medicine Protelos / Osseor (strontium ranelate), following an assessment of data showing an increased risk of serious heart problems. The CHMP recommended that Protelos / Osseor should only be used to treat severe osteoporosis in postmenopausal women at high risk of fracture and severe osteoporosis in men at increased risk of fracture. Additional measures, including restrictions in patients with heart or circulatory problems, were also recommended to minimise the heart risks of these medicines. **References:** EMA press release, 26 April 2014. WHO Pharmaceuticals Newsletter No. 2, 2014.
Chile	5 August 2014	The product inforamtion is updated with new indication restriction. The approved indications are: the treatment of severe osteoporosis in men and postmenopausal women with high risk of fracture, without cardiovascular pathology and who can not use another therapeutic alternative. **References:** Instituto de Salud Publica (www.ispch.cl).

PRODUCT NAME: sulfacetamide

C.A.S. NUMBER: 6209-17-2

OTHER NAMES: Spersacet

Country	Effective Date	Description of action taken
United Arab Emirates		Spersacet 20% drops were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: sulfacetamide sodium

C.A.S. NUMBER: 6209-17-2

OTHER NAMES: Isopto Cetamide

Country	Effective Date	Description of action taken

United Arab Emirates		Isopto Cetamide 15% drops were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: sulfaguanidine

C.A.S. NUMBER: 57-67-0

OTHER NAMES:

Country	Effective Date	Description of action taken
Viet Nam	20 September 2016 11 January 2018	In 2016, the registration of the inhalation format and importation of the products/ingredients were suspended due to reports of serious ADRs of respiratory disorders. The benefit-risk profile was not favorable. In 2018, the MAH was requested to provide more data to prove the product's characteristics of safety and efficacy of the oral form, due to limited safety and efficacy data. **References:** Drug Administration of Viet Nam Official documents No. 18276/QLD-DK, 20 September 2016, and No. 456/QLD-DK, 11 January 2018.

PRODUCT NAME: sulindac

C.A.S. NUMBER: 38194-50-2

OTHER NAMES: Clinoril

Country	Effective Date	Description of action taken
United Arab Emirates		Clinoril 200 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: sulpiride

C.A.S. NUMBER: 15676-16-1

OTHER NAMES: Dogmatil

Country	Effective Date	Description of action taken
United Arab Emirates		Dogmatil 100 mg injection and 25 mg/5 ml solution were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: suxamethonium

C.A.S. NUMBER: 306-40-1

OTHER NAMES: Brevidil M

Country	Effective Date	Description of action taken
United Arab Emirates		Brevidil M injection products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: tamoxifen

C.A.S. NUMBER: 10540-29-2

OTHER NAMES: Tamofen, Nolvadex, Genox, Istubal, Valodex

Country	Effective Date	Description of action taken
New Zealand	June 2011	Medsafe announced that recent evidence suggests there is a potential risk for higher rates of disease recurrence and death related to breast cancer in women taking tamoxifen concomitantly with CYP2D6 inhibitors. **References:** Prescriber Update Vol. 32 No. 2, June 2011 (www.medsafe.govt.nz). WHO Pharmaceuticals Newsletter No. 4, 2011.
United Arab Emirates		Tamofen 10 mg and 20 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: tegaserod

C.A.S. NUMBER: 145158-71-0

OTHER NAMES: Zelnorm

Country	Effective Date	Description of action taken
India	16 March 2011	Tegaserod and its formulations for human use are banned in India. **References:** The Gazette of India, No. 139, New Delhi 16 March 2011.

PRODUCT NAME: teicoplanin

C.A.S. NUMBER: 61036-62-2

OTHER NAMES: Targocid, Teico

Country	Effective Date	Description of action taken
United Arab Emirates		The application for Teico 200 and 400 injection products was rejected by the committee for various reasons. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: telaprevir

C.A.S. NUMBER: 402957-28-2

OTHER NAMES: Incivo, Incivek

Country	Effective Date	Description of action taken
Brazil	January 2013	Healthcare professionals were informed about safety update in the package leaflet under "Warnings and Precautions", in sub-section "Severe Rash", due to two reported cases in Japan of severe adverse skin reactions, such as toxic epidermal necrolysis, including a fatal case. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: telbivudine

C.A.S. NUMBER: 3424-98-4

OTHER NAMES: Sebivo, Tyzeka

Country	Effective Date	Description of action taken
United Arab Emirates		Sebivo solution and tablets were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: temozolomide

C.A.S. NUMBER: 85622-93-1

OTHER NAMES: Temodar, Temodal, Temcad

Country	Effective Date	Description of action taken
United Arab Emirates		Temodal 140 mg and 180 mg capsules were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety.

		References: Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: tenoxicam

C.A.S. NUMBER: 59804-37-4

OTHER NAMES: Tilcotil

Country	Effective Date	Description of action taken
United Arab Emirates		Tilcotil 20 mg tablet, injection, and suppository were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: terbutaline

C.A.S. NUMBER: 23031-25-7

OTHER NAMES: Bricanyl, Brethine, Brethaire, Terbulin

Country	Effective Date	Description of action taken
USA	17 February 2011	The U.S. Food and Drug Administration (US FDA) has notified the public that injectable terbutaline should not be used in pregnant women for prevention or prolonged treatment (beyond 48 to 72 hours) of preterm labor in either the hospital or outpatient setting because of the potential for serious maternal heart problems and death. The labelling of terbutaline injection will be revised to add a Boxed Warning and Contraindication to warn against this use. In addition, oral terbutaline should not be used for prevention or any treatment of preterm labor because it has not been shown to be effective and has similar safety concerns. The labeling of terbutaline tablet will be revised to add a Boxed Warning and Contraindication to warn against this use. **References:** FDA Drug Safety Communication, US FDA, 17 February 2011 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 2, 2011.
Saudi Arabia	23 May 2012	The SFDA advised health-care professionals that terbutaline MUST NOT be used in pregnant women for the management of preterm labor due to serious maternal heart adverse events and deaths. **References:** Communication from National Pharmacovigilance and Drug Safety Centre, SFDA, 23 May 2012. WHO Pharmaceuticals Newsletter No. 3, 2012.
United Arab Emirates		Bricanyl 0.3 mg/ml syrup were withdrawn by the MAH before getting approval.

		References: Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: terfenadine

C.A.S. NUMBER: 50679-08-8

OTHER NAMES:

Country	Effective Date	Description of action taken
Bhutan	22 July 2015	All forms of terfenadine-containing medicines are banned because the use of terfenadine products with certain other drugs or foods and in certain medical conditions is associated with the potential to result in rare and serious cardiac side effects primarily involving changes in heart rhythm. Pharmacies have been notified of the restrictions in their importation and sales. **References:** Bhutan Drug Regulatory Authority, List of Banned Drugs (www.dra.gov.bt).

PRODUCT NAME: terlipressin

C.A.S. NUMBER: 14636-12-5

OTHER NAMES: Glypressin

Country	Effective Date	Description of action taken
United Arab Emirates		Glypressin 1 mg injection products were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: testosterone

C.A.S. NUMBER: 58-22-0

OTHER NAMES:

Country	Effective Date	Description of action taken
Viet Nam	19 May 2017	The product information of testosterone was changed to clarify the approved uses: Hypogonadotropic hypogonadism (congenital or acquired)- gonadotropin or LHRH deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation. Safety and efficacy of testosterone in men with "age-related hypogonadism" had not been established. These cautions intend to clarify the approved uses of these medications.

		References: Drug Administration of Viet Nam Official Dispatch No. 6922/QLD-DK, 19 May, 2017.
United Arab Emirates		Primotestone Depot 100 mg and 250 mg solution for injection were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: tetracycline

C.A.S. NUMBER: 60-54-8

OTHER NAMES: Balkacycline, Hostacycline, Sumycin

Country	Effective Date	Description of action taken
United Arab Emirates		Balkacycline 250 mg and Hostacycline P 250 mg capsules, and Hostacycline 250 mg and 500 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: tetrazepam

C.A.S. NUMBER: 10379-14-3

OTHER NAMES: Myolastan

Country	Effective Date	Description of action taken
Montenegro	10 May 2013	Based on EMA referral and in accordance with Law on medicines, the Agency for Medicines and Medical Devices of Montenegro (CALIMS) has sent DHPC to relevant HCPs to inform them of the perceived increased risk of serious skin reactions related to tetrazepam. **References:** CALIMS, Direct healthcare professional communications.
Europe	29 May 2013	The Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) has endorsed the PRAC recommendation to suspend the marketing authorisations of tetrazepam-containing medicines across the European Union (EU). **References:** European Commission final decision (www.ema.europa.eu) WHO Pharmaceuticals Newsletter No. 2, 2013. WHO Pharmaceuticals Newsletter No. 3, 2013.
Viet Nam	20 March 2015	The marketing authorisation for tetrazepam-containing medicines is suspended due to increased risk of serious skin

		reactions (including SJS/TEN, DRESS syndrome). The products are recalled. **References:** Drug Administration of Viet Nam Official documents No. 5078/QLD-DK, 20 March 2015.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: thalidomide

C.A.S. NUMBER: 50-35-1

OTHER NAMES: Thalomid

Country	Effective Date	Description of action taken
United Kingdom	June 2011	The Medicines and Healthcare products Regulatory Agency (MHRA) reported that patients treated with thalidomide have an increased risk of arterial thromboembolism, including myocardial infarction and cerebrovascular events, in addition to the established risk of venous thromboembolism. The MHRA advised that healthcare professionals should consider venous and arterial thrombotic risk and administer antithrombotic prophylaxis for at least the first five months in patients commencing thalidomide. **References:** Drug Safety Update, February 2011, Volume 4, Issue 7, A3, MHRA (www.mhra.gov.uk). WHO Pharmaceuticals Newsletter No. 4, 2011. WHO Pharmaceuticals Newsletter No. 1, 2016.

PRODUCT NAME: theophylline

C.A.S. NUMBER: 58-55-9

OTHER NAMES: Quibron, Uniphyllin, Theolair, Slo-Bid

Country	Effective Date	Description of action taken
United Arab Emirates		Quibron T/Sr 300 mg, Uniphyllin Continus 200 mg, 300 mg, and 400 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: thiopental sodium

C.A.S. NUMBER: 76-75-5

OTHER NAMES: thiopentone, Trapanal, Intraval

Country	Effective Date	Description of action taken
United Arab Emirates		Intraval 0.5 g injection products were withdrawn by the MAH before getting approval.

		References: Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: thioridazine

C.A.S. NUMBER: 50-52-2

OTHER NAMES: Sonapax

Country	Effective Date	Description of action taken
Azerbaijan	24 November 2016	Thioridazine containing medicines have been suspended due to QTc prolongation and cardiac arrhythmias. **References:** Ministry of Health Pharmacology and Pharmacopeia Advisory Council, November 2016.

PRODUCT NAME: tianeptine

C.A.S. NUMBER: 66981-73-5

OTHER NAMES: Stablon

Country	Effective Date	Description of action taken
Brazil	March 2011	Due to the emergence of new cases of drug misuse in certain countries, a Letter to healthcare professionals was issued warning them about the potential abuse of tianeptine, especially in patients with a history of drug or alcohol dependence, for whom increased dosage should be avoided. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: tiapride

C.A.S. NUMBER: 51012-32-9

OTHER NAMES: Tiapridal

Country	Effective Date	Description of action taken
United Arab Emirates		Tiapridal 100 mg tablets and 100 mg/2 ml solution for injection were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: tigecycline

C.A.S. NUMBER: 220620-09-7

OTHER NAMES: Tygacil

Country	Effective Date	Description of action taken
United Kingdom	April 2011	The Medicines and Healthcare products Regulatory Agency (MHRA) has advised that tigecycline should only be used when other antibiotics are unsuitable, because an analysis of pooled results from clinical trials of tigecycline versus comparator drugs in a range of infections has shown numerically higher mortality rates in patients receiving tigecycline. **References:** Drug Safety Update, April 2011, Volume 4, Issue 9, A1, MHRA (www.mhra.gov.uk). WHO Pharmaceuticals Newsletter No. 3, 2011.

PRODUCT NAME: timolol maleate

C.A.S. NUMBER: 26839-75-8

OTHER NAMES: Nyolol, Betimol, Istalol

Country	Effective Date	Description of action taken
United Arab Emirates		Nyolol 0.5% drops were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: tinzaparin

C.A.S. NUMBER: 9041-08-01

OTHER NAMES: Innohep

Country	Effective Date	Description of action taken
Canada	19 October 2010	Health-care professionals have been advised that tinzaparin sodium is not recommended in elderly patients over 70 years of age with renal impairment. The company explains in the Dear Health Care Professional letter that a clinical study (Innohep in Renal Insufficiency Study (IRIS)) was stopped prematurely due to an interim finding of an increase in all-cause mortality in patients who received tinzaparin sodium compared to unfractionated heparin. **References:** Advisories, Warnings and Recalls, Health Canada, 19 October 2010 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 6, 2010.

PRODUCT NAME: tioconazole

C.A.S. NUMBER: 65899-73-2

OTHER NAMES: Trosyd, Gyno-Trosyd

Country	Effective Date	Description of action taken
United Arab Emirates		Trosyd 1% cream, and Gyno-Trosyd 100 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: tobramycin

C.A.S. NUMBER: 32986-56-4

OTHER NAMES: Tobrex, Tobi

Country	Effective Date	Description of action taken
United Arab Emirates		Tobrex 2X (3 mg/ml) drops were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: tolbutamide

C.A.S. NUMBER: 64-77-7

OTHER NAMES: Rastinon, Orinase

Country	Effective Date	Description of action taken
United Arab Emirates		Rastinon 0.5 g and 1 g tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: tolmetin

C.A.S. NUMBER: 26171-23-3

OTHER NAMES: Tolectin

Country	Effective Date	Description of action taken
United Arab Emirates		Tolectin 200 mg and 400 mg capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: tolperisone

C.A.S. NUMBER: 3644-61-9; 728-88-1

OTHER NAMES: Mydocalm

Country	Effective Date	Description of action taken
Europe	22 June 2012	The EMA's Committee for Medicinal Products for Human Use (CHMP) concluded that the benefits of tolperisone-containing medicines given orally continue to outweigh their risks, but that their use should be restricted to the treatment of adults with post-stroke spasticity (stiffness). The Committee also recommended that the marketing authorisations for tolperisone-containing medicines given by injection should be revoked throughout the European Union. **References:** EMA Referrals, 22 June 2012 (www.ema.europa.eu). WHO Pharmaceuticals Newsletter No. 4, 2012.
Azerbaijan	23 May 2018	Tolperisone hydrochloride containing injection form medicines have been suspended because the benefits of this formulation do not outweigh the identified risks. **References:** Ministry of Health Pharmacology and Pharmacopeia Advisory Council, May 2018 & Ministry of Health Analytical Expertise Center, April 2018.
Viet Nam	12 June 2013 15 July 2013	In June 2013, the use of oral toperisone was restricted to the treatment of adults with post-stroke spasticity (stiffness). The benefits of oral tolperisone outweighed its risks only when used in the treatment of post-stroke spasticity in adults, based on EMA's decision. In July 2013, the marketing authorisation of injectable tolperisone-containing medicines was suspended due to hypersensitivity (allergic) reactions. In addition, extremely limited data were available to support the safety and dosing recommendations of injectable tolperisone, the benefits of this formulation did not outweigh the identified risks. The products were recalled. **References:** Drug Administration of Viet Nam Official documents No. 10126/QLD-CL, 12 June 2013, and Official Dispatch No. 11147/QLD-DK, 15 July 2013.

PRODUCT NAME: tolvaptan

C.A.S. NUMBER: 150683-30-0

OTHER NAMES: Samsca

Country	Effective Date	Description of action taken

United Kingdom	February 2012	The MHRA reported that treatment with tolvaptan can result in over rapid correction of hyponatraemia, which can lead to serious neurological events. Careful monitoring of serum sodium is therefore important and co-administration of other drugs that may increase serum sodium is not recommended. Tolvaptan may also reduce the effect of vasopressin analogues used to control or prevent bleeding. **References:** Drug Safety Update, February 2012, Volume 5, issue 9, A3, MHRA, (www.mhra.gov.uk). WHO Pharmaceuticals Newsletter No. 3, 2012.

PRODUCT NAME: topical ketoprofen

C.A.S. NUMBER: 22071-15-4

OTHER NAMES: Fastum, Ketospray

Country	Effective Date	Description of action taken
Egypt	16 June 2011	It was decided to add the following to the product insert: - Do not use for more than 12 days. - Do not expose treated areas to sunlight during the treatment and 2 weeks after its discontinuation. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.

PRODUCT NAME: topiramate

C.A.S. NUMBER: 97240-79-4

OTHER NAMES: Topamax, Trokendi XR, Qudexy XR

Country	Effective Date	Description of action taken
Brazil	March 2011	Health professionals were reminded of the increased risk of leporine lip development in children whose mothers were treated with topiramate during pregnancy, information that was already included in the medicine package leaflet. It is recommended that topiramate be use on pregnant women only if its benefits justify the potential risks to the fetus, in which case the patient should be informed about the potential danger to the fetus. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).
USA	4 March 2011	The US FDA notified health-care professionals and patients of an increased risk of development of cleft lip and/or cleft palate in infants born to women treated with topiramate during pregnancy. Because of the increased risk for oral clefts, topiramate is being placed in Pregnancy Category D, which means that there is positive evidence of fetal risk

		based on human data, but the benefits of the medicine in pregnant women may outweigh the risks in certain situations. **References:** FDA Drug Safety Communication, US FDA, 4 March 2011 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 2, 2011.
Switzerland	24 May 2011	Exposure during pregnancy increases the risk of cleft palate. **References:** Communication from Swissmedic, July 2012.
Australia	April 2012	The Therapeutic Goods Administration (TGA) advised health-care professionals of the change in the pregnancy category for topiramate-containing products from B3 to D. The Australian Product Information (PI) already contains warnings regarding the potential effects on the fetus, and recommends that women considering using topiramate receive pregnancy counselling to ensure they are aware of the potential risks to the fetus. Category D medicines are defined as drugs which have caused, are suspected to have caused or may be expected to cause, an increased incidence of human fetal malformations or irreversible damage. The TGA also advised that health-care professionals should advise women of childbearing age of the increased risk for oral clefts when topiramate is used during pregnancy. Topiramate should be used in pregnancy only if the potential benefits outweigh the potential risks to the fetus. **References:** Medicines Safety Update Vol 3, No. 2, April 2012 (www.tga.gov.au). WHO Pharmaceuticals Newsletter No. 3, 2012. WHO Pharmaceuticals Newsletter No. 1, 2015.
United Arab Emirates		Topamax 200 mg tablets, Topamax Sprinkle 25 mg and 50 mg capsules were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: tretinoin

C.A.S. NUMBER: 302-79-4

OTHER NAMES: Airol, Vesanoid, Avita, Renova, Retin-a

Country	Effective Date	Description of action taken
United Arab Emirates		Retin-A gel, and 0.025% and 0.05% cream were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. Airol lotion and ointment were withdrawn by the MAH before getting approval. **References:**

		Ministry of Health and Prevention Ministerial Decree No. 366.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: triamcinolone

C.A.S. NUMBER: 124-94-7

OTHER NAMES: Kenacort-A, Kenalog, Azmacort, Nasacort AQ

Country	Effective Date	Description of action taken
United Arab Emirates		Azmacort inhaler, Nasacort AQ 55 mcg/actuation spary, Kenacort-A solution for injection and Kenalog in orabase 0.1% were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: tribenoside

C.A.S. NUMBER: 10310-32-4

OTHER NAMES: Glyvenol

Country	Effective Date	Description of action taken
United Arab Emirates		Glyvenol 400 mg capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: trimetazidine

C.A.S. NUMBER: 13171-25-0

OTHER NAMES: Vastarel

Country	Effective Date	Description of action taken
Viet Nam	29 November 2012	The marketing authorisation of trimetazidin-containing medicines is suspended due to safety concerns following reports of Parkinson syndrome and other motor disorders such as tremor (shaking), muscle rigidity and walking disorders, and restless-legs syndrome, associated with their use. **References:** Drug Administration of Viet Nam Official documents No. 18614/QLD-DK, 29 November 2012.
Brazil	January 2013	Following a positive risk-benefit balance from a reassessment of Vastarel carried out by the EMA, ANVISA reminded that the product is contraindicated in patients with Parkinson's disease or symptoms of parkinsonism, and

		in case of severely reduced renal function; whereas in patients with moderate renal failure, as well as the elderly, the dose should be reduced. The package leaflet of the drug has been updated. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).
United Arab Emirates		Vastarel 20 mg/ml drops were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: trimethoprim

C.A.S. NUMBER: 738-70-5

OTHER NAMES: Proloprim, Methostat, Monotrim, Triprim

Country	Effective Date	Description of action taken
United Arab Emirates		Methostat 100 mg tablets and 50 mg/5 ml suspension were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: trimipramine

C.A.S. NUMBER: 521-78-8

OTHER NAMES: Surmontil

Country	Effective Date	Description of action taken
United Arab Emirates		Surmontil 50 mg capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: triprolidine

C.A.S. NUMBER: 486-12-4

OTHER NAMES: Actidil, Myidil

Country	Effective Date	Description of action taken
Egypt	13 October 2011	Medicinal products containing triprolidine are contraindicated in children under the age of 6 years. **References:**

		Communication from the Egypt National Pharmacovigilance Centre, July 2012.

PRODUCT NAME: tropicamide

C.A.S. NUMBER: 1508-75-4

OTHER NAMES: Ciclomidrin, Tropinom, Mydriacyl

Country	Effective Date	Description of action taken
Brazil	October 2015	ANVISA warned about the risk associated with the use of tropicamide-based mydriatic eye drops in children (especially in neonates and children from 0 to 1 year of age), with the possibility of triggering severe adverse reactions. The events occurred after the use of mydriatic eye drops to perform the eye test/red reflex test in health facilities in Brazil. It should be noted that this test does not require the use of mydriatic eye drops for its effectiveness. **References:** ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia).
United Arab Emirates		Mydriaticum 0.5% drops were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: tyrothricin

C.A.S. NUMBER: 1404-88-2

OTHER NAMES: Herit

Country	Effective Date	Description of action taken
United Arab Emirates		Herit gel were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ulipristal acetate

C.A.S. NUMBER: 126784-99-4

OTHER NAMES: Esmya

Country	Effective Date	Description of action taken
Europe	November 2017	The European Medicines Agency (EMA) recommended that several measures be put in place to minimise the risk of rare but serious liver injury with Esmya (ulipristal acetate).

		Certain women may start treatment with Esmya once the new measures are implemented. The measures include: contraindication in women with known liver problems; liver tests before, during and after stopping treatment; a card for patients to inform them about the need for liver monitoring and to contact their doctor should they develop symptoms of liver injury. In addition, use of the medicine for more than one treatment course has been restricted to women who are not eligible for surgery. **References:** EMA Referrals (www.ema.europa.eu) WHO Pharmaceuticals Newsletter No. 4, 2018. WHO Pharmaceuticals Newsletter No. 5, 2018.
Montenegro	2 February 2018	Based on EMA referral and in accordance with Law on medicines, the Agency for Medicines and Medical Devices of Montenegro (CALIMS) has sent DHPC to relevant HCPs to inform them of serious liver injury, including liver failure leading to transplantation. **References:** CALIMS, Direct healthcare professional communications. WHO Pharmaceuticals Newsletter No. 2, 2018.

PRODUCT NAME: urapidil

C.A.S. NUMBER: 64887-14-5

OTHER NAMES: Tachyben

Country	Effective Date	Description of action taken
United Arab Emirates		Tachyben 100 mg injection products were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ursodiol

C.A.S. NUMBER: 128-13-2

OTHER NAMES: Actigall, Ursosan, Ursofalk, Egyurso, Urso, Urso Forte

Country	Effective Date	Description of action taken
Canada	5 December 2011	In a clinical trial patients taking twice the daily dose of ursodiol for primary sclerosing cholangitis (PSC) had improved serum liver tests, but overall survival was not improved and patients experienced higher rates of serious adverse events (including death or liver transplantation). The product monograph has been revised to advise that improved serum liver tests do not always correlate with improved liver disease status. **References:**

		Advisories, Warnings and Recalls, Health Canada, 5 December 2011 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 1, 2012.

PRODUCT NAME: valdecoxib

C.A.S. NUMBER: 181695-72-7

OTHER NAMES:

Country	Effective Date	Description of action taken
Bhutan	22 July 2015	All forms of valdecoxib are banned due to increased risk of heart attack. Pharmacies have been notified of the restrictions in their importation and sales. **References:** Bhutan Drug Regulatory Authority, List of Banned Drugs (www.dra.gov.bt).

PRODUCT NAME: valsartan

C.A.S. NUMBER: 137862-53-4

OTHER NAMES: Cinfaval, Diovan, ExTenz, Valdio, Valzar

Country	Effective Date	Description of action taken
Armenia	2018	After an assessment by the Scientific Centre of Drug and Medical Technology Expertise after Academician E. Gabrielyan (SCDMTE), marketing authorisations of valsartan-containing products with API manufacturer of Zheijang Huahai Pharmacetuicals Co. LTD were suspended due to contamination with NDMA (N-nitrosodimethylamine), a chemical that could cause cancer. **References:** Communication from Armenian National Pharmacovigilance Centre, 2018.
Oman	2018	Certain valsartan-containing medicines werer recalled due to contamination of impurity, NMDA, in the API used. **References:** Oman Ministry of Health Circular No. 52, 2018.
United Arab Emirates	2018	Cinfaval (40 mg, 160 mg, 320 mg), ExTenz (80 mg, 160 mg, 320 mg), Valdio (80 mg, 160 mg), Valzar (40 mg to 320 mg) tablets were suspended. Valis 40 tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.
Bosnia and Herzegovina	7 May 2018	The distribution of valsartan and request for variation of marketing authorisation were suspended. Some batches of the product were recalled from the market.

		References: Agency for Medicinal Products and Medical Devices news release (www.almbih.gov.ba).
Uganda	18 August 2018	The marketing authorisation of valsartans is suspended due to the identification of an unexpected impurity, N-nitrosodimethylamine (NDMA). **References:** Uganda National Drug Authority news release, 18 August 2018.
Europe	13 September 2018	The EMA has conducted a risk assessment of valsartan medicines containing the active substance manufactured by Zhejiang Huahai and Zhejiang Tianyu where unacceptable levels of NDMA have been confirmed. It concluded that the risk from NDMA remains low, while the impact of a related substance, N-nitrosodiethylamine (NDEA), which has been detected in valsartan made by the same manufacturers still need to be further assessed. Meanwhile, medicines containing valsartan from Zhejiang Huahai and Zhejiang Tianyu are no longer being distributed in the EU or have been recalled. Both companies are not currently authorised to produce valsartan for medicines in the EU. **References:** EMA press release, 13 September 2018. WHO Pharmaceuticals Newsletter No. 4, 2018. WHO Pharmaceuticals Newsletter No. 4, 2018.

PRODUCT NAME: vandetanib

C.A.S. NUMBER: 443913-73-3

OTHER NAMES: Caprelsa

Country	Effective Date	Description of action taken
Canada	15 February 2012	Serious risks of QTc prolongation, Torsade de Pointes, and sudden death have been reported with vandetanib. In addition, rash and other skin reactions, diarrhea, hypertension and vision abnormalities have also been reported. Vandetanib is only available through a Restricted Distribution Program. Only prescribers enrolled in the CAPRELSA Restricted Distribution Program can prescribe the drug. **References:** Advisories, Warnings and Recalls, Health Canada, 15 February 2012 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 2, 2012.

PRODUCT NAME: varenicline

C.A.S. NUMBER: 249296-44-5

OTHER NAMES: Champix, Chantix

Country	Effective Date	Description of action taken
USA	22 July 2011	The US FDA notified the public that the smoking cessation aid varenicline may be associated with a small, increased risk of certain cardiovascular adverse events in patients who have cardiovascular disease. Cardiovascular adverse events were infrequent overall; however, certain events, including heart attack, were reported more frequently in patients treated with varenicline than in patients treated with placebo. **References:** FDA Drug Safety Communication, US FDA 22 July 2011 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 4, 2011. WHO Pharmaceuticals Newsletter No. 2, 2015.
Brazil	July 2011 January 2012	In 2011, folowing a study published in the Canadian Medical Association Journal, ANVISA issued an alert about an increased cardiac risk for Champix® users. The Agency has assessed that the benefits of varenicline outweigh its risks, a decision corroborated by the publications from the US FDA, EMA and Health Canada. Health professionals were recommended to monitor patients for identification, early intervention and notification of adverse reactions. The product package leaflet has been updated. In January 2012, ANVISA issued a new alert stating that the Champix package leaflet was updated with new information about the cardiovascular risks associated with its use. Signs and symptoms indicative of a heart attack or stroke were highlighted. **References:** ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia). WHO Pharmaceuticals Newsletter No. 2, 2012.

PRODUCT NAME: vecuronium bromide

C.A.S. NUMBER: 50700-72-6

OTHER NAMES: Norcuron

Country	Effective Date	Description of action taken
United Arab Emirates		Norcuron 10 mg injection products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: vemurafenib

C.A.S. NUMBER:

1029872-54-5; 918504-65-1

OTHER NAMES: Zelboraf

Country	Effective Date	Description of action taken
Brazil	February 2014 October 2015 March 2017	In 2014, health professionals were informed of the occurrence of liver lesions with the use of Zelboraf, advising them to monitor liver function before starting treatment and follow up monthly during treatment, or according to clinical indication. Management of liver injury should be accomplished with dose reduction, temporary discontinuation, or discontinuation of treatment. The package leaflet was updated. In 2015, health professionals were informed about the risk of potentiating radiation toxicity associated with Zelboraf due to the occurrence of severe cases of lesions, some with fatal outcome, reported in patients treated with radiation before, during, or after treatment with Zelboraf®. Therefore, the drug should be used with caution when administered before, during or after radiation treatment. The package leaflet was updated with the information. In 2017, health professionals were informed of the risk of Dupuytren contracture and plantar fibromatosis with Zelboraf®, which should be managed with temporary interruption or discontinuation of treatment, as directed by the updated product package insert. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: veralipride

C.A.S. NUMBER: 66644-81-4

OTHER NAMES: Agreal, Agradil

Country	Effective Date	Description of action taken
Egypt	23 September 2010	Withdrawal of the registered product containing this active ingredient because the risks outweigh the benefits. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.
United Arab Emirates		Agreal 100 mg capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: verapamil

C.A.S. NUMBER: 52-53-9

OTHER NAMES: Isoptin, Calan

Country	Effective Date	Description of action taken
United Arab Emirates		Isoptin 40 mg, 80 mg, and Isoptin Retard 120 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: vernakalant

C.A.S. NUMBER: 748810-28-8

OTHER NAMES: Brinavess, Kynapid

Country	Effective Date	Description of action taken
United Arab Emirates	2012	Brinavess 20 mg/ml infusion were suspended. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: vildagliptin

C.A.S. NUMBER: 274901-16-5

OTHER NAMES: Galvus

Country	Effective Date	Description of action taken
United Arab Emirates		Galvus 100 mg tablets were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: vismodegib

C.A.S. NUMBER: 879085-55-9

OTHER NAMES: Erivedge

Country	Effective Date	Description of action taken
Brazil	December 2016	After the reassessment of the teratogenic limit for Erivedge, health professionals were informed that the recommended contraception period for women of childbearing age has been changed from 9 to 24 months after receiving the last dose. The same period was extended for the post-treatment waiting period for breastfeeding and for blood donation and blood products for patients receiving treatment with Erivedge®. The medicine package leaflet has been updated.

		References: ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: vitamin E

C.A.S. NUMBER: 10191-41-0

OTHER NAMES: Ephynal, Hijuven

Country	Effective Date	Description of action taken
United Arab Emirates		Ephynal 100 mg injection and tablet, and Hijuven capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: voriconazole

C.A.S. NUMBER: 137234-62-9

OTHER NAMES: VFEND

Country	Effective Date	Description of action taken
Switzerland	13 January 2011	Malignant skin tumours and adverse eye reactions have been associated with voriconazole use. **References:** Communication from Swissmedic, July 2012.

PRODUCT NAME: water for injection

C.A.S. NUMBER: 7732-18-5

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		Sterile Water for Irrigation USP and Water for Injection BP were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: xylometazoline

C.A.S. NUMBER: 526-36-3

OTHER NAMES: Otrivin, Otrivine

Country	Effective Date	Description of action taken

United Arab Emirates	Otrivin gel and 0.1% solution were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: zaleplon

C.A.S. NUMBER: 151319-34-5

OTHER NAMES: Sonata, Starnoc

Country	Effective Date	Description of action taken
Egypt	7 June 2012	ue to its abuse potential, it was decided to restrict the package size to a maximum of 14 tablet/capsule and its distribution should be restricted to only one distributor. In addition, each pharmacy should not receive more than 10 packs per month. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.

PRODUCT NAME: zinc oxide

C.A.S. NUMBER: 1314-13-2

OTHER NAMES:

Country	Effective Date	Description of action taken
Egypt	12 April 2012	Zinc oxide is not allowed to be registered in oral dosage forms. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.

PRODUCT NAME: zoledronic acid

C.A.S. NUMBER: 118072-93-8

OTHER NAMES: Zometa, Zomera, Aclasta, Reclast

Country	Effective Date	Description of action taken
USA	1 September 2011	Zoledronic acid is contraindicated in patients with creatinine clearance less than 35 mL/min or in patients with evidence of acute renal impairment due to risk of kidney failure. The label also recommends that healthcare professionals screen patients prior to administering zoledronic acid in order to identify at-risk patients. **References:** FDA Drug Safety Communication, US FDA, 1 September 2011 (www.fda.gov).

WHO Pharmaceuticals Newsletter No. 5, 2011.

PRODUCT NAME: zuclopenthixol

C.A.S. NUMBER: 53772-83-1

OTHER NAMES: Cisordinol, Clopixol

Country	Effective Date	Description of action taken
United Arab Emirates		Clopixol Acuphase 100 mg/2 ml and Clopixol Depot 500 mg/ml injection products, and Clopixol 10 mg and 20 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

Combination of Products

PRODUCT NAME: acetylsalicylate + diphenylpyraline + lysozyme

C.A.S. NUMBER:

OTHER NAMES: Skainar

Country	Effective Date	Description of action taken
United Arab Emirates		Skainar capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: acetylsalicylic acid + atorvastatin + ramipril

C.A.S. NUMBER:

OTHER NAMES: Trinomia

Country	Effective Date	Description of action taken
United Arab Emirates		The application was rejected by the committee for various reasons. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: acridone acid + N-methylglucamine

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Viet Nam	9 April 2012	The marketing authorisation for the combination of acridone acid and N-methylglucamin is suspended due to limited safety and efficacy data. **References:** Drug Administration of Viet Nam Official documents No. 4996/QLD-DK, 09 April 2012.

PRODUCT NAME: aescinate + sodium heparin + essential phospholipids

C.A.S. NUMBER:

OTHER NAMES: Essaven

Country	Effective Date	Description of action taken
United Arab Emirates		Essaven gel and capsules were withdrawn by the MAH before getting approval. **References:**

	Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: alendronic acid + cholecalciferol

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		Alen-D3, alendronic acid 70 mg and cholecalciferol 2800 IU or 5600 IU were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: allopurinol + benzbromarone

C.A.S. NUMBER:

OTHER NAMES: Allomaron

Country	Effective Date	Description of action taken
United Arab Emirates		Allomaron tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: almitrine and raubasine

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Egypt	26 May 2011	Withdrawal of registered products containing this active ingredients because the risks outweigh the benefits. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.

PRODUCT NAME: aluminium hydroxide + magnesium hydroxide

C.A.S. NUMBER:

OTHER NAMES: Maalox No.2, Rialox

Country	Effective Date	Description of action taken

United Arab Emirates		Maalox No.2 were withdrawn by the MAH before approval; while Rialox were volutarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: aluminium hydroxide + magnesium hydroxide + activated dimethicone

C.A.S. NUMBER:

OTHER NAMES: Actonorm

Country	Effective Date	Description of action taken
United Arab Emirates		Actonorm powder were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: Aminovenos-N-pad

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		Aminovenos-N-pad 6% and 10% injection products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: amiodarone + (ledipasvir + sofosbuvir), or sofosbuvir, or daclatasvir, or simeprevir

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Brazil	August 2015	Warned about the risk of severe bradycardia when the antiarrhythmic amiodarone is used in conjunction with the medicines: Harvoni® (ledipasvir + sofosbuvir), Sovaldi® (sofosbuvir), Daklinza® (daclatasvir) and Olysio® (simeprevir), considering cases reported by the EMA. Co-administration of amiodarone with these new medicines is not recommended. Bradycardia usually resolves after discontinuation of medications.

	References: ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: amoxicillin and clavulanic acid

C.A.S. NUMBER:

OTHER NAMES: Flemoclave Solutab, Megamox, Ultramox, MedaClav

Country	Effective Date	Description of action taken
United Arab Emirates	2011	Megamox powder for reconstitution suspention is suspended. French language was being added in the product insert of Megamox in all forms and strengths. Upon company request, Megamox 625mg tablets x 14 pack was discontinued. Flemoxin Solutab 250 mg and 500 mg, and Flemoxin drops and suspension were withdrawn by the MAH before geeting approval. MedaClav ® 228.5 mg, to 1 g were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.
Armenia	2018	After an assessment by the Scientific Centre of Drug and Medical Technology Expertise after Academician E. Gabrielyan (SCDMTE), the product information of Flemoclave Solutab was updated to include information on posology and administration for reducing risk of fatal mechanical asphyxia due to inappropriate use of the medicine and ingestion of a whole tablet without prior dissolution in water. As a risk minimization measure a DHPC was circulated. **References:** Communication from Armenian National Pharmacovigilance Centre, 2018.

PRODUCT NAME: amphotericin B + tetracycline

C.A.S. NUMBER:

OTHER NAMES: Vagmycin

Country	Effective Date	Description of action taken
United Arab Emirates		Vagmycin tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ampicillin + cloxaxillin

C.A.S. NUMBER:

OTHER NAMES: Ampiclox

Country	Effective Date	Description of action taken
United Arab Emirates		These products were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ampicillin + sulbactam

C.A.S. NUMBER:

OTHER NAMES: Unasyn

Country	Effective Date	Description of action taken
United Arab Emirates		The products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: antazoline hydrochloride + tetryzoline hydrochloride

C.A.S. NUMBER:

OTHER NAMES: Spersallerg

Country	Effective Date	Description of action taken
United Arab Emirates		The products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: antazoline sulphate + naphazoline nitrate

C.A.S. NUMBER:

OTHER NAMES: Antistin Privin

Country	Effective Date	Description of action taken
United Arab Emirates		Antistin Privin Eye Drops were withdrawn by the MAH before getting approval. **References:**

	Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: anti-hemorrhoid products

C.A.S. NUMBER:

OTHER NAMES: Preparation H

Country	Effective Date	Description of action taken
United Arab Emirates		Preparation H ointment and suppository were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: arsenic trioxidum

C.A.S. NUMBER: -

OTHER NAMES: Caustinerf arsenical dental paste

Country	Effective Date	Description of action taken
Europe	25 April 2014	The European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) has recommended that the marketing authorisations for the dental pastes Caustinerf arsenical, Yranicid arsenical and associated names be revoked in the EU due to concerns over the risk of genotoxic effects (damage to the genetic material in cells) and cell death in tissues around the teeth. The dental pastes, which contain an arsenic-based compound, arsenic trioxide, have been used to remove the damaged nerves in the dental pulp. **References:** CHMP advice

PRODUCT NAME: artesunate + amodiaquine

C.A.S. NUMBER: -

OTHER NAMES:

Country	Effective Date	Description of action taken
Eritrea	October 2018	The Eritrea Medicines and Food Administration and the Communicable Disease Control program established a new dosing regimen based on evidence that the country's audlt poplulation is underweight, rendering the global weight-for-age band an inaccurate guide. The new dosing regimen, after approval by WHO malaria experts, triggered changes in national malaria guidelines and product labelling in Eritrea.

		The manufacturer communicated the safety issue and accordingly submitted risk management plans including direct heathcare communication, boxed warning, label change and dosing change. As part of the risk management plan, the National Malaria Control program changed its guideline and instructed all health facilities to use weight-based dosing instead of age; where possible. **References:** Medicines Information Bulletin. Sabur Printing Services. Ministry of Health. Vol. 30, June 2018

PRODUCT NAME: atropine + diphenoxylate

C.A.S. NUMBER:

OTHER NAMES: Reasec

Country	Effective Date	Description of action taken
United Arab Emirates		Reasec drops and tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: betamethasone + gentamicin

C.A.S. NUMBER:

OTHER NAMES: Garasone

Country	Effective Date	Description of action taken
United Arab Emirates		Garasone eye/ear drops and ointment were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: bevacizumab and docetaxel

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Switzerland	27 February 2012	The combination therapy of bevacizumab and docetaxel for treatment of metastatic breast cancer has been revoked. **References:** Communication from Swissmedic, July 2012.

PRODUCT NAME: bevacizumab and paclitaxel

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Canada	29 September 2011	Health Canada made the final decision to suspend the approval of bevacizumab in combination with paclitaxel for the use of metastatic breast cancer. **References:** Advisories, Warnings and Recalls, Health Canada, 29 November 2011 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 1, 2012.

PRODUCT NAME: bisoprolol + amlodipine

C.A.S. NUMBER:

OTHER NAMES: Concor AM

Country	Effective Date	Description of action taken
United Arab Emirates		The application was rejected by the committee for various reasons. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: bisoprolol fumarate + hydrochlorothiazide

C.A.S. NUMBER:

OTHER NAMES: Lodoz

Country	Effective Date	Description of action taken
United Arab Emirates		LODOZ ® 5mg/6.25mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: borneol + camphene + cineole + α-pinene + β-pinene + anethol + fenchone

C.A.S. NUMBER:

OTHER NAMES: Rowatinex

Country	Effective Date	Description of action taken
United Arab Emirates		Rowatinex drops were withdrawn by the MAH before getting approval. **References:**

	Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: borneol + camphene + cineole + α-pinene + β-pinene + menthol + menthone

C.A.S. NUMBER:

OTHER NAMES: Rowachol

Country	Effective Date	Description of action taken
United Arab Emirates		Rowachol drops were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: bromhexine + salbutamol + guaifenesin

C.A.S. NUMBER:

OTHER NAMES: Bronkovent

Country	Effective Date	Description of action taken
United Arab Emirates		The application for Bronkovent syrup was rejected by the committee for various reasons. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: buclosamide + salicylic with or without hydrocortisone

C.A.S. NUMBER:

OTHER NAMES: Jadit, Jadit H

Country	Effective Date	Description of action taken
United Arab Emirates		Jadit oinment, solution and spray, and Jadit H ointment and solution were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: budesonide + formoterol fumarate dihydrate

C.A.S. NUMBER:

OTHER NAMES: Foracort

Country	Effective Date	Description of action taken
United Arab Emirates		The application for Foracort 100 and Foracort 200 was rejected by the committee for various reasons. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: camphor + eucalyptus oil + peru balsam + rosemary Oil

C.A.S. NUMBER:

OTHER NAMES: Pulmex

Country	Effective Date	Description of action taken
United Arab Emirates		Pulmex ointment and capsules, Pulmex Baby capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: carbinoxamine + phenylephrine

C.A.S. NUMBER:

OTHER NAMES: Rhinopront

Country	Effective Date	Description of action taken
United Arab Emirates		Rhinopront capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: carbinoxamine + phenylephrine + dextromethorphanx

C.A.S. NUMBER:

OTHER NAMES: Rhinotussal

Country	Effective Date	Description of action taken
United Arab Emirates		Rhinotussal capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: carbinoxamine + phenylpropanolamine

C.A.S. NUMBER:

OTHER NAMES: Fluzal

Country	Effective Date	Description of action taken
United Arab Emirates		The application for Fluzalwas rejected by the committee for various reasons. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: carbocisteine + promethazine HCl

C.A.S. NUMBER:

OTHER NAMES: Rhinathiol syrup

Country	Effective Date	Description of action taken
Oman	2010	The product information for 2% rhinathiol syrup for child and infant is updated with new contraindication in children below 2 years of age, following similar regulatory decision by the French regulator. The Circular was sent to HCPs. **References:** Oman Ministry of Health Circular No. 60, 2010.
United Arab Emirates		The products were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: Celemin

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		The registration of Celemin 10-Plus and Celemin 5-S were suspended **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: Centrum Prenatal multivitamins

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		Centrum® Prenatal multivitamin tablets were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cephalosporin + beta lactamase inhibitor

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Viet Nam	13 September 2012	The marketing authorisation of the product was withdrawn due tot limited safety and efficacy data. **References:** Drug Administration of Viet Nam Official documents No. 13702/QLD-DK, 13 September 2012

PRODUCT NAME: Cernevit injection

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		Cernevit injection were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cetirizine + pseudoephedrine

C.A.S. NUMBER:

OTHER NAMES: Cirrus

Country	Effective Date	Description of action taken
United Arab Emirates		These products should not be used for children under the age of 6 years. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cetrimide + benzalkonium chloride

C.A.S. NUMBER:

OTHER NAMES: Neo Baby

Country	Effective Date	Description of action taken
United Arab Emirates		Neo Baby cream were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cetrimide + benzalkonium chloride + chlorobutanol + aldioxa

C.A.S. NUMBER:

OTHER NAMES: Cetanorm

Country	Effective Date	Description of action taken
United Arab Emirates		Cetanorm cream were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: chloramphenicol + benzocaine

C.A.S. NUMBER:

OTHER NAMES: Otocol

Country	Effective Date	Description of action taken
United Arab Emirates		The application for Otocol ear drops was rejected by the committee for various reasons. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: chlormidazole + fluocinolone

C.A.S. NUMBER:

OTHER NAMES: Myco-Synalar

Country	Effective Date	Description of action taken
United Arab Emirates		Myco-Synalar cream and solution were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: chlorpheniramine maleate 1mg + pseudoephedrine HCL 20mg + paracetamol 100mg

C.A.S. NUMBER: -

OTHER NAMES: Rhinostop

Country	Effective Date	Description of action taken
Eritrea	April 2013	The National Medicines and Food Administration restricted the Rhinostop syrup from children aged < 6 years. At the same time the manufacturer was instructed to make the label change accordingly. **References:** National Medicines and Food Administartion Notification Letter, April 2013
United Arab Emirates		The application for Kidikold was rejected by the committee for various reasons. Whle Adol Allergy Sinus Therapy products were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cinchocaine + hydrocortisone

C.A.S. NUMBER:

OTHER NAMES: Proctosedyl

Country	Effective Date	Description of action taken
United Arab Emirates		Proctosedyl ointment were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: clopamide + dihydroergocristine mesilate + reserpine

C.A.S. NUMBER:

OTHER NAMES: Brinderdin

Country	Effective Date	Description of action taken
United Arab Emirates		Binderdin was voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: combinations of vitamins

C.A.S. NUMBER:

OTHER NAMES: Juvelon, Redoxon, Theragran, Tri-Vi-Sol

Country	Effective Date	Description of action taken
United Arab Emirates		The following vitamin combinations products were withdrawn by the MAH before getting approval: Juvelon capsules, Redoxon 200 mg and 500 mg tablets, Theragran Helmatinic and Theragran M tablets, Tri-Vi-Sol drops. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: compound sodium lactate solution for infusion

C.A.S. NUMBER:

OTHER NAMES: e.g. Ringer Dextrose injection, lactated Ringer's injection

Country	Effective Date	Description of action taken
United Arab Emirates		Prodcuts containing compound sodium lactate solution for infusion were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: Cypro-BC

C.A.S. NUMBER:

OTHER NAMES: contains: cyproheptadine hydrochloride,pyridoxine HCL (Vitamin B6),ascorbic acid,niacinamide ,riboflavin (Vitamin B2),thiamine hydrochloride (vitamin B1)

Country	Effective Date	Description of action taken
United Arab Emirates		Cypro-BC were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: Dextran 70

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken

United Arab Emirates		Dextran(70) 6% w/v infusion solution were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: dextromethorphan and antihistamine

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Syrian Arab Republic	22 January 2015	The outer package and the package insert should contain the information that these products are prescription drugs. Treatment with these products beyond 5 days is not recommended. The statement "The product is not recommended for children under 6 years of age" should be added to the outer package. **References:** Circular from the Ministry of Health No. 1147/20/1, 2015.

PRODUCT NAME: dipyridamole + acetylsalicylic acid

C.A.S. NUMBER:

OTHER NAMES: Aggrenox

Country	Effective Date	Description of action taken
United Arab Emirates		Aggrenox® 200/25mg capsules were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ephedrine + naphazoline

C.A.S. NUMBER:

OTHER NAMES: Deltarhinol

Country	Effective Date	Description of action taken
United Arab Emirates		Deltarhinol nasal spray were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: esdepallethrine + piperonyl butoxide

C.A.S. NUMBER:

OTHER NAMES: Spregal

Country	Effective Date	Description of action taken
Togo	12 April 2018	The MAH voluntarily withdrew the marketing authorisation of Spregal (esdepallethrine and piperonyl butoxide) nasal spray and lotion. **References:**

PRODUCT NAME: estradiol hemihydrate + drospirenone

C.A.S. NUMBER:

OTHER NAMES: Angeliq

Country	Effective Date	Description of action taken
United Arab Emirates		Angeliq® were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: estradiol valerate + cyproterone

C.A.S. NUMBER:

OTHER NAMES: Climen

Country	Effective Date	Description of action taken
United Arab Emirates		Climen were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ethinylestradiol + levonorgestrel

C.A.S. NUMBER:

OTHER NAMES: Microgynon 30

Country	Effective Date	Description of action taken
United Arab Emirates		Microgynon 30 were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ethinylestradiol + norethindrone

C.A.S. NUMBER:

OTHER NAMES: Ortho Novum, Ortho-Vaginal

Country	Effective Date	Description of action taken
United Arab Emirates		Ortho Novum tablet and Ortho-Vaginal cream were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: eye vitamin and mineral supplement

C.A.S. NUMBER:

OTHER NAMES: ICAPS Lutein & Zeaxanthin Formula

Country	Effective Date	Description of action taken
United Arab Emirates		ICAPS Lutein & Zeaxanthin Formula tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: felodipine + metoprolol

C.A.S. NUMBER:

OTHER NAMES: Logimax 5/50

Country	Effective Date	Description of action taken
United Arab Emirates		Logimax 5/50 were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ferrous (II)- glycine sulphate complex

C.A.S. NUMBER:

OTHER NAMES: r.g. ferro sanol®, ferro sanol® gyn

Country	Effective Date	Description of action taken
United Arab Emirates		ferro sanol® duodenal capsules and ferro sanol ® drops were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety.

		References: Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ferrous sulfate + hematinic

C.A.S. NUMBER:

OTHER NAMES: Fer-In-Sol

Country	Effective Date	Description of action taken
United Arab Emirates		Fer-In-Sol drops were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: flumethasone + coal tar + salicylic acid

C.A.S. NUMBER:

OTHER NAMES: Locacorten-Tar

Country	Effective Date	Description of action taken
United Arab Emirates		Locacorten-Tar ointment were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: fluorometholone + sodium cromoglycate

C.A.S. NUMBER:

OTHER NAMES: Fluca

Country	Effective Date	Description of action taken
United Arab Emirates		The application for Fluca was rejected by the committee for various reasons. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: fluorometholone + tetryzoline

C.A.S. NUMBER:

OTHER NAMES: Efemoline

Country	Effective Date	Description of action taken

United Arab Emirates		Efemoline® were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: fluoxetine + olanzapine

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Egypt	15 April 2010	Unauthorized for use in children and adolescents. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.

PRODUCT NAME: framycetin sulfate + gramicidin

C.A.S. NUMBER:

OTHER NAMES: Sofradex

Country	Effective Date	Description of action taken
United Arab Emirates		Sofradex drops and ointment were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: glycerol + lecithin + soybean oil

C.A.S. NUMBER:

OTHER NAMES: Lipovenos

Country	Effective Date	Description of action taken
United Arab Emirates		Lipovenos 10% solution for injection were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: glycosaminoglycan polysulphate + salicylic acid + suprarenal extract

C.A.S. NUMBER:

OTHER NAMES: Mobilat

Country	Effective Date	Description of action taken
United Arab Emirates		Mobilat cream were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: Haemosol

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		Haemosol (lysozyme + Vitamin E + Vitamin K1 etc.) capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: heparin + dexpanthenol + dimethyl sulfoxide

C.A.S. NUMBER:

OTHER NAMES: Dolobene

Country	Effective Date	Description of action taken
United Arab Emirates		Dolobene was withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: hydrochlorothiazide + amiloride hydrochloride,

C.A.S. NUMBER:

OTHER NAMES: Amitrid

Country	Effective Date	Description of action taken
United Arab Emirates		Amitrid 50 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: hydrochlorothiazide + bisoprolol fumarate

C.A.S. NUMBER:

OTHER NAMES: Lodoz

Country	Effective Date	Description of action taken
United Arab Emirates		Lodoz 2.5 mg/6.25 mg and 10 mg/6.25 mg were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: hypotonic saline solution (0.18% saline/4% glucose)

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Oman	2012	The product information for hypotonic saline solution was updated to restrict the use in children except in specialist settings under expert supervision. The decision took into consideration similar action by the Medicines and Healthcare products Regulatory Agency (MHRA). **References:** Oman Ministry of Health Circular No. 94, 2012.

PRODUCT NAME: indapamide + perindopril

C.A.S. NUMBER:

OTHER NAMES: bi Preterax, Preterax

Country	Effective Date	Description of action taken
United Arab Emirates		Preterax and bi Preterax were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: interferon alfa-2a, recombinant

C.A.S. NUMBER:

OTHER NAMES: Roferon-A

Country	Effective Date	Description of action taken
United Arab Emirates		Roferon-A 18 MIU/0.6 ml multidose and 18 MIU/ml injection products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ioxaglate meglumine + ioxaglate sodium

C.A.S. NUMBER:

OTHER NAMES: Hexabrix

Country	Effective Date	Description of action taken
United Arab Emirates		Hexabrix 320 solution for injection were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: kaolin + pectin

C.A.S. NUMBER:

OTHER NAMES: Kaonorm

Country	Effective Date	Description of action taken
United Arab Emirates		Kaonorm suspension were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: lidocaine + cetylpyridinium

C.A.S. NUMBER:

OTHER NAMES: Calgel

Country	Effective Date	Description of action taken
United Arab Emirates		Calgel was withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: lopinavir + ritonavir

C.A.S. NUMBER:

OTHER NAMES: Kaletra

Country	Effective Date	Description of action taken
Brazil	March 2011	ANVISA published a guidance stipulating that Kaletra oral solution should not be used in premature neonates in the immediate postnatal period, due to possible toxicity caused

		by the excipient propylene glycol contained in its formulation. Other guidelines included dosage calculation, overdose and administration in infants and children. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).
USA	8 March 2011	The use of lopinavir/ritonavir (Kaletra) oral solution should be avoided in neonates before a postmenstrual age of 42 weeks and a postnatal age of at least 14 days has been attained. Kaletra oral solution contains alcohol and propylene glycol as excipients. Preterm neonates may be at increased risk of propylene glycol associated adverse events due to diminished ability to metabolize propylene glycol, thereby leading to accumulation and potential adverse events such as serious heart, kidney or breathing problems. Be aware that toxicity in preterm neonates can be severe or possibly fatal, and it can be mistaken for neonatal sepsis. Immediate discontinuation of the drug is critical in these settings. **References:** FDA Drug Safety Communication, US FDA, 8 March 2011 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 2, 2011.

PRODUCT NAME: malathion + permethrin + piperonyl butoxide

C.A.S. NUMBER:

OTHER NAMES: Para Plus

Country	Effective Date	Description of action taken
Togo	12 April 2018	The MAH voluntarily withdrew the marketing authorisation of malathion with permethrin and piperonyl butoxide (Para Plus) in the form of cutaneous spray solution. **References:**

PRODUCT NAME: melatonin + pyridoxine

C.A.S. NUMBER:

OTHER NAMES: Viva-Max

Country	Effective Date	Description of action taken
United Arab Emirates		Viva-Max Micro 0.3 mg, Viva-Max 1 mg and 3 mg tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: melitracen + flupenthixol

C.A.S. NUMBER:

OTHER NAMES: Deanxit

Country	Effective Date	Description of action taken
United Arab Emirates		Deanxit were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: meprobamate and Valerian (herbal)

C.A.S. NUMBER: meprobamate (57-53-4)

OTHER NAMES:

Country	Effective Date	Description of action taken
Viet Nam	24 April 2012	The marketing authorisation for combination products of meprobamate and Valerian (herbal) is suspended due to unfavorable risk-benefit profile, and to prevent risk of overdose and drug abuse. **References:** Drug Administration of Viet Nam Official documents No. 5865/QLD-DK, 24 April 2012.

PRODUCT NAME: methocarbamol + acetylsalicylic acid (ASA)

C.A.S. NUMBER:

OTHER NAMES: Robaxisal

Country	Effective Date	Description of action taken
United Arab Emirates		Robaxisal tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: misoprostol + mifepristone

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Viet Nam	7 December 2017	The use of mifepristone combined with misoprostol is restricted to the medical termination of pregnancy up to 22 weeks' gestation.

		The restriction was based on Viet Nam National Guidelines for Reproductive Health (2016). **References:** Drug Administration of Viet Nam Official Dispatch No. 20534/QLD-DK, 07 December 2017.

PRODUCT NAME: Multivitaplex

C.A.S. NUMBER:

OTHER NAMES: (Nicotinamide,Vitamin B2,Vitamin B1 mononitrate,Vitamin B12,Calcium pantothenate,Vitamin B6,Alpha-Tocopheryl acetate,Eergocalciferol,Vitamin A,Vitamin C,Menadione)

Country	Effective Date	Description of action taken
United Arab Emirates		Multivitaplex were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: neomycin + dexamethasone phosphate

C.A.S. NUMBER:

OTHER NAMES: NEODECADRON occumeter

Country	Effective Date	Description of action taken
United Arab Emirates		Buffered Ophthalmic Solution Decadron/Neomycin were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: neomycin + hydrocortisone

C.A.S. NUMBER:

OTHER NAMES: Neo-Cortef

Country	Effective Date	Description of action taken
United Arab Emirates		Neo-Cortef 1.5% drops were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: neomycin + methylprednisolone

C.A.S. NUMBER:

OTHER NAMES: Neo-Medrol

Country	Effective Date	Description of action taken
United Arab Emirates		Neo-Medrol lotion were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: neomycin + nystatin + clobetasol propionate

C.A.S. NUMBER:

OTHER NAMES: Dermovate NN

Country	Effective Date	Description of action taken
United Arab Emirates		Dermovate NN ointment were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: neomycin + polymyxin B

C.A.S. NUMBER:

OTHER NAMES: Statrol®

Country	Effective Date	Description of action taken
United Arab Emirates		Statrol® drops were withdrawn by the MAH before getting approval. Statrol® ointment were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.
United Arab Emirates		Spersapolymixin drops were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: nicotinic acid (niacin) + laropiprant

C.A.S. NUMBER:

OTHER NAMES: Tredaptive, Pelzont, Trevaclyn, Cordaptive

Country	Effective Date	Description of action taken
Brazil	January 2013	The combination product will no longer be commercialized in Brazil and worldwide, after the outcome of a study indicated that the medicine did not reach its primary outcome of reduction of major cardiovascular events, as well as a demonstrated statistically significant increase in the incidence of serious non-fatal adverse events in the group receiving Cordaptive® and statin compared to the group that received only statin. Patients and health professionals were informed of the recommendations. **References:** ANVISA Pharmacovigilance Alert, and Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia). Official Gazette, cancellation of registration, 09 November 2015 (Resolution-RE No. 3054).
Europe	17 January 2013	the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) confirmed the recommendation to suspend the marketing authorisations of Tredaptive, Pelzont and Trevaclyn (nicotinic acid / laropiprant) used to treat adults with dyslipidaemia (abnormally high blood levels of fats such as triglycerides and cholesterol). Preliminary results from a large, long-term study, HPS2-THRIVE, indicated that taking nicotinic acid / laropiprant together with a statin has no significant additional benefit in reducing the risk of major vascular events such as heart attack and stroke, compared with statin therapy alone. In addition, a higher frequency of non-fatal but serious side effects was seen in patients taking these medicines. Subsequently the CHMP concluded that the benefits of Tredaptive, Pelzont and Trevaclyn no longer outweigh the risks and that their marketing authorisations should be suspended. **References:** EMA Referrals (www.ema.europa.eu) WHO Pharmaceuticals Newsletter No. 2, 2013.
Singapore	21 January 2013	The HSA suspended the marketing and supply of niacin/laropiprant in Singapore. The decision came after preliminary results from HPS2-THRIVE study failed to show a statistically significant beneficial effect of Tredaptive on the reduction of major vascular events. The study also showed an increase in the incidence of some types of non-fatal serious adverse events in the group that received Tredaptive. Consequently the balance of risks and benefits is no longer considered to be favourable. **References:** Dear Healthcare Professional Letter (DHCPL), 23 January 2013. (http://www.hsa.gov.sg/).

Chile	10 June 2013	Marketing authorisation for niacin/laropiprant is suspended. Based on information from AGEMED and EMA, the product failed to demonstrate the cardiovascular utility while known side effects of niacin, such as skin rashes, gastrointestinal problems and complications related to diabetes, and new adverse reactions such as infections and bleeding were identified. Overall it was concluded that the benefits provided by the drug do not outweigh the risks. **References:** Instituto de Salud Publica (www.ispch.cl)

PRODUCT NAME: nicotinic acid (niacin) + pentifylline

C.A.S. NUMBER:

OTHER NAMES: Cosaldon

Country	Effective Date	Description of action taken
United Arab Emirates		Cosaldon Retard prolonged release tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: nitrendipine + enalapril maleate

C.A.S. NUMBER:

OTHER NAMES: Eneas

Country	Effective Date	Description of action taken
United Arab Emirates		The application for ENEAS 10 mg/20 mg tablets (enalapril maleate / nitrendipine) was rejected by the committee for various reasons. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ombitasvir + veruprevir + ritonavir + dasabuvir

C.A.S. NUMBER:

OTHER NAMES: Viekira Pak

Country	Effective Date	Description of action taken
Brazil	December 2015 June 2017	In 2015, due to post-marketing reports of liver decompensation and liver failure, including liver transplantation or fatal outcomes, in patients treated with Viekira Pak with and without ribavirin, information has been published that the drug is not recommended for patients

		with moderate liver failure (Child-Pugh B), where the decision regarding initiation of treatment in these patients should be guided by the assessment of potential benefits and risks to the patient. Viekira Pak must not be used for patients with severe liver failure (Child-Pugh C). In 2017, ANVISA reinforced the information on the package leaflet that women who are being treated for Hepatitis C with Viekira Park should not use oral contraceptives containing ethinylestradiol, which should be discontinued approximately 2 weeks before the start of therapy with Viekira Pak. It should be noted that clinical trials showed that about 1% of patients using Viekira Pak demonstrated transient and asymptomatic elevations of alanine aminotransferase (ALT) that were 5 times or more than normal, being more frequent in women who also used medicines containing ethinylestradiol. **References:** ANVISA Pharmacovigilance Alert, and Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: orciprenaline + clobutinol + ammonium chloride

C.A.S. NUMBER:

OTHER NAMES: Orcinol

Country	Effective Date	Description of action taken
United Arab Emirates		Orcinol sugar free syrup were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: oxetacaine + polymigel

C.A.S. NUMBER:

OTHER NAMES: Strocain

Country	Effective Date	Description of action taken
United Arab Emirates		Strocain tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: oxethazaine + magnesium hydroxide + aluminium hydroxide

C.A.S. NUMBER:

OTHER NAMES: Mucacid

Country	Effective Date	Description of action taken
United Arab Emirates		The application for Mucacid was rejected by the committee for various reasons. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: oxytetracycline + hydrocortisone

C.A.S. NUMBER:

OTHER NAMES: Terracortril

Country	Effective Date	Description of action taken
United Arab Emirates		Terracortril drops and ointment were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: paracetamol + codeine

C.A.S. NUMBER:

OTHER NAMES: Tylex

Country	Effective Date	Description of action taken
Brazil	August 2013	ANVISA reminded of the contraindication of the product for the control of postoperative pain in children undergoing tonsillectomy and/or adenoidectomy. This followed the occurrence of cases of respiratory depression and death in children who received codeine in the postoperative period after tonsillectomy and/or adenoidectomy, with evidence of being ultrafast metabolisers of codeine; as well as cases of death in exposed infants, via breast milk, at high concentrations of morphine, because their mothers were ultrafast metabolisers of codeine. The medicine package leaflet in Brazil already includes these contraindications. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: paracetamol + salicylamide + caffeine + Codeine

C.A.S. NUMBER:

OTHER NAMES: Adol Compound

Country	Effective Date	Description of action taken
United Arab Emirates		Adol Compound tablest were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: peritoneal dialysis solution

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		peritoneal dialysis solution (lactate) in glucose 7% were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: Pharmaton Kiddi Syrup

C.A.S. NUMBER:

OTHER NAMES: (Nicotinamide,Riboflavin sodium phosphate,Thiamine hydrochloride,Colecalciferol 600IU equivaelnt to Colecalciferol,Dexapanthenol,Pyridoxine hydrochloride,Lysine hydrochloride,Vitamin E (all-rac-alpha-tocopheryl acetate),Calcium,Phosphorus)

Country	Effective Date	Description of action taken
United Arab Emirates		Pharmaton® Kiddi® Syrup were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: phenobarbital + pipenzolate bromide

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Egypt	27 January 2011	Withdrawal of registered oral drops containing combination of phenobarbital 0.6 mg/100 ml + pipenzolate bromide 0.4 mg/100ml.

		References: Communication from the Egypt National Pharmacovigilance Centre July, 2012.

PRODUCT NAME: pholcodine citrate + promethazine hydrochloride

C.A.S. NUMBER:

OTHER NAMES: Tixylix Linctus

Country	Effective Date	Description of action taken
United Arab Emirates		Tixylix Linctus syrup were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: pindolol + clopamide

C.A.S. NUMBER:

OTHER NAMES: Viskaldix

Country	Effective Date	Description of action taken
United Arab Emirates		Viskaldix tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: piperacillin and Tazobactam

C.A.S. NUMBER: -

OTHER NAMES:

Country	Effective Date	Description of action taken
India	23 December 2015	The Central Drugs Standard Control Organization (CDSCO) has requested all states/Union Territories drug controllers to instruct all manufacturers of piperacillin and tazobactam fixed-dose combination products to include hypokalaemia and bronchospasm in their package inserts as well as any other promotional literature. **References:** Letter issued by CDSCO on 23 December 2015. WHO Pharmaceuticals Newsletter No. 2, 2016.

PRODUCT NAME: potassium iodide + sodium iodide

C.A.S. NUMBER:

OTHER NAMES: Vitreolent

Country	Effective Date	Description of action taken
United Arab Emirates		Vitreolent drops were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: promethazine + carbocisteine

C.A.S. NUMBER:

OTHER NAMES: Rhinathiol Promethazine

Country	Effective Date	Description of action taken
United Arab Emirates		Rhinathiol Promethazine syrup were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: pseudoephedrine + triprolidine

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Viet Nam	21 July 2011	The product information was updated with a new contraindication in children under 6 years old to ensure drug safety because the use of this combination in children under 6 years old was associated with serious adverse events including death, based on EMA's decision. **References:** Drug Administration of Viet Nam Official Dispatch No. 9992/QLD-DK, 21 July 2011.

PRODUCT NAME: rosiglitazone + glimepiride

C.A.S. NUMBER:

OTHER NAMES: Avandaryl

Country	Effective Date	Description of action taken
United Arab Emirates		Avandaryl (rosiglitazone / glimepiride) 4 mg/1 mg, 4 mg/2 mg, and 4 mg/4 mg were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:**

		Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: rosiglitazone + metformin

C.A.S. NUMBER:

OTHER NAMES: Avandamet

Country	Effective Date	Description of action taken
United Arab Emirates		Avandamet 1 mg/500 mg, 2 mg/500 mg, 4 mg/500ml, 2 mg/1000 mg, 4 mg/1000 mg (rosiglitazone / metformin) were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ruscogenine + trimebutine

C.A.S. NUMBER: 472-11-7 (ruscogenine), 39133-31-8 (trimebutine)

OTHER NAMES:

Country	Effective Date	Description of action taken
Viet Nam	18 August 2017	The marketing authorisation for the combination of ruscogenine and trimebutine is suspended due to limited safety and efficacy data. The products are recalled. **References:** Drug Administration of Viet Nam Official documents No. 303/QĐ-QLD, 18 August 2017.

PRODUCT NAME: salmeterol + fluticasone propionate

C.A.S. NUMBER:

OTHER NAMES: Bexitrol-F

Country	Effective Date	Description of action taken
United Arab Emirates		The application for Bexitrol®-F 25/250 was rejected by the committee for various reasons. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: saxagliptin + metformin

C.A.S. NUMBER:

OTHER NAMES: Kombiglyze XR

Country	Effective Date	Description of action taken
Brazil	June 2016	The package leaflet of the product was updated with information on increased risk of of hospitalization for heart failure in patients treated with saxagliptin compared to placebo, as reported by a clinical study. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: Seroquel Patient Starter Pack

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		Seroquel patient starter pack (quetiapine, ovidone, calcium hydrogen phosphate dihydrate, microcrystalline cellulose, sodium starch glycollate Type A, lactose monohydrate, magnesium stearate) tablets were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: simethicone + Aspergillus oryzae dried extract

C.A.S. NUMBER:

OTHER NAMES: Elzym

Country	Effective Date	Description of action taken
United Arab Emirates		Elzym capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: simethicone + magnesium aluminium silicate

C.A.S. NUMBER:

OTHER NAMES: Alkasid

Country	Effective Date	Description of action taken
United Arab Emirates		Olysio 150 mg capsules were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: simvastatin AND amiodarone

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
USA	15 December 2011	In patients who are taking both simvastatin and amiodarone, the dose of simvastatin should not exceed 20 mg per day. **References:** FDA Drug Safety Communication, US FDA, 15 December 2011 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 2, 2012.

PRODUCT NAME: simvastatin and atorvastatin

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
New Zealand	June 2011	Medsafe reminded prescribers of the potential for serious adverse reactions when statins are prescribed with medicines that inhibit the CYP3A4 isoenzyme. Serious myopathies including life-threatening and fatal cases of rhabdomyolysis have been reported. **References:** Prescriber Update Vol. 32 No. 2, June 2011 (www.medsafe.govt.nz). WHO Pharmaceuticals Newsletter No. 4, 2011.

PRODUCT NAME: sodium benzoate + caffeine

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Viet Nam	2 July 2010	The use of this combination in the preterm neonate was rejected and the contraindication added . **References:** Drug Administration of Viet Nam Official Dispatch No. 6945/QLD-DK 02, July 2010.

PRODUCT NAME: sodium ferric gluconate complex

C.A.S. NUMBER:

OTHER NAMES: Ferrlecit

Country	Effective Date	Description of action taken

United Arab Emirates	Ferrlecit drops, tablets and solution for injection were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: soyabean oil + lecithin

C.A.S. NUMBER:

OTHER NAMES: Celepid

Country	Effective Date	Description of action taken
United Arab Emirates	2012	Registration for Celepid 10% and 20% infusion were suspended. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: streptokinase + streptodornase

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Viet Nam	13 September 2012	The marketing authorisation for this product is suspended due to limited safety and efficacy data. **References:** Drug Administration of Viet Nam Official documents No. 13702/QLD-DK, 13 September 2012.

PRODUCT NAME: Stresstabs ® with zinc

C.A.S. NUMBER:

OTHER NAMES: contains: Copper (Cupric oxide), Folic acid, Niacinamide, Pantothenic acid (Calcium Pantothenate), Vitamin B1 (Thiamine mononitrate) , Vitamin B 12 (Cyanocobalamin), Vitamin B2 (Riboflavin), Vitamin B6 (Pyridoxine Hydrochloride), Vitamin C (Ascorbic acid)

Country	Effective Date	Description of action taken
United Arab Emirates		Stresstabs ® with zinc were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: sulfadoxine + pyrimethamine

C.A.S. NUMBER:

OTHER NAMES: Fansidar

Country	Effective Date	Description of action taken
United Arab Emirates		Fancidar injection products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: sulfamethoxazole + trimethoprim

C.A.S. NUMBER:

OTHER NAMES: Bactrim

Country	Effective Date	Description of action taken
United Arab Emirates		Bactrim IM products were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: tetrahydrocannabinol (THC) + cannabidiol (CBD)

C.A.S. NUMBER:

OTHER NAMES: Sativex

Country	Effective Date	Description of action taken
United Arab Emirates		Sativex™ Oromucosal Spray products were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: triple sulfa (sulfabenzamide + sulfacetamide + sulfathiazole)

C.A.S. NUMBER:

OTHER NAMES: Sultrin

Country	Effective Date	Description of action taken
United Arab Emirates		Sultrin triple sulfa cream were withdrawn by the MAH before getting approval. **References:**

	Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: valsartan + hydrochlorothiazide

C.A.S. NUMBER:

OTHER NAMES: ExTenz H, Co-cinfaval, Covalis, Diostar-plus, Valzaar H

Country	Effective Date	Description of action taken
United Arab Emirates	2018	Valsartan / hydrochlorothiazide combination products were temporarily suspended. The MAH was requested submit relationship letter including flow chart mentioning the parties involved in bulk manufacturing, batch releasing, primary packaging, secondary packaging & marketing with sign and stamp from both parties, with products involved under the agreement. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.
United Arab Emirates	2018	ExTenz H (160/12.5 mg, 160/25 mg, 320/25 mg), Co-Cinfaval 160 mg/25 mg, and Diostar-Plus 160/25 mg tablets were suspended. Covalis 320/12.5 mg and 320/25 mg tablets were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: vemurafenib + ipilimumab

C.A.S. NUMBER:

OTHER NAMES: Zelboraf (vemurafenib) Yervoy (ipilimumab)

Country	Effective Date	Description of action taken
Brazil	May 2013	Health professionals were warned about the risk of concomitant administration of Zelboraf® (vemurafenib) and Yervoy® (ipilimumab). Safety updates on the combined use of the products included: elevations of severe transaminases in patients receiving vemurafenib with ipilimumab in a phase I clinical study, bilirubin elevations in patients who had elevated transaminases, ranging from moderate to severe, indicating that the administration of both drugs may generate hepatic impairment. Thus it is not recommended to use the two concomitantly. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

Group Products

PRODUCT NAME: acetaminophen prescription products

C.A.S. NUMBER: 103-90-2

OTHER NAMES:

Country	Effective Date	Description of action taken
USA	13 January 2011	The U.S. Food and Drug Administration (The US FDA) decided to limit the strength of acetaminophen in prescription drug products, which are predominantly combinations of acetaminophen and opioids, to 325 mg per tablet, capsule, or other dosage unit. In addition, a Boxed Warning highlighting the potential for severe liver injury and a Warning highlighting the potential for allergic reactions (swelling of the face, mouth, and throat, difficulty breathing, itching or rash) will be added to the label of all prescription products that contain acetaminophen. **References:** MedWatch Safety Information, US FDA, 13 January 2011 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 1, 2011. WHO Pharmaceuticals Newsletter No. 5, 2013. WHO Pharmaceuticals Newsletter No. 1, 2014.

PRODUCT NAME: acetylcysteine-containing products

C.A.S. NUMBER: 616-91-2

OTHER NAMES: Exomuc

Country	Effective Date	Description of action taken
Madagascar	28 July 2010	Mucolytics and thinners containing acetylcysteine are contraindicated in children less than 2 years of age. **References:** Communication from the Madagascar National Pharmacovigilance Centre July, 2012.

PRODUCT NAME: anhydrous glucose containing injection solution

C.A.S. NUMBER: 50-99-7

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		Andydrous glucose containing products (e.g. Glucose IV infusion, Dextrose injection), including combination products with calcium chloride,magnesium chloride, sodium acetate, and sodium chloride (e.g. peritoneal dialysis solution in glucose, Dextran IV infusion in glucose, etc.) were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:**

		Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: antihistamines, first generation

C.A.S. NUMBER:

OTHER NAMES: chlorpheniramine, oxomemazine, alimemazine, phenylephrine

Country	Effective Date	Description of action taken
Syrian Arab Republic	29 May 2011	Updates in the package insert to add the following contraindication: First generation antihistamines are contraindicated in children less than two years old. **References:** Circular from the Ministry of Health No. 14852/20/1, 2011.

PRODUCT NAME: antipsychotics

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
USA	22 February 2011	The U.S. Food and Drug Administration (US FDA) notified health-care professionals that the pregnancy section of drug labels for the entire class of antipsychotic medicines has been updated to include consistent information about the potential risk for extrapyramidal signs (EPS) and withdrawal symptoms in newborns whose mothers were treated with these medicines during the third trimester of pregnancy. The EPS and withdrawal symptoms in newborns may include agitation, abnormally increased or decreased muscle tone, tremor, sleepiness, severe difficulty of breathing, and difficulty in feeding. **References:** FDA Drug Safety Communication, US FDA, 22 February 2011 (www.fda.gov). WHO Pharmaceuticals Newsletter No 2, 2011.

PRODUCT NAME: apixaban, dabigatran, rivaroxaban

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Brazil	March 2013	Based on findings from clinical studies and post-marketing evidence, which indicated major bleeding events, including events with fatal outcome, were significant for the new oral anticoagulants, health professionals were reminded of the contraindications common to the products as well as those specific to each product, attention to renal function, and

		warnings and precautions of use to minimize the risk of bleeding. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: artemisinin and its derivatives

C.A.S. NUMBER:

OTHER NAMES: e.g. artemisinin (63968-64-9), artemether (CAS 71963-77-4)

Country	Effective Date	Description of action taken
Viet Nam	20 May 2013	The marketing authorisation for artemisinin-containing medicine and its derivatives are withdrawn to prevent artemisinin resistance. **References:** Drug Administration of Viet Nam Official documents No.112/QĐ-QLD, 20 May 2013.

PRODUCT NAME: benzocaine topical products

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
USA	7 April 2011	The US FDA recommended that benzocaine products, including sprays, gels, and liquids, should not be used on children less than two years of age, except under the advice and supervision of a health-care professional. The US FDA continues to receive reports of methemoglobinaemia, a serious and potentially fatal adverse effect, associated with benzocaine products. **References:** FDA Drug Safety Communication, US FDA, 7 April 2011 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 3, 2011. WHO Pharmaceuticals Newsletter No. 4, 2018.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: benzyl alcohol containing products

C.A.S. NUMBER: 100-51-6

OTHER NAMES:

Country	Effective Date	Description of action taken
Egypt	5 January 2012	Product information has been updated to include a Black Box Warning to not use benzyl alcohol in neonates and infants. A contraindication has been added to no administer injections preserved with benzyl alcohol to premature

		infants, neonates, children below 13 years, pregnant women, or nursing mothers. Benzyl alcohol is potentially toxic when administered locally to neural tissue. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.
Saudi Arabia	25 February 2012	According to the Saudi Food and Drug Authority (SFDA) it is not recommended to use benzyl alcohol containing diluents in preparing injectable medicines for pa ediatric patients due to the potential risk of developing gasping syndrome. **References:** Personal communication from SFDA, 25 February 2012. WHO Pharmaceuticals Newsletter No. 2, 2012.

PRODUCT NAME: bisphosphonates

C.A.S. NUMBER:

OTHER NAMES: e.g. alendronate , ibandronate , risedronate , pamidronate , clodronate, zoledronic acid

Country	Effective Date	Description of action taken
New Zealand	September 2011	Medsafe reminded prescribers that bisphosphonates have been associated with a number of rare but serious ocular inflammatory effects, including uveitis and scleritis. **References:** Prescriber Update Vol. 32 No. 3, September 2011 (www.medsafe.govt.nz). WHO Pharmaceuticals Newsletter No. 5, 2011.
Canada	19 December 2011	Health Canada updated its review of bisphosphonates to include a slightly increased risk of atypical femur fracture. Although the risk is higher, it is still extremely small and the benefits of using bisphosphonate drugs to prevent fractures associated with osteoporosis outweigh the risk of an atypical femur fracture. **References:** Advisories, Warnings and Recalls, Health Canada, 19 December 2011 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 1, 2012. WHO Pharmaceuticals Newsletter No. 1, 2017. WHO Pharmaceuticals Newsletter No. 2, 2017.
Brazil	October 2013	Based on recent study outcomes, ANVISA warned about possible risk factors for osteonecrosis of the jaw and atypical femoral fractures related to the long-term use of bisphosphonates. **References:** ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: carbocisteine and acetylcysteine containing mucolytics

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Madagascar	29 July 2010	Mucolytics and thinners containing carbocysteine are contraindicated in children less than 2 years of age. **References:** Communication from the Madagascar National Pharmacovigilance Centre July, 2012.
Viet Nam	31 August 2010	The product information was updated with a new contraindication in children under 2 years old to ensure drug safety dur to the risk of increased bronchial congestion in infants (according to ANSM's decision). The decision took into consideration similar action by the French regulator. **References:** Drug Administration of Viet Nam Official Dispatch No. 10367/QLD-DK, 31 August 2010.
Egypt	2 September 2010	Contraindicated for children less than 2 years for all products containing mucolytic substances including carbocsteine, acetylcisteine, essential terpentine oil, meglumine benzoate, helicidine. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.

PRODUCT NAME: cetirizine/levocetirizine

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Egypt	9 December 2010	Communication from the Egypt National Pharmacovigilance Centre July, 2012. **References:**

PRODUCT NAME: chloramphenicol containing medicines

C.A.S. NUMBER:

OTHER NAMES: e.g. Chloroptic, Isopto Fenicol, Spersadex, Spersacet C, Cortiphenol H, Spersadexoline, Spersanicol, Synthomycetine

Country	Effective Date	Description of action taken
United Arab Emirates		Chloramphenicol-containing products were withdrawn by the MAH before getting approval. **References:**

	Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: chlormezanone and chlormezanone combinations

C.A.S. NUMBER: 80-77-3

OTHER NAMES: chlormezanone; chlormezanone + paracetamol; chlormezanone + diazepam; chlormezanone + diazepam + pentaerythritol; chlormezanone + diazepam + anisotropine;chlormezanone + ibuprofen + metamizole

Country	Effective Date	Description of action taken
Chile	17 April 2012	The conditions of sale for chlormezanone and chlormezanone combination products are modified, from sale with medical prescription to sale with retained medical prescription. The decision follows reports of ADRs invoving these products in Chile, among which one reported Stevens-Johnson syndrome (SJS). Other regulators, EMA, Agence Nationale de Sécurité du Médicament (ANSM) and PAHO, also reported similar SJS cases. **References:** Instituto de Salud Publica (www.ispch.cl)

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: codeine-containing over-the-counter medicines

C.A.S. NUMBER: -

OTHER NAMES:

Country	Effective Date	Description of action taken
Armenia	2015	After an assessment by the Scientific Centre of Drug and Medical Technology Expertise after Academician E. Gabrielyan (SCDMTE), the product information of codeine-containing medicinal products was updated to include a contraindication for use in children up tp 12 years for cough and cold because of the risk of respiratory depression associated with codeine use. **References:** Communication from Armenian National Pharmacovigilance Centre, 2015. EMA press release, April 2015.
United Kingdom	October 2010	Medicines and Healthcare products Regulatory Agency (MHRA) has announced that a UK review on the benefits and risks of over-the-counter (OTC) oral liquid cough medicines containing codeine has concluded that the risks outweigh the benefits in children and young people under 18 years. Therefore, it has been advised that codeine-containing OTC liquid medicines should not be used for cough suppression in children and people younger than age 18 years. **References:**

		Drug Safety Update, MHRA, Volume 4, Issue 3, H3 October 2010 (www.mhra.gov.uk). WHO Pharmaceuticals Newsletter No. 6, 2010. WHO Pharmaceuticals Newsletter No. 4, 2013.
Europe	26 June 2013	The Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) has endorsed by consensus a series of risk-minimisation measures to address safety concerns with codeine-containing medicines when used for the management of pain in children. The recommendations are: - Codeine-containing medicines should only be used to treat acute (short-lived) moderate pain in children above 12 years of age, and only if it cannot be relieved by other painkillers such as paracetamol or ibuprofen, because of the risk of respiratory depression associated with codeine use. - Codeine should not be used at all in children (aged below 18 years) who undergo surgery for the removal of the tonsils or adenoids to treat obstructive sleep apnoea, as these patients are more susceptible to respiratory problems. - The product information of these medicines should carry a warning that children with conditions associated with breathing problems should not use codeine. In addition, codeine should not be used in people of any age who are known to be ultra-rapid metabolisers nor in breastfeeding mothers (because codeine can pass to the baby through breast milk). The product information for codeine should also include general information for healthcare professionals, patients and carers on the risk of morphine side effects with codeine, and how to recognise their symptoms. **References:** EMA Referrals (www.ema.europa.eu) WHO Pharmaceuticals Newsletter No. 5, 2013.
Europe	13 March 2015	EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has recommended restrictions on the use of codeine-containing medicines for cough and cold in children because of the risk of serious side effects with these medicines, including the risk of breathing problems. The PRAC recommended specifically that: - Codeine should be contraindicated in children below 12 years. This means it must not be used in this patient group. - Use of codeine for cough and cold is not recommended in children and adolescents between 12 and 18 years who have problems with breathing. - All liquid codeine medicines should be available in child-resistant containers to avoid accidental ingestion. The PRAC further recommended that codeine must not be used in people of any age who are known to convert codeine into morphine at a faster rate than normal ('ultra-rapid metabolisers') nor in breastfeeding mothers, because codeine can pass to the baby through breast milk. **References:**

		EMA press release, 13 March 2015. WHO Pharmaceuticals Newsletter No. 3, 2015.
Indonesia	16 March 2016	The National Agency of Drug and Food Control (NADFC) has informed that the product information of codeine should be revised with additional information due to risk of respiratory depression. product information should provide contraindication in children **References:** Dear Healthcare Professional Communication PW.02.03.343.3.03.16.1166
Chile	30 May 2016	New indication restrictions and contraindications are introducted for codeine + paracetamol, and codeine + chlorphenamine + pseudoephedrine. The approved indications must start with "In adults and children over 12 years of age it is indicated in ..." In addition, in cases where it is indicated as an analgesic, it must be specified as "In children older than 12 years, it can only be used after having ruled out the use of other analgesics." New contraindications: This medicine should not be used by children under 12 years of age. Neither should be used in older adolescents, if it is for the purpose of controlling pain after an operation to remove tonsils or adenoids. Women who are breastfeeding should not use codeine-based medications, as it can pass into breast milk and affect the child. In addition, people who can process codeine at a faster rate than normal, should not take this medicine as it may give rise to an excessive amount of an active metabolite in a very short period of time, which can cause serious health problems. The decision took into consideration similar actions by the US FDA and the EMA. **References:** Instituto de Salud Publica (www.ispch.cl). US FDA Drug Safety Communication, 15 August 2012 (https://www.fda.gov/drugs). EMA Referrals, 14 June 2013 (www.ema.europa.eu).
Viet Nam	7 July 2016	The use of codeine is restricted to: - The treatment of acute moderate pain which is not considered to be relieved by other analgesics such as paracetamol or ibuprofen (alone) in patients older than 12 years of age. - The symptomatic relief of an unproductive dry cough in patients older than 12 years of age. The product information is updated with new contraindications: - In women during breastfeeding. - In patients for whom it is known they are CYP2D6 ultra-rapid metabolisers.

		- In all paediatric patients (0-18 years of age) who undergo tonsillectomy and/or adenoidectomy for obstructive sleep apnoea syndrome. - In children below the age of 12 years for the symptomatic treatment of cough. The decision took into consideration similar actions by EMA and US FDA. **References:** Drug Administration of Viet Nam Official Dispatch No. 20534/QLD-DK, 07 July 2016.
Oman	2013 2015	Following PRAC recommendations, in 2013, the use of codeine-containing OTC medicines for pain relief in children is restricted. The HCPs are informed through the Circular. In 2015, codeine-containing medicines are not to be used in children below 12 years for cough and cold. **References:** Oman Ministry of Health Circular No. 89, 2013, and No. 41, 2015.
United Arab Emirates		Codipront capsules and syrup were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: combined hormonal contraceptives

C.A.S. NUMBER: -

OTHER NAMES: all contraceptives containing low-dose estrogen and the following progestogens: chlormadinone, desogestrel, dienogest, drospirenone, etonogestrel, gestodene, nomegestrol, norelgestromin and norgestimate;

e.g. Zoely (nomegestrol acetate/estradiol), Ioa (no

Country	Effective Date	Description of action taken
Armenia	2013	After an assessment by the Scientific Centre of Drug and Medical Technology Expertise after Academician E. Gabrielyan (SCDMTE), the product information of cyproterone/ethinylestradiol containing medicinal products was updated to include the information on risk of tromboembolism. **References:** Communication from Armenian National Pharmacovigilance Centre, 2013. EMA press release, 08 February 2013.
Oman	2013	Temporary suspension of Diane-35 due to safety concern raised by French regulator. The suspension was later lifted as the product was allowed for specific indications.

		References: Oman Ministry of Health Circular No. 11, 2013, and No. 131, 2013.
Australia	October 2011	The Therapeutic Goods Administration (TGA) announced that the risk of venous thromboembolism (VTE) is being included in the product information for drospirenone containing combined oral contraceptives. Oral contraceptives are contraindicated in women with severe or multiple risk factor(s) for venous or arterial thrombosis. **References:** Medicines Safety Update Vol. 2, No. 5, October 2011 (www.tga.gov.au). WHO Pharmaceuticals Newsletter No. 6, 2011. WHO Pharmaceuticals Newsletter No. 2, 2015. WHO Pharmaceuticals Newsletter No. 1, 2017.
Chile	17 June 2013	New contraindications are added for combined hormonal contraceptives drospirenone + ethynyl estradiol, drospirenone + ethynyl estradiol + levomefolate calcium, drospirenone + estradiol. The products are contraindicated in: • Presence or history of venous thrombosis (deep vein thrombosis, pulmonary embolism). • Presence or history of arterial thrombosis (eg, stroke, myocardial infarction) or prodromal conditions (eg, angina pectoris and transient ischemic attack). • Presence or history of stroke • Presence of one or more serious or multiple risk factors for arterial thrombosis: • diabetes mellitus with vascular symptoms, • severe hypertension, • severe dyslipoproteinemia. • Hereditary or acquired predisposition to venous or arterial thrombosis, such as resistance to activated protein C, antithrombin III deficiency, protein C deficiency, protein S deficiency, hyperhomocysteinemia and antiphospholipid antibodies (anticardiolipin antibodies, lupus anticoagulant). **References:** Instituto de Salud Publica (www.ispch.cl)
Europe	16 January 2014	European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) concluded that the benefits of combined hormonal contraceptives (CHCs) in preventing unwanted pregnancies continue to outweigh their risks, and that the well-known risk of venous thromboembolism (VTE) with all CHCs is small. The review reinforced the importance of ensuring that clear and up-to-date information is provided to women who use these medicines and to the healthcare professionals giving advice and clinical care. **References:** European Commission final decision (www.ema.europa.eu)

		WHO Pharmaceuticals Newsletter No. 2, 2013. WHO Pharmaceuticals Newsletter No. 4, 2013. WHO Pharmaceuticals Newsletter No. 6, 2013.
Montenegro	12 February 2014	Based on EMA referral and in accordance with Law on medicines, the Agency for Medicines and Medical Devices of Montenegro (CALIMS) has sent DHPC to relevant HCPs to inform them of the perceived increased risk of venous thromboembolism. **References:** CALIMS, Direct healthcare professional communications.
Viet Nam	3 June 2014	Cyproterone and ethinylestradiol containing medicines are restricted to the treatment of moderate to severe acne related to androgen-sensitivity (with or without seborrhoea) or hirsutism, in women of reproductive age. For the treatment of acne, these medicines should only be used after topical therapy or systemic antibiotic treatment has failed. **References:** Drug Administration of Viet Nam Official Dispatch No. 9049/QLD-DK, 03 June 2014.
Brazil	January 2013 April 2013 November 2013 December 2014 June 2015 May 2017	In January 2013, following a statement from the French regulator that it would perform a benefit-risk assessment of Diane® 35 and its generics used for the treatment of acne, ANVISA emphasized the contraindication for this product in patients with a history of thrombotic processes. No indication of health risk signal was detected in the database of the Agency's notification system at the point. It reminded that the package leaflet already included contraindication in the presence or history of arterial or venous thromboembolic/thromboembolic processes. In April 2013, ANVISA informed of the restrictions on the use of estrogen-androgen hormone therapies after the withdrawal of Diane 35® by the French regulator in January. ANVISA warned of the risk of venous and arterial thromboembolic events, which is elevated when the product is administered as long-term therapy and when there are other concomitant factors such as smoking, overweight, dyslipidemias and advanced age. Recommendations for risk mitigation were also communicated. In November 2013, ANVISA warned about the risks of thrombotic/thromboembolic disorders associated with 3rd or 4th generation combined oral contraceptives (COC). following safety reviews performed by the US FDA and EMA. ANVISA emphasized the recommendations already included in the package leaflets of the products available in Brazil. In 2014, ANVISA updated and reinforced the guidelines for prescribing and use of COCs. Adequate medical evaluation was recommended, with inquiry of individual and family history of the patient which serves to determine the

	appropriate contraceptive method. Women should always be informed by health professionals about the risks associated with the use of oral contraceptives. Some risk factors that cause the use of contraceptive medications to be contraindicated are highlighted, as well as warnings about the impact of smoking and the increased risks with age. Another alert specially addressed to physicians was issued in June 2015, reinforcing the recommendations already made and highlighting the situations that contraindicate its use.chlormadinone + ethinylestradiol In 2017, Health professionals were informed of the introduction of a new indication for Belara® (chlormadinone 2mg + ethinylestradiol 0.03 mg): treatment of moderate papulopustular acne, strictly limited for women who desire contraception and for whom the safe use of the drug for contraception has been carefully evaluated. They were reminded that for the treatment of acne only, there is a negative risk-benefit profile for the use of Belara®, where the risk related to venous thromboembolism events outweighs the benefits related to acne treatment. Thus, for patients undergoing treatment of moderate papulopustular acne with Belara®, who no longer desire the contraceptive effects of the product, treatment should be discontinued. **References:** ANVISA Pharmacovigilance Alert, and Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: corticosteroids-containing eye drops

C.A.S. NUMBER:

OTHER NAMES: e.g. prednisolone, loteprednol, dexamethasone and fluormetolone

Country	Effective Date	Description of action taken
Brazil	June 2014	Upon learning about the indiscriminate use of eye drops containing corticosteroids, ANVISA issued an alert highlighting the risks of prolonged use , which includ increased intraocular pressure in certain patients, a fact that can cause damage to the optic nerve, visual field failures, cataract formation or, in some cases, occurrence of corneal perforations. It has been stressed that these should be used appropriately, based on medical prescription and with the appropriate follow-up of a health professional. **References:** ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia).

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: cough & cold preparations

C.A.S. NUMBER:

OTHER NAMES: brompheniramine, chlorpheniramine, diphenhydramine, doxylamine, promethazine, triprolidine, dextromethorphan, phenylephrine, pseudoephedrine, oxymetazoline

Country	Effective Date	Description of action taken
Sudan	9 April 2012	The packaging and/or inner labels for all the products will be required to carry advisory information and directions for use such as: •The specified active ingredients included in orally administered nonprescription cough and cold products should not be used in children under 6 years of age • Children aged 6 to 12 years: o A strengthened warning and requirement for child resistant packaging were introduced. o Do not use for longer than 7 days. o Read the complete label and package insert prior to use and follow all label instructions. o For liquid formulations the following statement should be included with the directions of use: "Use only the measuring device provided." o Do not exceed the single and maximum daily dose and duration of use recommended, higher doses may result in serious harm. o Do not give with any other cough and cold medications since serious harm may occur. o Consult a physician or pharmacist prior to combining with other medications, including herbal or natural health products, prescription drugs or nonprescription drugs. **References:** Communication from the Sudan National Pharmacovigilance Centre, July 2012.
Syrian Arab Republic	22 January 2015	Updates in the package insert to add the following warnings: these products are not recommended for children under 6 years of age. Treatment beyond 5 days is not recommended. **References:** Circular from the Ministry of Health No. 1147/20/1, 2015/

PRODUCT NAME: dextromethorphan-containing products

C.A.S. NUMBER:

OTHER NAMES: e.g. Riaphan, Emikoff, Adol Cold Hot Therapy, Romilar

Country	Effective Date	Description of action taken
United Arab Emirates		Riaphan (dextromethorphan) and Adol Cold Hot Therapy (dextromethorphan + paracetamol + pseudoephedrine) were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. Romilar (dextromethorphan) tablets, drops, Romilar

		Expectorant syrup, and Emikoff (dextromethorphan + pseudoephedrine + chlorphenamine) were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: dextrose (+ sodium chloride)

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		Dextrose injection and infusion products were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: diiodohydroxy quinoline, phthalyl sulfathiazole, streptomycin sulfate, homatropine methyl bromide

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Egypt	12 May 2011	Contraindicated in cases of enlarged prostate, glaucoma and the elderly. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.

PRODUCT NAME: diloxanide-containing products

C.A.S. NUMBER:

OTHER NAMES: Furamide (diloxanide), Entamizole (diloxanide + metronidazole)

Country	Effective Date	Description of action taken
United Arab Emirates		Furamide and Entamizole were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: diphenhydramine-containing products

C.A.S. NUMBER:

OTHER NAMES: e.g. Histergan, Amydramine-II (diphenhydramine), Adol PM Hot Therapy (diphenhydramine + paracetamol), B-Calm (diphenhydramine + belladonna tincture + chloral hydrate)

Country	Effective Date	Description of action taken
United Arab Emirates		The application for B-Calm was rejected by the committee for various reasons. Amydramine-II and Adol PM Hot Therapy were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. While Histergan tablets and syrup were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: econazole-containing products

C.A.S. NUMBER:

OTHER NAMES: Pevaryl, Spectazole, Ecostatin, Gyno-pevaryl, Pevisone (econazole + triamcinolone)

Country	Effective Date	Description of action taken
United Arab Emirates		Pevison, as well as Pevaryl 1% lotion, powder solution, gel and shampoo were withdrawn by the MAH before getting approval; while Pevaryl 1% spray and Gyno-Pevaryl Depot 150 mg pessary were voluntarily withdrawn by the MAH either for commercial reasons other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: fibrate, fenofibrate

C.A.S. NUMBER:

OTHER NAMES: fenofibrate, fenofibrate + pravastatin, fenofibrate + simvastatin;

Country	Effective Date	Description of action taken
Chile	18 June 2013	The products' information is updated with new indication restrictions. The approved indications are: Supplement to diet and non-pharmacological management (such as exercise, weight loss) in the cases indicated in the treatment of severe hypertriglyceridemia with or without low HDL cholesterol, and in mixed hyperlipidemia when statins are contraindicated or not tolerated by the patient. The decision was based on CHMP recommendation that fibrates should not be used as first-line drugs in the treatment of dyslipidemias, except in severe

	hypertriglyceridemia, in cases of intolerance to statins and in other specific and well-defined cases that do not include the active principles bezafibrate, ciprofibrate and gemfibrozil, nd one of which specifically covers the active principle fenofibrate. **References:** Instituto de Salud Publica (www.ispch.cl). EMA Referrals (www.ema.europa.eu), 28 February 2011.

PRODUCT NAME: fibrinogen-containing sealant

C.A.S. NUMBER:

OTHER NAMES: Evicel, Beriplast, Tissucol, Tisseel Duo, Tachosil

Country	Effective Date	Description of action taken
Brazil	July 2013 February 2016	In 2013, ANVISA warned about the risk of gas embolism related to the use of fibrogen-containing solutions as a sealant administered by spray, by the use of the spray device at a pressure higher than recommended or with the distance of application of the surface lower than indicated by the manufacturer, following an evaluation report issued by the Committee of Medicinal Products for Human Use (CHMP) of the EMA. Thus, ANVISA requested the MAH to minimize risks for these drugs when administered in spray form. Letter to healthcare professionals was issued. In 2016, ANVISA recommended to avoid adhesions of tissues in unwanted locations. It took into consideration similar recommendations by EMA and the Health Products Regulatory Authority (HPRA, Ireland), issued after evaluating case reports related to abdominal surgeries near the intestine, which reported the risk of adhesions to gastrointestinal tissues, leading to intestinal obstruction associated with TachoSil. **References:** ANVISA Pharmacovigilance Alert, and Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: finasteride, dutasteride

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
USA	9 June 2011	The US FDA notified health-care professionals that the Warnings and Precautions section of the labels for the 5-alpha reductase inhibitor (5-ARI) class of drugs which include finasteride and dutasteride has been revised to include new

		safety information about the increased risk of being diagnosed with a more serious form of prostate cancer. **References:** FDA Drug Safety Communication, US FDA, 9 June 2011 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 4, 2011.
Canada	19 March 2012	Health Canada informed health-care professionals and the public that finasteride (Proscar®, Propecia® and their generic equivalents) and dutasteride (Avodart® and Jalyn® (a combination drug product containing dutasteride and tamsulosin)) may be associated with an increased risk of developing a serious form of prostate cancer known as high-grade prostate cancer. High-grade prostate cancer is an aggressive type of prostate cancer that grows and spreads more quickly than low-grade prostate cancer. This type of cancer is rare, and the increased risk seen with finasteride and dutasteride drugs is still considered very small. **References:** Advisories, Warnings and Recalls, Health Canada, 19 March 2012 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 3, 2012.

PRODUCT NAME: fluocinolone acetonide containing products

C.A.S. NUMBER:

OTHER NAMES: Synalar, Procto Synalar (fluocinolone acetonide + lidocaine), Synalar®-N (fluocinolone acetonide + neomycin)

Country	Effective Date	Description of action taken
United Arab Emirates		Synalar (fluocinolone acetonide) cream and ointment, Procto Synalar (fluocinolone acetonide + lidocaine) ointment and suppository, as well as Synalar®-N (fluocinolone acetonide + neomycin) cream and ointment were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: fluoroquinolones

C.A.S. NUMBER:

OTHER NAMES: ciprofloxacin, gemifloxacin, levofloxacin, moxifloxacin, norfloxacin, ofloxacin, pefloxacin, lomefloxacin

Country	Effective Date	Description of action taken
Egypt	16 February 2012	Avoid fluoroquinolones in patients with known history of myasthenia gravis. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.

Canada	9 March 2012	Fluoroquinolone antibiotics should be avoided in patients with a known history of myasthenia gravis because they may exacerbate symptoms of myasthenia gravis. **References:** Advisories, Warnings and Recalls, Health Canada, 9 March 2012 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 6, 2011. WHO Pharmaceuticals Newsletter No. 2, 2012. WHO Pharmaceuticals Newsletter No. 1, 2016. WHO Pharmaceuticals Newsletter No. 2, 2017.
Indonesia	3 October 2013	The product information of all fluoroquinolone containing products should be revised to inform the risk of peripheral neuropathy. **References:** Dear Healthcare Professional Communication PW.02.03.342.3.10.4186
Viet Nam	27 April 2017	The use of fluoroquinolones in the treatment of acute bacterial sinusitis (ABS), acute bacterial exacerbation of chronic bronchitis (ABECB) and uncomplicated urinary tract infections (UTIs) are restricted for those who do not have alternative treatment options. These restrictions intend to enhance warnings about disabling and potentially permanent side effects and to limit their use in patients with less serious bacterial infections. **References:** Drug Administration of Viet Nam Official Dispatch No. 5748/QLD-DK, 27 April 2017.

PRODUCT NAME: fluticasone propionate containing products

C.A.S. NUMBER: 80474-14-2

OTHER NAMES: Flutiderm, Flovent, Flixotide, Flonase, Bexitrol® F 25/125 (salmeterol + fluticasone propionate)

Country	Effective Date	Description of action taken
United Arab Emirates		The application for Bexitrol® F 25/125 inhaler was rejected by the committee for various reasons. Flutiderm cream and ointment were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: folic acid containing products

C.A.S. NUMBER:

OTHER NAMES: Neoferon (folic acid + carbonyl iron), 4M6 (folic acid + sildenafil + cyanocobalamin + pyridoxine)

Country	Effective Date	Description of action taken
United Arab Emirates		Neoferon were withdrawn by the MAH before getting approval. 4M6 products were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: gadolinium-based contrast agents (GBCA)

C.A.S. NUMBER:

OTHER NAMES: "gado-" e.g. Gadovist, Omniscan, Magnevist, Magnegita, OptiMark

Country	Effective Date	Description of action taken
Egypt	3 June 2010	Medicinal products containing Gadversetamide will now be contraindicated in patients with 1) acute or chronic severe renal insufficiency (glomerular filtration rate <30 mL/min/1.73m2), or 2) acute renal insufficiency of any severity due to the hepato-renal syndrome or in the perioperative liver transplantation period. Medicinal products containing Gadversetamide are not recommended for use in children below the age of two years. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.
Europe	21 July 2017	Based on a review of the PRAC's recommendation, the CHMP found that the benefit-risk balance is no longer favorable for certain linear GBCAs. **References:** European Commission final decision (www.ema.europa.eu) WHO Pharmaceuticals Newsletter No. 3, 2017.
Montenegro	6 December 2017	Based on EMA referral and in accordance with Law on medicines, the Agency for Medicines and Medical Devices of Montenegro (CALIMS) has sent DHPC to relevant HCPs to inform them of the perceived increased risk of deposition of gadolinium in brain and other tissues. **References:** CALIMS, Direct healthcare professional communications.
Indonesia	6 August 2018	The product information for GBCA should provide box warning on the risk of gadolinium deposits in brain. **References:** Dear Healthcare Professional Communication T-PW.04.35.351.08.18.75

United Arab Emirates		OptiMark 0.5mmol/ml were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: glucosamine-containing medicines

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Viet Nam	16 June 2010 5 August 2013	The use of glucosamine was restricted to the following indication: symptomatic relief of mild to moderate osteoarthritis of the knee. The product information was also changed to include contraindications in pregnancy and lactation, children under 18 years old. **References:** Drug Administration of Viet Nam Official Dispatch No. 6132/QLD-DK, 16 June 2010, and No. 12509/QLD-DK, 05 August 2013.

PRODUCT NAME: gonadotropin-releasing hormone agonist

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
canada	8 September 2011	The labeling for GnRH agonist drugs has been updated to add a warning on the potential increased risk of heart-related side effects. **References:** Advisories, Warnings and Recalls, Health Canada, 8 September 2011 (www.hc-sc.gc.ca). WHO Pharmaceuticals Newsletter No. 5, 2011.

PRODUCT NAME: hydrochlorothiazide-containing products

C.A.S. NUMBER:

OTHER NAMES: e.g. lisiniopril hydrochlorothiazide, ramipril hydrochlorothiazide, enalapril hydrochlorothiazide, losartan hydrochlorothiazide, valsartan hydrochlorothiazide, Clorana, Diurix

Country	Effective Date	Description of action taken
Europe	1 October 2018	The PRAC assessment considered there was a biologically plausible mechanistic model supporting the increased risk of nonmelanoma skin cancer (NMSC) following higher

		cumulative doses of hydrochlorothiazide (HCTZ). Therefore, the PRAC has agreed that the MAHs for the hydrochlorothiazide-containing products are to submit a variation within 2 months, to amend the product information. Meanwhile, Patients taking HCTZ should be informed of the risk of NMSC and advised to regularly check their skin for any new lesions and promptly report any suspicious skin lesions. Possible preventive measures such as limited exposure to sunlight and UV rays and, in case of exposure, adequate protection should be advised to the patients in order to minimize the risk of skin cancer. Suspicious skin lesions should be promptly examined potentially including histological examinations of biopsies. The use of HCTZ may also need to be reconsidered in patients who have experienced previous NMSC. **References:** EMA , PRAC recommendations on signals (www.ema.europa.eu)
Montenegro	29 October 2018	Based on PRAC recommendation following evaluation of safety signals and in accordance with Law on medicines, the Agency for Medicines and Medical Devices of Montenegro (CALIMS) has sent DHPC to relevant HCPs to inform them of non melanoma skin cancer related to the use of high cumulative dose of hydrochlothiazide. **References:** CALIMS, Direct healthcare professional communications.
Brazil	October 2018 November 2018	Following data from epidemiological studies, which demonstrated a cumulative dose-dependent association between hydrochlorothiazide and non-melanoma skin cancer, health professionals were recommended to inform patients treated with hydrochlorothiazide about this risk, especially those were use the drug long term. It was recommended that patients be instructed to regularly check their skin for new lesions and to immediately notify the physician of any suspected skin lesions, as well as to take preventive measures regarding exposure to sunlight and UV rays. Letters were addressed to health professionals. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: hydroxyethyl starch (HES)

C.A.S. NUMBER: 9005-27-0

OTHER NAMES: Hespan, Voluven, Volulyte, Voluven, Tetrahes, Hestar, Istarthes, Plasmin, Plasmo-Tech 6, Plasmo-Tech 10, OslaDex

Country	Effective Date	Description of action taken

United Arab Emirates	2012	HESTAR - 200 (Pentastarch 6%) was suspended. Plasmasteril injection were withdrawn by the MAH before the product getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: ibuprofen- and dexibuprofen-containing medicines

C.A.S. NUMBER: -

OTHER NAMES: E.g. Blokmax, Defrinol, Rapidol, Nurofen, Spedifen

Country	Effective Date	Description of action taken
Europe	20 May 2015	The Coordination Group for Mutual Recognition and Decentralised procedures-Human (CMDh) has endorsed by consensus updated advice on the use of high-dose ibuprofen, following a review carried out by EMA's Pharmacovigilance Risk Assessment Committee (PRAC), which confirmed a small increased cardiovascular risk with daily doses at or above 2,400 mg. A high dose of dexibuprofen is a dose at or above 1,200 mg per day. The review clarifies that the risk with high-dose ibuprofen is similar to the risk seen with some other non-steroidal anti-inflammatory drugs (NSAIDs), including COX-2 inhibitors and diclofenac. **References:** CMDh position (consensus)
Montenegro	29 July 2015	Based on CMDh final decision and in accordance with Law on medicines, the Agency for Medicines and Medical Devices of Montenegro (CALIMS) has sent DHPC to relevant HCPs to inform them of the perceived increased risk of serious cardiovascular reactions. **References:** CALIMS, Direct healthcare professional communications.

PRODUCT NAME: Incretin mimetic drugs

C.A.S. NUMBER:

OTHER NAMES: exenatide (Byetta, Bydureon), liraglutide (Victoza), sitagliptin (Januvia, Janumet, Janumet XR, Juvisync), saxagliptin (Onglyza, Kombiglyze XR), alogliptin (Nesina, Kazano, Oseni), linagliptin (Tradjenta, Jentadueto)

Country	Effective Date	Description of action taken
Brazil	March 2014	Following US FDA's Drug Safety Communication regarding incretin mimetic drugs for type 2 diabetes, ANVISA warned of a higher risk of pancreatitis and the detection of precancerous cells in the pancreas of patients with type 2 diabetes treated with this class of medications. The Health

		Surveillance Center of the State Secretariat of São Paulo (CVS/SES/SP) also published an alert on the subject. **References:** ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: iron parenteral preparations

C.A.S. NUMBER: -

OTHER NAMES: ferric carboxymaltose, iron dextran, sodium ferric gluconate, iron isomaltoside, iron sucrose

Country	Effective Date	Description of action taken
Europe	13 September 2013	EMA's CHMP completed its review of intravenous iron-containing medicines used to treat iron deficiency and anaemia associated with low iron levels. The CHMP concluded that the benefits of these medicines are greater than their risks, provided that adequate measures are taken to minimise the risk of allergic reactions. **References:** European Commission final decision (www.ema.europa.eu)
Montenegro	13 March 2014	Based on EMA referral and in accordance with Law on medicines, the Agency for Medicines and Medical Devices of Montenegro (CALIMS) has sent DHPC to relevant HCPs to inform them of the perceived increased risk of serious allergic reactions. **References:** CALIMS, Direct healthcare professional communications.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: long-acting beta-agonists (LABA)

C.A.S. NUMBER:

OTHER NAMES: e.g. indacaterol, salmeterol, formoterol

Country	Effective Date	Description of action taken
Brazil	February 2010	In accordance with the recommendations made by the US FDA, based on analyses of studies that demonstrated an increased risk of severe exacerbation of asthma symptoms, leading to hospitalization of adult and pediatric patients, as well as the death of some patients using these medications, an alert was published with safety recommendations to prescribers and patients. The product lable was updated accordingly; the MAH was requested to submit Risk Minimization Plans with an educational focus to health professionals. **References:** ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia).

USA	3 June 2010	Use of a long-acting beta-agonist (LABA) alone without use of a long-term asthma control medication, such as an inhaled corticosteroid, is contraindicated in the treatment of asthma. In addition, LABAs should not be used in patients whose asthma is adequately controlled on low or medium dose inhaled corticosteroids. **References:** Safety Information, US FDA 3 June 2010 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 4, 2010. WHO Pharmaceuticals Newsletter No. 3, 2011. WHO Pharmaceuticals Newsletter No. 1, 2018.
Egypt	25 November 2010	1.The products should not be used alone, instead it should be used in combination with corticosteroid derivative inhalation. 2. The long-term use of these products is reserved only for cases that do not response to use of corticosteroid products alone. 3. These drugs should be used for the shortest time possible to control the symptoms of respiratory crisis and treatment should be completed after that by corticosteroid product. 4. Children and adolescents should use a pharmaceutical formulation containing LABA in addition to the corticosteroid products. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.

PRODUCT NAME: meprobamate-containing medicines

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Europe	20 January 2011	The European Medicines Agency (EMA) has recommended the suspension of all marketing authorizations for meprobamate-containig medicines for oral use in the European Union (EU) because their risks, particularly the risk of serious side effects affecting the nervous system, are greater than their benefits. It has been recommended that the medicines be withdrawn gradually within 15 months to ensure prescribers have enough time to determine the most appropriate treatments for their patients. **References:** Press release, EMA, 20 January 2011 (www.ema.europa.eu). WHO Pharmaceuticals Newsletter No. 1, 2012.

PRODUCT NAME: methyl paraben, propyl paraben

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Egypt	12 April 2012	Methyl paraben and propyl paraben should not be used for children less than 3 years of age. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.

PRODUCT NAME: modified-release oral opioids

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Europe	23 July 2010	The Committee for Medicinal Products for Human Use (CHMP) concluded that modified-release oral opioids using a polymethacrylate-triethylcitrate controlled-release system are highly sensitive to alcohol and that there is a risk of the active ingredient being released too quickly (a.k.a. dose dumping) if patients drink alcohol while taking them. Therefore, the Committee recommended that the marketing authorizations for these medicines should be suspended until the manufacturers have reformulated them so that they are more stable in alcohol. **References:** Press release, Questions and answers, EMA, 23 July 2010 (www.ema.europa.eu). WHO Pharmaceuticals Newsletter No. 5, 2010.

PRODUCT NAME: OTC drugs brompheniramine, chlorphenamine, diphenhydramine, doxylamine, promethazine, OR triprolidine; dextromethorphan OR pholcodine; guaifenesin OR ipecacuanha; ephedrine, oxymetazoline, OR xylometazoline

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Egypt	26 May 2011	OTC medicinal products containing these substances are contraindicated in children less than two years. For children under 6 years they should ONLY be used under medical supervision. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.

PRODUCT NAME: OTC nasal decongestant: phenylephrine and lerymazoline, oxymetazoline, xylometazoline, ephedrine,

C.A.S. NUMBER: -

OTHER NAMES:

Country	Effective Date	Description of action taken
Montenegro	August 2014	Following MHRA decision to implement measures to improve the safe use of OTC cough and cold medicines for children under 12 years, the Agency for Medicines and Medical Devices of Montenegro (CALIMS) has sent DHPC to relevant HCPs to inform them of the perceived increased risk of serious allergic reactions, overdosing and sleep disorders. **References:** CALIMS, Direct healthcare professional communications.

PRODUCT NAME: OTC topical teething preparations lidocane or benzocaine

C.A.S. NUMBER: 137-58-6

OTHER NAMES: lidocaine (lignocaine), benzocaine (Anbesol, Hurricaine, Orajel, Baby Orajel, Orabase etc.)

Country	Effective Date	Description of action taken
Chile	23 July 2014	Product label is updated to indicate indications banned: those related to dentition discomfort treatment or similar ones, as well as new contraindications: children under 3 years old and the use as dentition reliever. The decision took into consideration US FDA's decision in 2012 and 2014. **References:** Instituto de Salud Publica (www.ispch.cl). US FDA Drug Safety Communication, 2012 and 2014 (https://www.fda.gov/drugs).

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: paracetamol combinations

C.A.S. NUMBER:

OTHER NAMES: e.g. Agud, Naldecon Dia, Tylex, Neomol CF, ADOL ® Sinus Hot Therapy, Distalgesic

Country	Effective Date	Description of action taken
Egypt	2010	Paracetamol + phenylephrine combination is not to be used for children less than 12 years. In addition it was decided not to receive new authorization application for products containing the combination of (Cetirizine 10mg + Paracetamol 400 mg + Pseudoephedrine 30 mg). **References:**

Brazil	January 2014	ANVISA issued an alert about liver risks related to the use of combinations with paracetamol in doses above 325mg. ANVISA clarified that it would conduct a risk assessment in the database of the adverse event notification system and make recommendations to health professionals and patients. This took into consideration of a US FDA Drug Safety Communication, which recommended the discontinuation of prescribing and dispensing of drugs containing paracetamol in access of dose above 325mg, because there were no data available that demonstrated any additional benefit that compensated for the risk of liver injury. **References:** ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia).
United Arab Emirates		Midrone Extra (paracetamol + caffeine) tablets were suspended. Neomol CF(paracetamol + pseudoephedrine + chlorphenamine maleate) syrup, paranormv(paracetamol + metoclopramide) syrup and Distalgesic (paracetamol + dextropropoxyphene) tablets were withdrawn by the MAH before getting approval. ADOL ® Sinus Hot Therapy (paracetamol + pseudoephedrine) granules and Panadol Cold & Flu Hot Lemon (paracetamol + phenylephrine + ascorbic acid) powder were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: paracetamol, modified release, with or without tramadol

C.A.S. NUMBER: -

OTHER NAMES: Alvedon, Doreta, Panodol, and others

Country	Effective Date	Description of action taken
Europe	March 2018	The CMDh recommended that modified-release paracetamol-containing products to be suspended from EU market, based on a review by PRAC that determined the advantages of a longer-acting product did not outweigh the complications of managing an overdose of the medicine. **References:** European Commission final decision (www.ema.europa.eu). WHO Pharmaceuticals Newsletter No. 5, 2017. WHO Pharmaceuticals Newsletter No. 1, 2018.

Viet Nam	15 March 2018	The marketing authorisation for modified release, paracetamol containing tablets are withdrawn to prevent overdose and hepatic injury. **References:** Drug Administration of Viet Nam Official No. 4430/QLD-DK, 15 March 2018.

PRODUCT NAME: phenylephrine OR pseudoephedrine

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Egypt	27 October 2011	The restriction of using OTC medicinal products containing these substances has been strengthened as follows: "Not to be used for children under the age of 6 years" instead of "Not used for children under the age of 2 years" Also it was decided not to accept new authorization application for medicinal products containing pseudoephedrine. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.

PRODUCT NAME: prednisolone containing products

C.A.S. NUMBER: 1953-03-02

OTHER NAMES: Deltacortril, UltraCortenol, Econopred, Pred, Cetapred (prednisolone acetate + sodium sulphacetamide)

Country	Effective Date	Description of action taken
United Arab Emirates		Deltacortril 5 mg tablets, Ultracortenol drops and 0.5% ointment, and Pred Mild drops were withdrawn by the MAH before getting approval. Econopred Plus 1% drops and Cetapred ointment were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: prochlorperazine, haloperidol, loxapine, thioridazine, molindone, thithixene, pimozide, trifluperazine, trifluoperazine, chlorpromazine, perphenazine

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Egypt	29 September 2011	These drugs are not indicated in the treatment of dementia-related psychosis. These products should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Neonates exposed to antipsychotic drugs, during the third trimester of pregnancy are at risk for extrapyramidal and/or withdrawal symptoms following delivery. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.

PRODUCT NAME: proton pump inhibitors (PPI)

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
United Kingdom	February 2012	The MHRA reported that there is recent epidemiological evidence of an increased risk of fracture with long-term use of PPIs. Patients at risk of osteoporosis should be treated according to current clinical guidelines to ensure they have an adequate intake of vitamin D and calcium. In addition, prolonged use of PPIs has been associated with hypomagnesaemia. The MHRA advised that health-care professionals should consider measuring magnesium levels before starting PPI treatment and repeat measurements periodically during treatment for patients expected to be on prolonged treatment, and especially for those who take PPIs with digoxin or drugs that may cause hypomagnesaemia (e.g. diuretics). **References:** Drug Safety Update, February 2012, Volume 5, issue 9, A1 MHRA, (www.mhra.gov.uk). WHO Pharmaceuticals Newsletter No. 3, 2012. WHO Pharmaceuticals Newsletter No. 5, 2015.

PRODUCT NAME: rosiglitazone & rosiglitazone-containing products

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Sudan	3 October 2010	There has been a suspension & recall of the products from markets along with withdrawal of the products from clinical use. Prescribers are requested to strictly follow the following recommendations:

		1. Prescribers should put in place a system to ensure that all patients are reviewed and changed to another suitable treatment in line with NICE recommendations. 2. Thiazolidinediones group may increase the risk of cardiovascular events. Therefore, healthcare professionals should consider this group as a last choice in treatment of diabetes mellitus and should take appropriate precautions when prescribing thiazolidinediones. **References:** Communication from the Sudan National Pharmacovigilance Centre, July 2012.

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: short-acting beta-agonists (SABA)

C.A.S. NUMBER:

OTHER NAMES: e.g. fenoterol, hexoprenaline, isoxsuprine, ritodrine, salbutamol, terbutaline

Country	Effective Date	Description of action taken
Oman	2013	Following PRAC recommendation, short acting beta agonists should no longer be used in obstetric indications. The HCPs were informed throught the Circular. **References:** Oman Ministry of Health Circular No. 149, 2013.
Europe	25 October 2013	The CMDh has endorsed by consensus the revocation of marketing authorisations for use of short-acting beta-agonists. They should no longer be used in oral or suppository forms in obstetric indications, such as for suppressing premature labour or excessive labour contractions. However, injectable forms of these medicines can still be given for short-term obstetric use under specific conditions. The PRAC review concluded that there was a risk of serious cardiovascular side effects to both the mother and unborn baby when high-dose short-acting beta-agonists are used in obstetric indications, with the data suggesting these mostly occur with prolonged use. Given the cardiovascular risk and the very limited data on the effectiveness of the oral and suppository forms of these medicines, the PRAC concluded that their benefit-risk balance is not favourable and these medicines should no longer be used in obstetric indications. **References:** EMA press release, 25 October 2013.
Montenegro	8 November 2013	Based on EMA referral and in accordance with Law on medicines, the Agency for Medicines and Medical Devices of Montenegro (CALIMS) has sent DHPC to relevant HCPs to inform them of the perceived increased risk of cardiovascular toxicity and pulmonary edem. **References:** CALIMS, Direct healthcare professional communications.

PRODUCT NAME: sodium-glucose cotransporter type 2 (SGLT2) inhibitors

C.A.S. NUMBER:

OTHER NAMES: e.g. canagliflozin (Invokana), dapagliflozin (Forxiga), empagliflozin (Xigduo XR), ertugliflozin (Jardiance)

Country	Effective Date	Description of action taken
Brazil	June 2015 April 2016 September 2018	Due to the occurrence of severe and possibly life-threatening diabetic ketoacidosis reported in patients with type 2 and type 1 diabetes treated with SGLT2 inhibitors (canagliflozin, dapagliflozin or empagliflozin), health professionals were informed about the need to assess ketone levels in patients using SGLT2 inhibitors when they experience acidosis symptoms, to prevent delay in diagnosis and treatment. It noted also that type 1 diabetes is not an approved indication for this class of medications. In 2018, based on scientific publication and information released by the US FDA, ANVISA warned of the occurrence of cases of necrotizing fasciitis or Fournier gangrene, in patients with type II diabetes treated with SGLT2 inhibitors. Health professionals were recommended to guide patients on the identification of related symptoms, with emphasis on the importance of seeking immediate care, considering that symptoms can worsen rapidly. Upon first symptoms therapy with SGLT2 inhibitors should be discontinued and alternative therapy should be instituted. **References:** ANVISA Pharmacovigilance Alert, and Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: statins

C.A.S. NUMBER:

OTHER NAMES: atorvastatin, lovastatin, pravastatin, rosuvastatin, simvastatin

Country	Effective Date	Description of action taken
United Arab Emirates	2015	Simcor 10 mg and 20 mg (simvastatin) tablets were suspended. Juvicor (simvastatin + sitaglitpin) tablets were withdrawn by the MAH before getting approval. Simcard 10 and 20 (simvastatin) tablets were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

Brazil	February 2012	Based on the comprehensive review of this class of medications, ANVISA warns of changes in statin leaflets associated with the risk of liver problems and potential cognitive adverse events, usually non-serious and reversible (memory loss, confusion, etc.), as well as increased levels of sugar and glycosylated hemoglobin (HbA1c) in the blood. In addition, the lovastatin package leaflet has been updated with new contraindications and dose limitations in cases of administration with other drugs that have the risk of muscle injury. Recommendations are addressed to health professionals and patients. **References:** ANVISA, Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).
USA	March 2012	HIV or hepatitis C protease inhibitors and certain statin drugs taken together may raise the blood levels of statins and increase the risk for myopathy. **References:** FDA Drug Safety Communication, US FDA, 1 March 2012 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 2, 2012.
Viet Nam	5 April 2013	The product information of simvastatin/lovastatin was updated with a new contraindications againist concomitant uses of potent CYP3A4 inhibitors. The restrictions intend to reduce the risk of myopathy and/or rhabdomyolysis associated with the concomitant use of simvastatin/lovastatin with other drugs, according to US. FDA's decision. **References:** Drug Administration of Viet Nam Official Dispatch No. 5074/QLD-DK, 05 April 2013.

PRODUCT NAME: topical nasal decongestants

C.A.S. NUMBER:

OTHER NAMES: naphazoline, phenoxazoline, oxymetazoline, xylometazoline

Country	Effective Date	Description of action taken
Brazil	July 2013 February 2016	In 2013, after receiving notifications reporting cases of intoxication due to the use of naphazoline in children, ANVISA warned about the risk of intoxication and reinforces the contraindication of use in children. Naphazoline is still available on the market for sale with a prescription and only for adult use. In 2016, INVISA warned about the risks related to the indiscriminate use of nasal decongestants based on vasoconstrictor substric substances. Inadequate or excessive use of these medications may lead to nasal rebound congestion, desensitization, and pharmacodependence. It was recommended the maximum treatment time of up to

		three days. Patients with heart disease, hypertension, thyroid disease, diabetes, chronic rhinitis, glaucoma or difficulty urinating due to increased size of the prostate gland should not use the medications. **References:** ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: tumor necrosis factor (TNF) alpha blockers

C.A.S. NUMBER:

OTHER NAMES: e.g. infliximab (Remicade), etanercept (Enbrel), adalimumab (Humira), certolizumab (Cimzia), golimumab (Simponi)

Country	Effective Date	Description of action taken
USA	7 September 2011	The US FDA notified healthcare professionals that the Boxed Warning for the entire class of Tumor Necrosis Factor-alpha (TNFO) blockers has been updated to include the risk of infection from two bacterial pathogens, Legionella and Listeria. Patients treated with TNFO blockers are at increased risk for developing serious infections involving multiple organ systems and sites that may lead to hospitalization or death due to bacterial, mycobacterial, fungal, viral, parasitic, and other opportunistic pathogens. **References:** FDA Drug Safety Communication, US FDA, 7 September 2011 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 5, 2011.
Brazil	September 2011 June 2014	In 2011, ANVISA warned that the use of tumor necrosis factor(TNF) alpha blocking drugs is associated with the risk of serious bacterial infections by the opportunistic pathogens Legionella (pneumonia) and Listeria (meningitis, bacteremia, endophthalm and sepsis), sometimes with fatal outcome. Recommendations were made to patients and prescribers. Changes in the package leaflet were being evaluated, according to the US FDA review. In 2014, health professionals were alerted to the management of Enbrel patients and the risk of tuberculosis. Before starting treatment with TNF-alpha inhibitors, patients should be evaluated for the possibility of tuberculosis or latent infection by Mycobacterium tuberculosis. If any of the cases are confirmed, treatment with TNF-alpha inhibitor should not be initiated. **References:** ANVISA Pharmacovigilance Alert, and Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

PRODUCT NAME: valproate sodium (valproic acid), calcium valproate

C.A.S. NUMBER:

OTHER NAMES: Valproate containing medicinal products e.g. Convulex, Depakine, Depakine enteric 300, Depakine Chrono ,Convulsofin, Depakote, Depakene, Epilim, Convulex, Valpakine

Country	Effective Date	Description of action taken
Armenia	2018	After an assessment by the Scientific Centre of Drug and Medical Technology Expertise after Academician E. Gabrielyan (SCDMTE), the product information of valproate containing medicinal products was updated to include new measures to avoid valproate exposure in pregnancy. As a risk minimization measure a DHPC was circulated. **References:** Communication from Armenian National Pharmacovigilance Centre, 2018. EMA press release, 09 February 2018.
USA	30 June 2011	The US FDA notified health-care professionals that children born to mothers who take the anti-seizure medication valproate sodium or related products (valproic acid and divalproex sodium) during pregnancy have an increased risk of lower cognitive test scores than children exposed to other antiseizure medications during pregnancy. **References:** FDA Drug Safety Communication, US FDA 30 June 2011 (www.fda.gov). WHO Pharmaceuticals Newsletter No. 4, 2011. WHO Pharmaceuticals Newsletter No. 3, 2013.
Indonesia	3 October 2013	The product information of all valproate containing products should be revised to inform the risk of decreased IQ. **References:** Dear Healthcare Professional Communication PW.02.03.342.3.10.13.4187
Viet Nam	8 June 2015	The product information (where migraine prevention was authorised) was updated with the following contraindications: The use of valproate for women of childbearing age who are not using effective methods of contraception or if they are already pregnant was contraindicated. Pregnancy should be ruled out before starting a female patient on valproate treatment for migraine. The restrictions intend to strengthen warnings on the use of valproate medicines in women and girls due to the risk of malformations and developmental problems in babies who are exposed to valproate in the womb. **References:** Drug Administration of Viet Nam Official Dispatch No. 10107/QLD-DK, 08 June 2015.
Europe	9 February 2018	The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) recommended strengthening

		restrictions on the use of valproate and related substances and introducing new measures to require appropriate counselling and information for affected women in order to avoid exposure of babies to valproate medicines in the womb. Babies exposed are at risk of malformations and developmental problems. The PRAC also recommended that the companies marketing these medicines carry out additional studies to further characterise the nature and extent of the risks posed by valproate and to monitor ongoing valproate use and the long-term effects from affected pregnancies. In the meantime, women who have any concerns should consult their doctor. Women and girls who have been prescribed valproate should not stop taking their medicines without consulting their doctor as doing so could result in harm to themselves or to an unborn child. **References:** EMA press release, 09 February 2018.
Brazil	July 2011 August 2016 November 2016	In 2011, ANVISA warned about the risk of congenital malformations in children whose mothers use the drug during pregnancy. For women who are pregnant or planning to become pregnant, the decision to use a valproate-containing drug should be based on rigorous analysis of the benefits compared to the inherent risk of the fetus, in consultation with the doctor. Patients already on valproate-containing medicaiton should not stop taking their medication or make any changes in treatment before talking to a healthcare professional, as abrupt discontinuation of the use of the drug can cause serious problems. The product package leaflet has been updated. In August 2016, warnings about the risk of congenital anomalies was reinforced, considering that children exposed to sodium valproate in utero are at a high risk of serious developmental disorders (in up to 30-40% of cases) and/or congenital malformations (approximately 10% of cases). Thus, valproate should not be prescribed to children and female adolescents, or to pregnant women, unless at medical discretion when other treatments are considered ineffective or not tolerated. The medicine package leaflet has been updated. In November 2016, ANVISA re-emphasized the Alert published in 2011 on contraindication and warnings for the use of drugs containing sodium valproate and related substances, such as valproic acid and sodium divalproate, by children and female adolescents, women of childbearing age and pregnant women, due to the increased risk of malformations and developmental problems in infants. **References:** ANVISA Pharmacovigilance Alert, and Letter to healthcare professionals (http://portal.ANVISA.gov.br/farmacovigilancia).

Other Products

PRODUCT NAME: anti-rabies vaccine

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
India	4 October 2016	All manufacturers and importers of the rabies vaccine are directed to ensure that erythema multiforme is inserted in the drug safety label of the rabies vaccine. **References:** Letter issued by CDSCO on 04 October 2016. WHO Pharmaceuticals Newsletter No. 5, 2016.

PRODUCT NAME: Biovital

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		Biovital tablet and Biovital (paediatric) syrup were withdrawn by the MAH before getting approval. Biovital (adult) were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: cerebrolysin

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		The application for Cerebrolysin injection products was rejected by the committee for various reasons. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: Enervit nutritional supplement

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		Enervit nutritional supplement as tablet were withdrawn by the MAH before getting approval.

		References: Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: essential phospholipids

C.A.S. NUMBER:

OTHER NAMES: Essentiale

Country	Effective Date	Description of action taken
United Arab Emirates		Essentiale capsules were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: follitropin alfa

C.A.S. NUMBER:

OTHER NAMES: Gonal-F

Country	Effective Date	Description of action taken
United Arab Emirates		Gonal-f® 150 IU were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. Gonal-f® 1050 IU were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: Hiberix (haemophilus b conjugate) vaccine, multiple dose

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		Hiberix™ vaccine (Multiple dose) were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: human albumin

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		Human albumin 20% by Biotest Pharma were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: immunoglobulin

C.A.S. NUMBER:

OTHER NAMES: Gamimune N 10%

Country	Effective Date	Description of action taken
United Arab Emirates		Gamimune N 10% were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: Infanrix ™ Hib

C.A.S. NUMBER:

OTHER NAMES: combined vaccine against diphtheria, tetanus, pertussis, poliomyelitis and Haemophilus influenzae type b

Country	Effective Date	Description of action taken
United Arab Emirates		Infanrix ™ Hib were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: influenza vaccine

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
United Kingdom	October 2011	Prescribers are reminded that Enzira and CSL Biotherapies generic influenza vaccines (both manufactured by CSL and marketed by Pfizer) should not be given to children younger than 5 years. These vaccines are not authorised for use in

		this age-group after the increased risk of febrile convulsions observed in Australia last year. **References:** Drug Safety Update, volume 5, issue 3, October 2011. (www.mhra.gov.uk).

* Refer to Pharmaceuticals: Restrictions In Use and Availability, 2010 for more regulatory actions related to this product.

PRODUCT NAME: Kava-Kava

C.A.S. NUMBER: 900-38-8

OTHER NAMES:

Country	Effective Date	Description of action taken
Egypt	19 May 2011	Withdrawal of registered products containing this active ingredient due to the liver toxicity associated with kava-kava. **References:** Communication from the Egypt National Pharmacovigilance Centre July, 2012.

PRODUCT NAME: levonorgestrel-releasing implant

C.A.S. NUMBER:

OTHER NAMES: Norplant System Kit

Country	Effective Date	Description of action taken
United Arab Emirates		Norplant System Kit were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: oral polio vaccine, trivalent

C.A.S. NUMBER:

OTHER NAMES: Opvero

Country	Effective Date	Description of action taken
United Arab Emirates		Opvero were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: Pandemic influenza vaccine (H1N1)

C.A.S. NUMBER:

OTHER NAMES: Celvapan, Pandemrix

Country	Effective Date	Description of action taken
United Arab Emirates		Celvapan were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.
Europe	21 July 2011	The European Medicines Agency (EMA) announced that the Committee for Medicinal Products for Human Use (CHMP) finalized its review of Pandemrix and narcolepsy and recommended that in persons under 20 years of age Pandemrix may only be used if the recommend **References:** Press release, EMA, 21 July 2011 (www.ema.europa.eu). WHO Pharmaceuticals Newsletter No. 2, 2011. WHO Pharmaceuticals Newsletter No. 4, 2011.

PRODUCT NAME: pneumococcal vaccine, polyvalent

C.A.S. NUMBER:

OTHER NAMES: Pneumovax 23

Country	Effective Date	Description of action taken
Australia	1 February 2012	Immunocompetent individuals should not be routinely revaccinated with Pneumovax 23. Revaccination should be considered for patients at high risk of serious pneumococcal disease provided at least five years have passed since their previous dose of Pneumovax 23. **References:** Medicines Safety Update Vol. 3, No. 1, February 2012 (www.tga.gov.au). WHO Pharmaceuticals Newsletter No. 2, 2012.

PRODUCT NAME: rotavirus vaccine

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Oman	2010	The marketing authorisation of rotarix vaccine was suspended following US FDA finding that DNA from porcine circovirus type1 was present in Rotarix. Subsequent investigation did not find similar problem; hence the suspension was lifted. **References:** Oman Ministry of Health Circular No. 42, 2010, and No. 72, 2010.
Brazil	March 2010	A Pharmacovigilance Alert was published, after US FDA suspended the use of Rotarix vaccine, following the

		identification of DNA from Circovirus Pig 1 (CS1) in two batches of rotarix® vaccine. Agência Nacional de Vigilância Sanitária (ANVISA) maintains the recommendation for the use of Rotarix oral vaccine, according to WHO recommendation, also adopted by the EMA, considering that the benefits produced by the vaccine are greater than its interruption, even if temporary. The Health Surveillance Secretariat (SVS) of the Ministry of Health, together with ANVISA, will continue monitoring the use of the vaccine. **References:** ANVISA Pharmacovigilance Alert (http://portal.ANVISA.gov.br/farmacovigilancia).
Chile	4 June 2013	The product information is updated with new contraindications in 1) patients with uncorrected congenital malformations of the gastrointestinal tract (such as Meckel's diverticulum) that could predispose to intestinal intussusception; and in 2) subjects wi **References:** Instituto de Salud Publica (www.ispch.cl)

PRODUCT NAME: Saccharomyces boulardii

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Chile	24 February 2015	The product information is updated to include new indication restrictions. The approved indications are: for the symptomatic treatment of nonspecific acute diarrhea, as a complement to rehydration, and in the prevention and symptomatic treatment of diarr **References:** Instituto de Salud Publica (www.ispch.cl). WHO (2012) Guidelines for the Evaluation of Probiotics in Food. US agency Agency for Healthcare Research and Quality (2011) Safety of Probiotics to Reduce Risk and Prevent or Treat Disease.

PRODUCT NAME: selenium sulfide

C.A.S. NUMBER:

OTHER NAMES: Exsel

Country	Effective Date	Description of action taken
United Arab Emirates		Exsel 2.5% lotion were withdrawn by the MAH before getting approval. **References:**

		Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: Serratiopeptidase

C.A.S. NUMBER: 37312-62-2; 95077-02-4

OTHER NAMES:

Country	Effective Date	Description of action taken
Viet Nam	24 April 2012	The marketing authorisation of serratiopeptidase-containing medicines is suspended due to limited efficacy data. **References:** Drug Administration of Viet Nam Official documents No. 5865/QLD-DK, 24 April 2012.

PRODUCT NAME: Solcoseryl

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		Solcoseryl gel were withdrawn by the MAH before getting approval. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: terpenic derivatives

C.A.S. NUMBER:

OTHER NAMES: camphor, cineole, niaouli, wild thyme, terpineol, terpine, citral, menthol and essential oils of pine needle, eucalyptus and turpentine

Country	Effective Date	Description of action taken
Europe	23 September 2011	The EMA's Committee for Medicinal Products for Human Use (CHMP) has concluded that the use of these medicines should be contraindicated in children under 30 months old, children with a history of epilepsy or febrile convulsion and children with a recent history of anorectal lesion (precancerous growths in the anus or rectum). **References:** EMA Referrals, 23 September 2011 (www.ema.europa.eu). WHO Pharmaceuticals Newsletter No. 5, 2011.
Viet Nam	6 December 2012	Suppositories containing terpenic derivatives are contraindicated for use in children under 30 months, children with a history of febrile convulsion or epilepsy and children with a recent history of anorectal lesion. The restrictions intended to ensure drug safety because there

		was a risk of neurological disorders, especially convulsions, in infants and small children. There was also a risk of these medicines causing local anorectal lesions, based on EMA's decision. **References:** Drug Administration of Viet Nam Official Dispatch No. 19109/QLD-DK, 06 December 2012.

PRODUCT NAME: thymomodulin

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Viet Nam	3 April 2012	The use of thymomodulin was restricted to the following indications: - Adjunct to prevention of recurrent respiratory infections in children and adults. - Treatment of acute episodes of allergic rhinitis. - Adjunct to prevention of recurrent food allergy. **References:** Drug Administration of Viet Nam Official Dispatch No. 4397/QLD-DK, 03 April 2012.

PRODUCT NAME: turpentine

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
Madagascar	16 December 2011	The product has been withdrawn due to reevaluation of risk/benefit ratio of paediatric suppositories containing terpene derivatives. **References:** Communication from the Madagascar National Pharmacovigilance Centre July, 2012.

PRODUCT NAME: Typherix vaccine

C.A.S. NUMBER:

OTHER NAMES:

Country	Effective Date	Description of action taken
United Arab Emirates		Typherix vaccine were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:**

	Ministry of Health and Prevention Ministerial Decree No. 366.

PRODUCT NAME: vaccine, Diphtheria-Tetanus-Pertussis (whole cell)-Hepatitis B-Haemophilus influenzae type b

C.A.S. NUMBER:

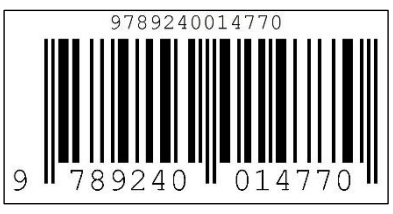
OTHER NAMES: Tritanrix-Hib

Country	Effective Date	Description of action taken
United Arab Emirates		Tritanrix™Hib vaccine were voluntarily withdrawn by the MAH either for commercial reasons or any reason other than safety. **References:** Ministry of Health and Prevention Ministerial Decree No. 366.

Annex

Web links to pharmaceutical safety information from select regulatory authorities
(Accessed on 14 August 2020)

Country/Region	Regulatory Agency & Link to Safety Information for Pharmaceuticals
Australia	Department of Health - Therapeutic Goods Administration (TGA) https://www.tga.gov.au/publication/medicines-safety-update
Canada	Health Canada https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/safety-reviews.html
European Union	European Medicines Agency (EMA) https://www.ema.europa.eu/en/human-regulatory/post-authorisation/pharmacovigilance/signal-management/prac-recommendations-safety-signals
Ireland	Health Products Regulatory Authority (HPRA) http://www.hpra.ie/homepage/about-us/publications-forms/newsletters
Japan	Pharmaceuticals and Medical Devices Agency (PMDA) https://www.pmda.go.jp/english/safety/info-services/drugs/0001.html
New Zealand	Medcines and Medical Devices Safety Authority (MEDSAFE) https://medsafe.govt.nz/publications/prescriber-update.asp https://medsafe.govt.nz/safety/SafetyCommunications.asp
Singapore	Health Sciences Authority (HSA) https://www.hsa.gov.sg/announcements?contenttype=Safety%20Alerts
Switzerland	SwissMedic https://www.swissmedic.ch/swissmedic/en/home/humanarzneimittel/market-surveillance/pharmacovigilance/vigilance-news.html
United Kingdom	Medicines and Healthcare Products Regulatory Agency (MHRA) https://www.gov.uk/drug-safety-update
United States	U.S. Food & Drug Administration (US FDA) https://www.fda.gov/drugs/drug-safety-and-availability https://www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program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