WHO/EMP/QSM/2010.3

PHARMACEUTICALS:

RESTRICTIONS IN USE

AND AVAILABILITY

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Prepared within the context of the United Nations publication

"Consolidated List of Products whose Consumption and/or Sale have been Banned, Withdrawn, Severely Restricted or Not Approved by Governments"

Update of the Fourteenth Issue

2010

Essential Medicines and Pharmaceutical Policies
Quality Assurance and Safety: Medicines
Health Systems and Services

Printed in Switzerland.

Acknowledgements:

WHO expresses its sincere appreciation to the National Pharmacovigilance Centres and / or National Medicines Regulatory Agencies, for providing the information contained in this publication. Sincere thanks are due to Ms Cecilia Biriell, the Uppsala Monitoring Centre, Sweden, and to Ms Jackie Lu and Mr Dominick Bailey, University of Maryland-Baltimore, USA for their assistance with content editing, layout and technical support.

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Fourteenth Issue of the United Nations Consolidated List of Products whose Consumption and/or Sale have been Banned, Withdrawn, Severely Restricted or Not Approved by Governments - Pharmaceuticals (UN General Assembly Resolutions 37/137, 1982; 38/149, 1983; 39/229, 1984; 44/226, 1989).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 and consolidates other drug-related information issued by the World Health Organization, including the WHO Rapid Alerts, WHO Pharmaceuticals Newsletter and the quarterly subscription journal WHO Drug Information.

Scope and presentation

This volume presents information on new national regulatory decisions and on voluntary withdrawal of products by manufacturers on grounds of safety from 2009, 2010 (up to May 2010), and earlier years that had not been included in the last update.

Products are listed alphabetically within sections; 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 chemical names; the effective date on which the regulation came into force; a summary of regulatory measures taken by governments; 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 38 governments on 99 products. 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.

Criteria for the inclusion of products in the Consolidated List were developed in 1985 and revised in the light of the comments received from governments. However, governments' interpretation of the criterion "severely restricted", in particular, continues to vary widely, leading to considerable unevenness in reporting. When necessary, additional information and/or clarification have been requested from governments; products which 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.

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Alphabetical listing

Monocomponent Products

Combination Products

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Product Name: **Aliskiren**

CAS Number: **173334-57-1**

Other Names: Tekturna, Rasilezt

Country	Effective Date	Description of action taken Grounds for decision
European Union	2009	The European Medicines Agency (EMA) has added contraindication to the Product Information for aliskiren, which states that it is not to be used in patients who have experienced angioedema when taking aliskiren in the past. The Agency has also recommended that patients who develop signs of angioedema should stop treatment and seek medical attention. **Reference:** 1. Press Release, EMA, 19 Feb 2009 (www.ema.euopa.eu). 2. WHO Pharmaceuticals Newsletter No. 2, 2009.
UK	2009	The Medicines and Healthcare products Regulatory Agency (MHRA) has warned about the risk of angioedema and renal dysfuntion with the use of aliskiren and the risk associated with the concomitant use of aliskiren and non-steroidal anti-inflammatory drugs (NSAIDs). Aliskiren treatment may lead to renal insufficiency and acute renal failure in patients with renal artery stenosis. Concomitant use of NSAIDs may reduce the antihypertensive effect of aliskiren, which may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible when treatment is stopped. Health-care professionals are advised not to use aliskiren in patients who have previously had angioedema after using it. **Reference:** 1. Drug Safety Update, MHRA, Volume 2, Issue 10, May 2009 (www.mhra.gov.uk). 2. WHO Pharmaceuticals Newsletter No. 3, 2009.

Product Name: **Aprotinin**

CAS Number: **9087-70-1**

Other Names: Trasylol

Country	Effective Date	Description of action taken Grounds for decision
Chile	November 2007	In Chile, products with aprotinin injectable were withdrawn from the market in November 2007 due to the increased risk of death compared to tranexamic acid and aminocaproic acid. **Reference:** Communication from the Chile National Pharmacovigilance

		Centre, February 2008.
Singapore	August 2008	In Singapore, the sales of aprotinin was temporarily suspended as of 7 November 2007 due to the increased mortality rate when compared to the epsolon-aminocaproic acid or tranexamic acid. Currently, the drug manufacturer is allowed to supply aprotinin when physicians deem there are no therapeutic alternatives and its benefits outweigh its risks. Physicians are required to undertake in writing that they will inform patients of the risks of using aprotinin and patients' signed consent is required. **Reference:** Communication from the Singapore National Pharmacovigilance Centre, August 2008.

Product Name: Becaplermin

CAS Number: **165101-51-9**

Other Names: Regranex

Country	Effective Date	Description of action taken Grounds for decision
European Union	2010	The EMA has recommended contraindication for becaplermin in patients with any pre-existing cancer, following a review of the available data at the Agency's Committee for Medicinal Products for Human Use (CHMP) on a possible risk of cancer associated with becaplermin use. **Reference:** 1. Press Release, Questions & Answers, EMA, 18 Feb 2010 (www.ema.europa.eu). 2. WHO Pharmaceuticals Newsletter No. 2, 2010.

Product Name: Benzyl alcohol

CAS Number: **100-51-6**

Other Names: Ulesfia, Zilactin-L

Country	Effective Date	Description of action taken Grounds for decision
Iraq	July 2008	All intravenous injection preparations for infants containing benzyl alcohol have been banned. **Reference:** Communication from the Iraq National Pharmacovigilance Centre, May 2010.

Product Name: **Bufexamac**

CAS Number: **2438-72-4**

Other Names: Parfenac

Country	Effective Date	Description of action taken Grounds for decision
European Union	22 April 2010	The EMA's CHMP has recommended that marketing authorizations for bufexamac-containing medicines be revoked throughout the European Union (EU). The risk of developing a contact allergic reaction to bufexamac is high, and the risk is even higher in patients with pre-disposing conditions, such as certain forms of eczema, for which bufexamac is frequently prescribed. **Reference:** 1. Press release, Questions and Answers, EMA, 22 April 2010 (www.ema.europa.eu). 2. WHO Pharmaceuticals Newsletter No.3, 2010.

Product Name: **Cabergoline**

CAS Number: **81409-90-7**

Other Names: Cabaser

Country	Effective Date	Description of action taken Grounds for decision
Switzerland	3 December 2008	The maximal daily dose of cabergoline has been restricted (reduced to 3 mg from 4 and 6 mg, respectively; tablets with 4 mg are not marketed any more by 31 December 2008) due to known risk of cardiac valvulopathy. Additionally, a cardiovascular examination prior to treatment has become mandatory. **Reference:** Communication from Swissmedic, April 2010.

Product Name: **Carbinoxamine**

CAS Number: **486-16-8**

Other Names: Cristin, Palgic

Country	Effective Date	Description of action taken Grounds for decision
Iraq	April 2008	Carbinoxamine has been banned because of high incidence of adverse drug reactions (ADRs) at therapeutic levels. **Reference:** Communication from the Iraq National Pharmacovigilance Centre, May 2010.

Product Name: **Ceftriaxone**

CAS Number: **73384-59-5**

Other Names: Rocephin

Country	Effective Date	Description of action taken Grounds for decision
Canada	2008	The antibiotic ceftriaxone should not be mixed or co-administered with calcium-containing solutions. Health Canada issued the warning to hospitals after cases of fatal reactions in neonates and infants were reported. The Agency also advised that for patients aged less than 10 weeks, intravenous ceftriaxone and calcium-containing solutions should not be administered within five days of each other. **Reference:** 1. Health Canada, 31 July 2008 (www.hc-sc.gc.ca). 2. WHO Pharmaceuticals Newsletter No. 4, 2008.
Malaysia	December 2009	Updates to the previous warning on potential interaction with calcium-containing intravenous solutions were incorporated in the package insert as follows. - Ceftriaxone is contraindicated in neonates (≤ 28 days of age) if they require treatment with calcium-containing intravenous solutions because of the risk of ceftriaxone-calcium precipitation. - In patients other than neonates, ceftriaxone and calcium-containing solutions may be administered sequentially if the infusion lines are thoroughly flushed between infusions with a compatible fluid. - Diluents containing calcium are not to be used to reconstitute ceftriaxone vials or to further dilute a reconstituted vial for intravenous administration because a precipitate can form. Ceftriaxone must not be administered simultaneously with calcium-containing intravenous solutions

		because precipitation of can occur. **Reference:** 1. Information for Healthcare Professionals: Ceftriaxone (marketed as Rocephin and generics), FDA MedWatch, 2008 (www.fda.gov),. 2. Updated prescribing information for all ceftriaxone products marketed in Canada, Health Canada, 2008 (www.hc-sc.gc.ca).
USA	2009	Based on studies, the U.S. Food and Drug Administration (US FDA) has recommended the following: - Concomitant use of ceftriaxone and intravenous calcium-containing products is contraindicated in neonates (28 days of age and under). - Ceftriaxone should not be used in neonates (28 days of age and under) if they are receiving (or are expected to receive) calcium-containing products. - In patients aged over 28 days, ceftriaxone and calcium-containing products may be administered sequentially, provided the infusion lines are thoroughly flushed between infusions with a compatiblefluid. - Ceftriaxone must not be administered simultaneously with intravenous calcium-containing solutions via a Y-site in any age group. - Ceftriaxone and calcium-containing products may be used concomitantly in patients aged over 28 days, using the precautionary steps above because the risk of precipitation is low in this population. **Reference:** 1. Information for Healthcare Professionals, US FDA, 21 April 2009 (www.fda.gov). 2. WHO Pharmaceuticals Newsletter No. 3, 2009.

Product Name: **Chloroquine**

CAS Number: **54-05-7**

Other Names: Cloquine

Country	Effective Date	Description of action taken Grounds for decision
Guinea-Bissau	October 2008	From October 2008, tablets and syrup containing chloroquine have been withdrawn in Guinea-Bissau. Coartem (combination of artemether and lumefantrine) has replaced chloroquine. **Reference:**

Communication from the Guinea-Bissau National Pharmacovigilance Centre, October 2010.

Product Name: **Chromic-phosphate-P-32**

CAS Number: **14596-37-3**

Other Names: Phosphocol P 32, Phosphorus-32

Country	Effective Date	Description of action taken Grounds for decision
USA	2008	Chromic-phosphate-P-32 suspension (Phosphocol P 32) use may increase the risk of leukaemia after receiving intra-articular Phosphocol P 32 injections. This route of administration is not approved by the US FDA. The Phosphocol P 32 package insert now contains a Warnings statement with above information, and an Adverse Reactions statement that reports that leukaemia in children has been identified during postmarketing experience. An additional Adverse Reactions statement highlights that radiation injury to the bladder, caecum and small bowel following Phosphocol P 32 administration into the peritoneal cavity has also been identified. **Reference:** 1. Dear Health-care Provider letter from Covidien, Mallinckrodt Inc., 29 August 2008 (www.fda.gov). 2. WHO Pharmaceuticals Newsletters No. 5 & No. 6, 2008.

Product Name: **Clindamycin**

CAS Number: **18323-44-9**

Other Names: Cleocin

Country	Effective Date	Description of action taken Grounds for decision
Iraq	April 2009	Clindamycin injection 150 mg has been added to the health care list of restricted medicines and is to be used only for patients with penicillin allergy. **Reference:** Communication from the Iraq National Pharmacovigilance Centre, May 2010.

Product Name: **Clopidogrel**

CAS Number: **113665-84-2**

Other Names: Plavix

Country	Effective Date	Description of action taken Grounds for decision
European Union	2009	The EMA recommended updating the existing warning over the concomitant use of clopidogrel-containing medicines and proton-pump inhibitors (PPIs). In May 2009, the Agency's CHMP recommended that the product information for all clopidogrel-containing medicines be amended to discourage the concomitant use of PPIs and clopidogrel unless absolutely necessary. **Reference:** 1. Public statement, EMA, 17 March 2010 (www.ema.europa.eu). 2. WHO Pharmaceuticals Newsletter No. 2, 2010.
Malaysia	July 2009	Updates in the package insert to inform that patients with genetically reduced CYP2C19 function have lower systemic exposure to the active metabolite of clopidogrel and diminished antiplatelet responses, and generally exhibit higher cardiovascular event rates following myocardial infarction. Also, concomitant use of drugs that inhibit CYP2C19 (e.g. proton pump inhibitors) should be discouraged. **Reference:** Communication from the Malaysia National Pharmcacovigilance Centre, May 2010.
New Zealand	2009	The New Zealand Medicines and Medical Devices Safety Authority (Medsafe) have required the clopidogrel data sheets to be updated, to include information about genetic factors influencing clopidogrel metabolism, specifically in patients with genetically reduced CYP2C19 function. The information discouraging the use of concomitant medicines that inhibit CYP2C19 metabolism, e.g. omeprazole, will also be included as a precaution. **Reference:** 1. Prescriber Update Volume 30, No. 3, August 2009 (www.medsafe.govt.nz). 2. WHO Pharmaceuticals Newsletter No. 4, 2009.

Product Name: **Clozapine**

CAS Number: **5786-21-0**

Other Names: Leponex

Country	Effective Date	Description of action taken Grounds for decision
France	2010	- The initial prescription of the product should be made annually at hospital (at the initiation of the treatment by

		clozapine, and every year). - The prescription and the renewal of the prescription (every month) should be made by specialists in geriatry, neurology or psychiatry. - A specific monitoring is needed during treatment by clozapine to avoid the risk of agranulocytosis and myocarditis. **Reference:** Communication from the France National Pharmacovigilance Centre, March 2010.
Malaysia		In Malaysia, the clozapine label must include “For specialist’s use only” and the necessary warnings are related to hyperglycaemia and diabetes mellitus. **Reference:** Communication from the Malaysia National Pharmacovigilance Centre, February 2010.

Product Name: **Colchicine**

CAS Number: **64-86-8**

Other Names: Colsalide, Colcrys

Country	Effective Date	Description of action taken Grounds for decision
Malaysia	October 2009	Due to the potential risk of severe drug interactions, including death, observed in patients treated with colchicine and P-glycoprotein or strong CYP3A4 inhibitors, new warnings were added to advise against the concomitant use of these drugs in patients with renal or hepatic impairment. A dose reduction or interruption of colchicine treatment should be considered in patients with normal renal and hepatic function if treatment with a P-glycoprotein or a strong CYP3A4 inhibitor is required. In addition, patients should avoid consuming grapefruit and grapefruit juice while using colchicine. **Reference:** Communication from the Malaysia National Pharmacovigilance Centre, October 2009.
USA	2009	The US FDA has advised health-care professionals not to use P-glycoprotein or strong CYP3A4 inhibitors in patients with renal or hepatic impairment who are currently taking colchicine. Patients are advised to consult the Medication Guide for important safety information. The above advice has been issued because the US FDA has received reports of fatal colchicine toxicity in certain patients taking standard therapeutic doses of colchicine and concomitant medications that interact with colchicine, such as clarithromycin. **Reference:**

1. Safety Information, US FDA, 30 July 2009 (www.fda.gov).

2. WHO Pharmaceuticals Newsletter No. 4, 2009.

Product Name: **Cyproterone**

CAS Number: **2098-66-0**

Other Names: Cyprostat, Cyproteron

Country	Effective Date	Description of action taken Grounds for decision
Belarus	February 2010	Cyproterone-containing drugs with dosage higher than 2 mg are contraindicated in patients with meningioma or a history of meningioma. Treatment with cyproterone must be stopped if patient is diagnosed with meningioma. This decision was made on the basis of available evidences of a possible causal relationship between cyproterone acetate and the occurrence of meningioma. **Reference:** Communication from the Belarus National Pharmacovigilance Centre, April 2010.
UK	2009	The MHRA has advised health-care professionals that patients with existing meningioma or a history of meningioma must not be prescribed cyproterone acetate at doses of 25 mg per day or higher (Cyprostat-50, Cyprostat- 100, or Androcur-50). The occurrence of (multiple) meningiomas has been reported in association with longer-term use (years) of cyproterone acetate at doses of 25 mg/day or higher. **Reference:** 1. Drug Safety Update, MHRA, Volume 3, Issue 3, October 2009 (www.mhra.gov.uk). 2. WHO Pharmaceuticals Newsletters No. 6, 2009 & No.1, 2010.

Product Name: **Deferasirox**

CAS Number: **201530-41-8**

Other Names: Exjade

Country	Effective Date	Description of action taken Grounds for decision
Canada	2009	Canadian Product Monograph has been changed to include a contraindication in high risk myelodysplastic syndrome (MDS) patients and in those with advanced malignancies because these patients are not likely to benefit from iron chelation therapy due to the expected rapid progression of their disease.

Reference:

1. Advisories, Warnings and Recalls, Health Canada, 3 December 2009 (www.hc-sc.gc.ca).

2. WHO Pharmaceuticals Newsletter No. 6, 2009 & No. 1, 2010.

Product Name: Desmopressin

CAS Number: **16679-58-6**

Other Names: Minirin

Country	Effective Date	Description of action taken Grounds for decision
Iraq	January 2008	Desmopressin acetate in lingual tablets is restricted to be used in primary enuresis, central diabetes insipidus, and enuresis in adults. It is not to be used by patients over the age of 65 years. **Reference:** Communication from the Iraq National Pharmacovigilance Centre, May 2010.
Spain	2008	Desmopressin nasal product has new terms of use implemented because the nasal formulation was associated with more adverse drug reactions than the oral formulation. These new conditions are: - Dose reduction in primary nocturnal enuresis - Contraindicated in moderate and severe renal failure - To be used only when use of the oral formulation is not possible - Only for short duration treatment **Reference:** Alertas de Seguridad, AEMPS, 28 March 2008 (www.aemps.es).

Product Name: Dextropropoxyphene

CAS Number: **469-62-5**

Other Names: Darvocet-N, Capadex, Co-proxamol

Country	Effective Date	Description of action taken Grounds for decision
European Union	2009	The marketing authorizations for dextropropoxyphene containing medicines were withdrawn across the EU because the risks, particularly the risk of potentially fatal overdose, are greater than their benefits. The withdrawal was recommended because no other adequate measures could be identified to sufficiently minimize these risks.

		Reference: 1. Press Release, EMA, 25 June 2009 (www.ema.europa.eu). 2. WHO Pharmaceuticals Newsletter No. 4, 2009.
Iraq	March 2009	Dextropropoxyphen has been banned because of high incidence of adverse drug reactions. **Reference:** Communication from the Iraq National Pharmacovigilance Centre, May 2010.
New Zealand	1 August 2009	The consent to distribute dextropropoxyphene containing medicines will be revoked on 1 August 2010. From this date it will no longer be legal to sell, distribute, or advertise these medicines unless exempted under the Medicines Act 1981. This decision followed a review by the Medicines Adverse Reaction Committee, which concluded that, overall, the risks of these medicines exceed their benefits. **Reference:** 1. Prescriber Update, Volume 31, No. 1 February 2010 (www.medsafe.govt.nz). 2. WHO Pharmaceuticals Newsletter No. 2, 2010.

Product Name: **Efalizumab**

CAS Number: **214745-43-4**

Other Names: Raptiva

Country	Effective Date	Description of action taken Grounds for decision
Canada	2009	Health Canada has issued a recommendation to suspend efalizumab (Raptiva) in Canada, after the EMA has determined that the benefit/risk for the product has become unfavourable due to safety concerns. Prescribers in Canada are advised not to issue any new prescriptions for efalizumab and to review the treatment of patients taking this medicine to assess the most appropriate alternative. **Reference:** 1. Advisories, Warnings and Recalls, Health Canada, 20 January 2009 (www.hc-sc.gc.ca). 2. WHO Pharmaceuticals Newsletter No. 2, 2009.
European Union	2009	The EMA has recommended the suspension of the marketing authorization for efalizumab, which is authorized to treat adult patients with moderate to severe chronic plaque psoriasis. These decisions are based on reports of confirmed cases of progressive multifocal leukoencephalopathy (PML) in patients

		who had taken efalizumab for more than three years; two out of the three cases resulted in death. In addition to PML, efalizumab is associated with other serious side effects, including Guillain-Barré and Miller-Fisher syndromes, encephalitis, encephalopathy, meningitis, sepsis and opportunistic infections. There is not enough evidence to identify a group of patients in which the benefits of efalizumab outweigh its risks. **Reference:** 1. Press Release, EMA, 19 February 2009 (www.ema.europa.eu). 2. WHO Pharmaceuticals Newsletter No. 2, 2009.
Mexico	2010	Efalizumab has been withdrawn because of the risk of patients developing PML. **Reference:** Communication from the Mexico National Pharmacovigilance Centre, May 2010.
Switzerland	2009	The Swiss Agency for Therapeutic Products (Swissmedic) has banned the distribution and sales of efalizumab due to cases of PML. The drug is also suspected to be correlated with other serious adverse effects like Guillain-Barré- and Miller-Fisher-Syndrome, encephalitis, encephalopathy, meningitis, sepsis und opportunistic infections. The Agency has also warned that control by a physician is necessary to change the treatment for patients currently using the product, adding that stopping the product abruptly on a patient's own initiative can lead to an acute worsening of psoriasis and symptoms of inflammation. **Reference:** 1. Announcements, Swissmedic, 20 February 2009 (www.swissmedic.ch). 2. WHO Pharmaceuticals Newsletter No. 2, 2009.
Turkey	2009	Efalizumab has been withdrawn from the market in Turkey. **Reference:** WHO Pharmaceuticals Newsletter No. 2, 2009.
Ukraine	5 March 2009	Withdrawal of marketing authorization due to risk of serious side effects. **Reference:** Communication from the Ukraine National Pharmacovigilance Centre, May 2010.

Product Name: **Etoricoxib**

CAS Number: **202409-33-4**

Other Names: Arcoxia, Algix, Tauxib

Country	Effective Date	Description of action taken Grounds for decision
European Union	2008	The EMA recommended that the product information for etoricoxib-containing products should be updated concerning the risk of cardiovascular side effects. In addition, the CHMP recommended updating the existing contraindication in patients with hypertension that is not adequately controlled to state that patients whose blood pressure is persistently above 140/90 mmHg and has not been adequately controlled should not take etoricoxib. **Reference:** 1. Press Release, EMA, 26 June 2008 (www.ema.europa.eu). 2. WHO Pharmaceuticals Newsletter No. 3, 2008.

Product Name: **Etravirine**

CAS Number: **269055-15-4**

Other Names: Intellence

Country	Effective Date	Description of action taken Grounds for decision
Spain	October 2009	The Spanish Regulatory Agency (AEMPS) had instructed the company to update the data sheet about severe rash and hypersensitivity reaction. The AEMPS recommended that health-care professionals strictly follow the recommendations of the technical specifications and discontinue treatment in cases of severe rash or hypersensitivity reaction. **Reference:** AEMPS, Alertas de Seguridad, 21 October 2009 (www.aemps.es).

Product Name: **Fentanyl**

CAS Number: **437-38-7**

Other Names: Ionsys

Country	Effective Date	Description of action taken Grounds for decision
European Union	September 2008	The EMA has recommended the suspension of the marketing authorization of a system (Ionsys) for the transdermal delivery of fentanyl. This drug delivery system has a defect that could

		lead to overdose. **Reference:** 1. EMA, 20 November 2008 (www.ema.europa.eu). 2. WHO Pharmaceuticals Newsletters No. 5 & 6, 2008.

Product Name: **Flecainide**

CAS Number: **54143-55-4**

Other Names: Tambocor, Almarytm, Apocard

Country	Effective Date	Description of action taken Grounds for decision
New Zealand	2009	Flecainide is not recommended for use in patients with chronic atrial fibrillation due to the risk of inducing 1:1 atrioventricular conduction, with a consequent paradoxical increase in ventricular rate when used to treat atrial flutter. Flecainide is indicated only in patients without structural heart disease for the prevention, rapid control, or short-term prophylaxis of supraventricular and ventricular arrhythmias. **Reference:** 1. Prescriber Update Volume. 30, No.2, May 2009 (www.medsafe.govt.nz). 2. WHO Pharmaceuticals Newsletter No. 3, 2009.

Product Name: **Gadolinium**

CAS Number: **7440-54-2**

Other Names: Optimark, Omniscan, Magnevist, Magnegita and Gado-MRT ratiopharm

Country	Effective Date	Description of action taken Grounds for decision
European Union	November 2009	High-risk gadolinium-containing contrast agents (Optimark, Omniscan, Magnevist, Magnegita and Gado-MRT ratiopharm) are contraindicated in patients with severe kidney problems, in patients who are scheduled for or have recently received a liver transplant, and in newborn babies up to four weeks of age. The prescribing information for all gadolinium-containing contrast agents should include: - a warning that the elderly may be at particular risk of nephrogenic systemic fibrosis (NSF) due to impaired ability of their kidneys to clear gadolinium from the body - a statement that there is no evidence to support the initiation of haemodialysis to prevent or treat NSF in patients not already undergoing haemodialysis - a statement that the type and dose of contrast agent used

		should be recorded. These recommendations are aimed at minimizing the risk of NSF with gadolinium-containing contrast agents. **Reference:** 1. Press Release, EMA, 20 November 2009 (www.ema.europa.eu). 2. WHO Pharmaceuticals Newsletters No. 6, 2009 & No. 1, 2010.

Product Name: **Gadoversetamide**
CAS Number: **131069-91-5**
Other Names: Optimark

Country	Effective Date	Description of action taken Grounds for decision
Canada	2010	Due to the risk of NSF in patients with renal impairment, gadoversetamide (Optimark) is contraindicated in patients with: - acute or chronic severe renal insufficiency (glomerular filtration rate <30 mL/min/1.73m2), or - acute renal insufficiency of any severity due to the hepato-renal syndrome or in the perioperative liver transplantation period. Gadoversetamide is not recommended for use in children below the age of two years because the safety and efficacy of gadoversetamide, as well as impact of use in patients with an immature kidney function have not been studied. **Reference:** 1. Advisories, Warnings and Recalls, Health Canada, 12 January 2010 (www.hc-sc.gc.ca). 2. WHO Pharmaceuticals Newsletters No. 6, 2009 & No. 1, 2010.

Product Name: **Goserelin**
CAS Number: **65807-02-5**
Other Names: Zoladex

Country	Effective Date	Description of action taken Grounds for decision
Iraq	January 2008	Gosorelin (as acetate) implant, 10.8 mg in safe system syringe applicator is restricted to the use in prostate and breast cancers only. **Reference:**

Communication from the Iraq National Pharmacovigilance Centre, May 2010.

Product Name: **Human Chorionic Gonadotropin Hormone**

CAS Number:

Other Names: A.P.L., Chorex, Pregnyl, Profasi

Country	Effective Date	Description of action taken Grounds for decision
Iraq	April 2008	Registration withdrawn of non-recombinant Human Chorionic Gonadotropin Hormone, in the strengths 1500 and 5000 IU. **Reference:** Communication from the Iraq National Pharmacovigilance Centre, May 2010.

Product Name: **Human immune globulin**

CAS Number:

Other Names: WinRho

Country	Effective Date	Description of action taken Grounds for decision
Canada	2010	Due to rare but serious and sometime fatal adverse events of intravascular hemolysis (IVH) and its complications, human immune globulin is contraindicated for immune thrombocytopenic purpura (ITP) patients: - with ITP secondary to other conditions including leukemia, lymphoma, or active viral infections with Epstein-Barr virus (EBV) or hepatitis C (HCV) - who are elderly with co-morbidities predisposing to acute hemolytic reaction (AHR) or its complications - with evidence of autoimmune hemolytic anemia (Evan's Syndrome), or Systemic Lupus Erythematosus (SLE) or anti-phospholipid antibody syndrome (APS) - who are IgA deficient. **Reference:** 1. Advisories, Warnings and Recalls, Health Canada, 22 March 2010 (www.hc-sc.gc.ca). 2. WHO Pharmaceuticals Newsletter No. 2, 2010.

Product Name: **Iron sucrose**

CAS Number: **8047-67-4**

Other Names: Venofer

Country	Effective Date	Description of action taken Grounds for decision
Iraq	November 2008	The use of Iron sucrose for injection is restricted for use in hospitals, for in-patients only. **Reference:** Communication from the Iraq National Pharmacovigilance Centre, May 2010.

Product Name: **Isotretinoin**

CAS Number: **4759-48-2**

Other Names: Accutane, Amnesteem, Oratane

Country	Effective Date	Description of action taken Grounds for decision
New Zealand	2009	As a result of its teratogenicity, isotretinoin is contraindicated in women of childbearing potential unless an extensive list of conditions for prescribing are met. Medsafe is currently assessing the risk mitigation strategies used by the manufacturers of isotretinoin products in New Zealand. **Reference:** 1. Prescriber Update, Volume 30, No.2, Medsafe, May 2009 (www.medsafe.govt.nz). 2. WHO Pharmaceuticals Newsletter No. 3, 2009.
Switzerland	7 October 2008	The prescription and dispense of isotretinon has been restricted for female patients based on the teratogenic effect of isotretinoin. Female patients must confirm with their signature that they know the risks in connection with the treatment and will keep the safety measures by adhering to a strict contraception program. The prescription of isotretinoin must be restricted to 30 days for women in reproductive age. A new prescription is needed for continuation of therapy. Isotretinoin has to be dispensed within 7 days maximally following issue of the prescription. **Reference:** Communication from Swissmedic, April 2010.

Product Name: **Ivermectin**

CAS Number: **70288-86-7**

Other Names: Stromectol

Country	Effective Date	Description of action taken Grounds for decision
Iraq	July 2008	Ivermectin has been restricted to be used in scabies complicated with hyperkeratotic crusted lesions only. **Reference:** Communication from the Iraq National Pharmacovigilance Centre, May 2010.

Product Name: **Ketoprofen**

CAS Number: **22071-15-4**

Other Names: Ketum, Topfena

Country	Effective Date	Description of action taken Grounds for decision
Egypt	June 2008	A contraindication for ketoprofen dosage of more than 2 mg/kg/day has been decided. From 19 November 2009 ketoprofen injection and suppositories are contraindicated in children. From 1 January 2010 ketoprofen is contraindicated in children less than 6 months of age. All products containing ketoprofen in the form of a gel have been withdrawn. **Reference:** Communication from the Egypt National Pharmacovigilance Centre, April 2010.
France	12 January 2010	AFSSAPS is suspending the market authorization for specialties containing ketoprofen gel for which the benefit/risk is now seen as negative because of the risk of adverse skin reactions in rare but serious photoallergy. **Reference:** Retraits de lots et de produits, AFSSAPS, January 2010 (www.afssaps.fr).

Product Name: **Laronidase**

CAS Number: **210589-09-6**

Other Names: Aldurazyme

Country	Effective Date	Description of action taken Grounds for decision
Iraq	May 2009	Laronidase is restricted to distribution to specialized centers only. **Reference:** Communication from the Iraq National Pharmacovigilance Centre, May 2010.

Product Name: **Letrozole**

CAS Number: **112809-51-5**

Other Names: Femara

Country	Effective Date	Description of action taken Grounds for decision
Iraq	September 2009	Letrozole 205 mg tablets is restricted to be used in endometriosis and advanced breast cancer only. **Reference:** Communication from the Iraq National Pharmacovigilance Centre, May 2010.

Product Name: **Mefenamic acid**

CAS Number: **61-68-7**

Other Names: Dyfenamic, Dolfenal, Mafepain, Mephadolor, Meftal, Meyerdonal, Parkemed, Ponstel, Ponstan, Ponstal, Potarlon

Country	Effective Date	Description of action taken Grounds for decision
Iraq	April 2009	Mefenamic acid suspension should not be used in children under 12 years of age. **Reference:** Communication from the Iraq National Pharmacovigilance Centre, May 2010.
Switzerland		Mefenamic acid is registered in Switzerland as an analgesic and antipyretic agent for adults and children, but restricted to children older than 6 months. **Reference:**

Communication from the Switzerland National Pharmacovigilance Centre, April 2008.

Product Name: **Mefloquine**
CAS Number: **53230-10-7**
Other Names: Lariam

Country	Effective Date	Description of action taken Grounds for decision
Iraq	July 2009	Mefloquine hydrochloride in tablets and mefloquin lactate in 250 mg tablets have been restricted to control centres for tranmitted diseases only. **Reference:** Communication from the Iraq National Pharmacovigilance Centre, May 2010.

Product Name: **Metamizole**
CAS Number: **50567-35-6**
Other Names: Dipyrone, Analgin, Noramidopyrine, Novalgine, Minalgin

Country	Effective Date	Description of action taken Grounds for decision
Philippines		Metamizole has been banned in the Philippines. **Reference:** Communication from the Philippines National Pharmacovigilance Centre, June 2009.

Product Name: **Methylphenidate**
CAS Number: **113-45-1**
Other Names: Ritalin, Methylin, Equasym

Country	Effective Date	Description of action taken Grounds for decision
European Union	2009	The EMA has concluded that methylphenidate-containing medicines remain suitable for the treatment of children aged six years or older and adolescents with attention deficit/hyperactivity disorder (ADHD). All patients should be screened for any problems with blood pressure or heart rate and psychiatric disorders before starting treatment and monitored regularly during treatment. Treatment should be interrupted at least once a year to

determine whether continuation is needed.

Reference:

1. Press Release, EMA, 22 January 2009.

2. WHO Pharmaceuticals Newsletter No. 2, 2009.

Product Name: **Methylthioninium chloride**

CAS Number: **61-73-4**

Other Names: Methylene Blue

Country	Effective Date	Description of action taken Grounds for decision
UK	2009	Use of methylthioninium chloride is not approved in visualization in surgical procedures or in the management of intractable hypotension. The MHRA has provided an update on the risk of central nervous system (CNS) toxicity associated with an interaction between methylthioninium chloride (formerly called methylene blue) and serotonergics. In view of the new reports, the MHRA has strengthened the advice for health-care professionals, including emphasis on approved indication. It is also advised that intravenous methylthioninium chloride should be avoided in patients who have been treated recently with serotonergic antidepressants, including SSRIs, clomipramine and venlafaxine. **Reference:** 1. Drug Safety Update, MHRA, Volume 2, Issue 9, April 2009 (www.mhra.gov.uk). 2. WHO Pharmaceuticals Newsletter No. 3, 2009.

Product Name: **Metoclopramide**

CAS Number: **364-62-5**

Other Names: Reglan, Primperan

Country	Effective Date	Description of action taken Grounds for decision
USA	2009	The US FDA has required manufacturers of metoclopramide to add a boxed warning to the labels about the risk of its long-term or high-dose use. It is recommended that treatments not exceed three months. These warnings are based on reports of tardive dyskinesia in many patients who used metoclopramide for more than three months. **Reference:** 1. FDA News, US FDA, 26 February 2009 (www.fda.gov). 2. WHO Pharmaceuticals Newsletter No. 2, 2009.

Product Name: **Misoprostol**

CAS Number: **59122-46-2**

Other Names: Cytotec

Country	Effective Date	Description of action taken Grounds for decision
Cameroon		Misoprostol is registered in Cameroon as a prescription-only-medicine that may only be used in hospitals under strict supervision of the prescribers. **Reference:** Communication from theCameroon National Pharmacovigilance Centre, January 2008.

Product Name: **Moxifloxacin**

CAS Number: **151096-09-2**

Other Names: Avelox, Vigamox

Country	Effective Date	Description of action taken Grounds for decision
European Union	2008	Moxifloxacin-containing medicines for oral use should only be prescribed in the treatment of acute bacterial sinusitis, acute exacerbation of chronic bronchitis and community acquired pneumonia when other antibiotics cannot be used or have failed. The reason is increased risk of hepatic reactions. **Reference:** 1. Press Release, EMA, 24 July 2008. 2. WHO Pharmaceuticals Newsletter No. 3, 2008.

Product Name: **Mycophenolate mofetil**

CAS Number: **115007-34-6**

Other Names: CellCept, Myfortic

Country	Effective Date	Description of action taken Grounds for decision
USA	2009	Due to serious side effects including possible loss of pregnancy, and higher risk of birth defects, serious infections and certain cancers, a medication guide for mycophenolate mofetil (CellCept) has been interoduced to provide important safety information for patients. Pharmacists are required to distribute a copy of the medication guide to every patient who fills a prescription of this product.

Reference:

1. Media Release, US FDA, 12 February 2009 (www.fda.gov).

2. WHO Pharmaceuticals Newsletter No. 2, 2009.

Product Name: **Nifuroxazine**

CAS Number: **965-52-6**

Other Names:

Country	Effective Date	Description of action taken Grounds for decision
Belgium	2008	Nifuroxazine was withdrawn from the Belgian market due to its negative benefit-risk profile with a lack of proven efficacy in human therapy (no resorption in the gastro-intestinal tract) and the availability of many effective alternative therapies. **Reference:** Communication from the Belgium National Pharmacovigilance Centre, October 2008.

Product Name: **Nimesulide**

CAS Number: **51803-78-2**

Other Names: Aldoron, Nisulid, Redaflam, Scafan

Country	Effective Date	Description of action taken Grounds for decision
Argentina	September 2009	The National Agency for Drugs, Food and Medical Technology (ANMAT) through its Department of Evaluation of Medicinal Products (DEM) and its National Pharmacovigilance System ordered the prohibition of all medical specialties containing the NSAID nimesulide as the only active pharmaceutical ingredient or in combination products. **Reference:** Communication from the Argentina National Pharmacovigilance Centre, March 2010.
Bhutan	2008	The sale and use of nimesulide was suspended in Bhutan. **Reference:** Communication from the Bhutan National Pharmacovigilance Centre, December 2008.
Brazil	2008	Nimesulide is used in Brazil for children above 12 years of age. The leaflet information was changed after two cases of Reye's syndrome occurred in Portugal. **Reference:** Communication from the Brazil National Pharmacovigilance

		Centre, January 2008.
Egypt	October 2009	Nimesulide containing products are contraindicated in children under 12 years in Egypt. The use of systemic formulation of nimesulide should be restricted to limit the risk of liver injury. Packages must be modified to contain no more than 30 doses with duration no more than 15 days. Registration of new products will not be approved but may be registered for export only. **Reference:** Communication from the Egypt National Pharmacovigilance Centre, May 2010.
Malaysia	2008	The Ministry of Health has cancelled registration of all registered products containing nimesulide and prohibited the registration of new products containing nimesulide. **Reference:** Communication from the Malaysia National Pharmacovigilance Centre, November 2008.
Mexico		Nimesulide is restricted to be used in adults and in children over 2 years of age due to possible hepatotoxic effects. **Reference:** Communication from the Mexico National Pharmacovigilance Centre, May 2010.
Singapore	July 2008	The Health Sciences Authority (HSA) concluded that the benefit-risk profile of nimesulide is unfavourable as there is an increased risk of liver toxicity. Sale of oral preparations containing nimesulide is suspended. **Reference:** Communication from the Singapore National Pharmacovigilance Centre, November 2008.
Thailand	2008	A temporary decsion was taken in Thailand about nimesulide in early 2008 as follows: - Nimesulide is restricted to be used in hospitals only, and intensive monitoring for liver toxicity must be carried out in all patients. - The suspension formulation and 50 mg tablet are withdrawn. - A study will be conducted to find out the risks and benefits of this product in the country. **Reference:** Communication from the Thailand National Pharmacovigilance Centre, January 2008.
Ukraine	16 July 2008	The use of all products containing nimesulide has been restricted to the treatment of acute pain, symptomatic treatment of osteoarthritis and primary dysmenorrhoea and

		added contraindications for use in children under 12 years of age, in patients with fever and/or flu-like symptoms, and for use with potential hepatotoxic drugs, other NSAIDs and alcohol. **Reference:** Communication from the Ukraine National Pharmacovigilance Centre, May 2010.
Viet Nam	September 2008	Drug Administration of Viet Nam has stopped new applications for oral products containing nimesulide and has withdrawn all products containing nimesulide already on the market. This decision does not apply to topical products containing nimesulide. **Reference:** Communication from the Viet Nam National Pharmacovigilance Centre, November 2008.

Product Name: Nitrous oxide

CAS Number: 10024-97-2

Other Names:

Country	Effective Date	Description of action taken Grounds for decision
New Zealand	2009	Prescribers are advised to check vitamin B12 levels in those with risk factors for vitamin B12 deficiency prior to using nitrous oxide and to seek specialist advice if necessary. Prescribers are also advised not to use nitrous oxide continuously for more than 24 hours or more frequently than every four days without clinical supervision and haematological monitoring. **Reference:** 1. Prescriber Update Volume. 30, No. 3, August 2009 (www.medsafe.govt.nz). 2. WHO Pharmaceuticals Newsletter No. 5, 2009.
UK	2008	The MHRA has advised health-care professionals to assess vitamin B12 levels before nitrous oxide anaesthesia in people with risk factors for vitamin B12 deficiency. Prolonged use of nitrous oxide may lead to rare cases of megaloblastic anaemia and myelopathy resulting from vitamin B12 inactivation. **Reference:** 1. Drug Safety Update, MHRA, Volume 2, Issue 5, December 2008 (www.mhra.gov.uk). 2. WHO Pharmaceuticals Newsletter No. 1, 2009.

Product Name: **Norfloxacin**
CAS Number: **70458-96-7**
Other Names: Noroxin

Country	Effective Date	Description of action taken Grounds for decision
European Union	2008	The CHMP has advised against the use of oral norfloxacin-containing medicines in the treatment of acute or chronic complicated pyelonephritis (kidney infection) due to its poorly established efficacy and high risk for adverse effects. This recommendation does not apply to the use of oral norfloxacin-containing medicines in other types of infection. **Reference:** 1. EMA Press Release, 24 July 2008 (www.ema.europa.eu). 2. WHO Pharmaceuticals Newsletter No. 3, 2008.

Product Name: **Orciprenaline**
CAS Number: **586-06-1**
Other Names: Alupent Syrup

Country	Effective Date	Description of action taken Grounds for decision
UK	2009	The MHRA has annouced the withdrawal of orciprenaline sulphate due to its low bronchodilating efficacy (compared to salbutamol) and high incidence of cardiac side effects, mainly palpitations and tachycardia due to its nonselectivity. **Reference:** 1. Drug Safety Update, MHRA, Volume 3, Issue 4, November 2009 (www.mhra.gov.uk). 2. WHO Pharmaceuticals Newsletters No. 6, 2009 & No. 1, 2010.

Product Name: **Pergolide**
CAS Number: **76-19-7**
Other Names: Permax

Country	Effective Date	Description of action taken Grounds for decision
Switzerland	26 August 2008	The maximal daily dose of Permax has been restricted (reduced to 3 mg from 5 mg) due to known risk of cardiac valvulopathy. Additionally, a cardiovascular examination before treatment has become mandatory.

Reference:

Communication from Swissmedic, April 2010.

Product Name: Phenazone

CAS Number: **60-80-0**

Other Names: Saridon, Antipyrine

Country	Effective Date	Description of action taken Grounds for decision
Iraq	August 2008	Saridon tablets, which contain phenazone, have been banned because of the high incidence of adverse reactions (phenazone was banned in Iraq in 1980s). **Reference:** Communication from the Iraq National Pharmacovigilance Centre, May 2010.

Product Name: Phenylpropanolamine

CAS Number: **14838-15-4**

Other Names: Norephedrine

Country	Effective Date	Description of action taken Grounds for decision
Indonesia		In Indonesia phenylpropanolamine (PPA) is only approved as nasal decongenstant in cough and cold products with a recommended dosage of 10 - 25 mg and a maximum dosage per day of 75 mg (adults) and 37.5 mg (children 6 - 12 years old). **Reference:** Communication from the Indonesia National Pharmacovigilance Centre, April 2009.
Uganda		In Uganda, all products containing phenylpropanolamine have been de-registered. Market authorization holders were advised to reformulate products containing phenylpropanolamine, using a different composition, and re-apply for registration if interested. **Reference:** Communication from the Uganda National Pharmacovigilance Centre, December 2009.

Product Name: **Pimecrolimus**

CAS Number: **137071-32-0**

Other Names: Elidel

Country	Effective Date	Description of action taken Grounds for decision
Mexico	2010	Pimecrolimus should only be used for short periods of time at the lowest amount possible. It should not be used in children younger than 2 years or in immunocompromised patients. **Reference:** Communication from the Mexico National Pharmacovigilance Centre, May 2010.

Product Name: **Piroxicam**

CAS Number: **36322-90-4**

Other Names: Feldene

Country	Effective Date	Description of action taken Grounds for decision
Canada	2009	Health Canada has recommended that piroxicam should no longer be used to treat acute or short-term pain and inflammation due to an increased risk of serious skin reactions and gastrointestinal problems relative to other similar drugs. Piroxicam can still be prescribed for the symptomatic relief of chronic pain and inflammation in patients suffering from certain types of chronic arthritis (osteoarthritis, rheumatoid arthritis and ankylosing spondylitis). **Reference:** 1. Advisories, Warnings and Recalls, Health Canada, 25 June 2009 (www.hc-sc.gc.ca). 2. WHO Pharmaceuticals Newsletter No. 4, 2009.

Product Name: **Promethazine**

CAS Number: **60-87-7**

Other Names: Phenergan, Romergan, Avomine

Country	Effective Date	Description of action taken Grounds for decision
USA	16 September 2009	Due to the risks of of severe tissue injury, including gangrene, and subsequent amputation associated with intravenous administration of promethazine, the preferred route of administration for this product is deep intramuscular injection;

		subcutaneous injection is contraindicated. **Reference:** 1. Safety Information, US FDA, 16 September 2009 (www.fda.gov). 2. WHO Pharmaceuticals Newsletter No. 5, 2009.

Product Name: **Propylthiouracil**

CAS Number: **51-52-5**

Other Names: Prothiucil, Propacil

Country	Effective Date	Description of action taken Grounds for decision
Malaysia		Propylthiouracil should not be used in paediatric patients unless the patient is allergic or intolerant to available alternatives. Due to the potential risk of serious hepatotoxicity including liver failure and death, patients should be closely monitored for signs and symptoms of liver injury, espeically during the first six months of treatment. **Reference:** Communication from the Malaysia National Pharmacovigilance Centre, June 2009.
USA	3 June 2009	Because of the risk of serious liver injury, including liver failure and death, with the use of propylthiouracil (PTU), it is recommended only as a second-line therapy; it should be reserved for patients who are intolerant to methimazole or patients with Grave's disease, who are in their first trisemester of pregnancy, or who are allergic to or do not tolerate methimazole (MMI). It has also been advised that PTU should not be used in paediatric patients unless the patient is allergic to or does not tolerate MMI, and there are no other treatment options available. **Reference:** 1. FDA Alert, US FDA, 3 June 2009 (www.fda.gov). 2. WHO Pharmaceuticals Newsletter No. 4, 2009.

Product Name: **Pseudoephedrine**

CAS Number: **90-82-4**

Other Names: Genaphed, Robidrine, Sudafed

Country	Effective Date	Description of action taken Grounds for decision
Egypt	18 June 2009	Pseudoephedrine is contraindicated in children less than two years of age. Registration of new products containing

		pseudoephedrine will not be approved. **Reference:** Communication from the Egypt National Pharmacovigilance Centre, April 2010.
Iraq	May 2008	Pseudoephedrine hydrochloride has been banned because of an increased risk of adverse reactions. **Reference:** Communication from the Iraq National Pharmacovigilance Centre, May 2010.

Product Name: **Rimonabant**

CAS Number: **168273-06-1**

Other Names: Acomplia

Country	Effective Date	Description of action taken Grounds for decision
Switzerland	30 Ocotober 2008	The distribution and sale of rimonabant have been banned (suspension of marketing authorization) due to increased risk of serious psychiatric disorders. **Reference:** Communication from Swissmedic, April 2010.
Ukraine	29 January 2009	A voluntary recall has been conducted by Sanofi-Aventis. **Reference:** Communication from the Ukraine National Pharmacovigilance Centre, May 2010.

Product Name: **Sibutramine**

CAS Number: **106650-56-0**

Other Names: Lindaxa, Meridia, Minimectil, Redact, Reductil, Sibutral

Country	Effective Date	Description of action taken Grounds for decision
Armenia	2010	Scientific Centre of Drug and Medical Technology Expertise, Ministry of Health of the Republic of Armenia (SCDMTE MoH) suspended marketing authorization for sibutramine weight-loss medicine associated with increased risk of cardiovascular events, on the basis of unsatisfactory ”benefit/risk” index. **Reference:** Communication from the Armenia National Pharmacovigilance Centre, April 2010.

Belarus	March 2010	Sibutramine-containing medicines have been suspended and recalled from the market. The suspension will remain until the manufacturers are able to provide sufficient data that sibutramine's benefits clearly outweigh its risks in certain patient groups. This decision is based on currently available data suggesting that cardiovascular risks of sibutramine-containing medicines outweigh its therapeutical benefit in reducing body weight. **Reference:** Communication from the Belarus National Pharmacovigilance Centre, April 2010.
Brazil	February 2010	A decision was made in February 2010 to keep sibutramine available in Brazil, but under a stricter prescription scheme (changed from C to B2). A final decision will be made based on the report from the Sibutramine Cardiovascular Outcome Trial (SCOUT). **Reference:** Communication from the Brazil CEATOX Centre, March 2010.
Egypt	11 February 2010	The marketing authorizations for sibutramine (Reductil, Sibutral) have been cancelled. **Reference:** Communication from the Egypt National Pharmacovigilance Centre, April 2010.
European Union	21 January 2010	The EMA has advised a suspension on the prescription and distribution of sibutramine due an increased risk for serious cardiovascular events in patients with a history of cardiovascular disease. **Reference:** 1. Press Release, Questions and Answers, EMA, 21 January 2010 (www.ema.europa.eu). 2. WHO Pharmaceuticals Newsletters No. 6, 2009 & No. 1, 2010.
Saudi Arabia	2010	The marketing authorizations for sibutramine (Reductil, Sibutral) have been cancelled. **Reference:** WHO Pharmaceuticals Newsletters No. 6, 2009 & No. 1, 2010.
Sudan	2010	The registration of sibutramine in Sudan has been suspended. Sibutramine has been registered in Sudan but was never marketed. **Reference:** Communication from the Sudan National Pharmacovigilance Centre, March 2010.

Switzerland	29 March 2010	The distribution and sale of sibutramine have been banned (suspension of marketing authorization) due to increased cardiovascular risk observed in the SCOUT study. **Reference:** Communication from Swissmedic, April 2010.
Ukraine	15 April 2010	Marketing authorization of products containing sibutramine has been suspended due to adverse cardiovascular events associated with the drug. **Reference:** Communication from the Ukraine National Pharmacovigilance Centre, May 2010.
USA	November 2009	Sibutramine is contraindicated in patients with a history of cardiovascular disease, including coronary artery disease (e.g., heart attack, angina), stroke or transient ischaemic attack, cardiac arrhythmias, congestive heart failure, peripheral arterial disease, or uncontrolled hypertension (e.g. > 90/145 mmHg) since there are reports of cadiovascular events (heart attack, stroke, resuscitated cardiac arrest, or death) related to sibutramine use in patients with a history of cardiovascular disease. Patients' blood pressure and heart rate should be monitored regularly. Sibutramine should be discontinued in patients who do not lose at least 5% of their baseline body weight within the first three to six months of treatment. **Reference:** 1. Safety Information, US FDA, 20 November 2009, 21 January 2010 (www.fda.gov). 2. WHO Pharmaceuticals Newsletter No. 6, 2009 & No. 1, 2010.

Product Name: **Sodium phosphate**

CAS Number: **7632-05-5**

Other Names: Fleet Enema, LaCrosses Complete, Visicol

Country	Effective Date	Description of action taken Grounds for decision
Canada	March 2009	Health Canada has warned the public against using over-the-counter oral sodium phosphate products as bowel cleansers due to serious adverse effects, including electrolyte disturbances and kidney damage. However, these products are still considered to be safe and effective for laxative use. **Reference:** 1. Advisories, Warnings and Recalls, Health Canada, 5 August 2009 (www.hc-sc.gc.ca).

		2. WHO Pharmaceuticals Newsletter No. 5, 2009.
Iceland	17 May 2009	Phosphoral (oral solution, 10.8 g/45 ml g 24.4 g/45 ml) is no longer sold over the counter in Iceland, due to reports of serious adverse events. **Reference:** Communication from the Iceland National Pharmacovigilance Centre, May 2010.
USA	11 December 2008	The US FDA has issued an alert that over-the-counter oral sodium phosphate (OSP) laxative products should not be used for bowel cleansing prior to colonoscopy and other procedures due to the risk of acute phosphate nephropathy. The US FDA is requiring the manufacturers of the two prescription-only OSPs to add a Boxed Warning to the labelling, as well as to develop and implement a risk evaluation and mitigation strategy (REMS), which will include a Medication Guide. **Reference:** 1. FDA Alert, US FDA, 11 December 2008 (www.fda.gov). 2. WHO Pharmaceuticals Newsletter No. 1, 2009.

Product Name: ***Stichopus sp.* (*S. horrens*, *S. variegatus*)**

CAS Number:

Other Names: Sea Cucumber, Gamat

Country	Effective Date	Description of action taken Grounds for decision
Malaysia	2008	The registration of Gamat products from Healwell Pharmaceuticals was suspended and all products in the market containing *Stichopus sp.* were recalled following adverse reaction reports received on renal failure. **Reference:** Communication from the Malaysia National Pharmacovigilance Centre, November 2008.

Product Name: **Tacrolimus**

CAS Number: **104987-11-3**

Other Names: Protopic

Country	Effective Date	Description of action taken Grounds for decision
Mexico	2010	Tacrolimus (topical preparation) should not be used in children younger than 2 years and in immunocompromised patients. It should only be used for short periods of time at the

		lowest amount possible. **Reference:** Communication from the Mexico National Pharmacovigilance Centre, May 2010.

Product Name: **Telithromycin**

CAS Number: **173838-31-8**

Other Names: Ketek

Country	Effective Date	Description of action taken Grounds for decision
Egypt	30 October 2008	The use of telithromycin is restricted to the following indications: - acute bacterial sinusitis - acute bacterial exacerbations of chronic bronchitis. In addition, telithromycin is contraindicated in patients with myasthenia gravis. There is also a strengthened warning on specific drug-related adverse events including visual disturbances and loss of consciousness. **Reference:** Communication from Egypt National Pharmacovigilance Centre, April 2009.

Product Name: **Thalidomide**

CAS Number: **50-35-1**

Other Names: Thalix

Country	Effective Date	Description of action taken Grounds for decision
European Union	January 2009	Thalidomide is used to treat multiple myeloma in combination with melphalan and prednisone in patients who have not been treated for multiple myeloma before. It is only to be used in patients aged over 65 years, and in younger patients if they cannot be treated with high-dose chemotherapy. Thalidomide must be prescribed and dispensed according to a special programme to prevent the exposure of unborn children to the medicine. **Reference:** European Public Assessment Report (EPAR), EMA, January 2009 (www.ema.europa.eu/humandocs/PDFs/EPAR/thalidomidecel

		gene/H-823-en1.pdf).
Sudan	July 2009	Thalidomide was registered in Sudan in July 2009 under the name Thalix, for multiple myeloma, in concentrations 50 mg and 100 mg. The use of the medicince will be restricted to: - distribution in special myeloma centres only - prescription-only drug from specialists - prescription should be written in Arabic language. **Reference:** Communication from the Sudan National Pharmacovigilance Centre, February 2010.

Product Name: **Tibolone**
CAS Number: **5630-53-5**
Other Names: Livial

Country	Effective Date	Description of action taken Grounds for decision
UK	February 2009	Tibolone is contraindicated in women with known or suspected breast cancer and those with a history of breast cancer due to an increased risk for recurrence of breast cancer. **Reference:** 1. Drug Safety Update, MHRA, Volume 2, Issue 7, February 2009 (www.mhra.gov.uk). 2. WHO Pharmaceuticals Newsletter No. 2, 2009.

Product Name: **Tinzaparin**
CAS Number: **9041-08-1**
Other Names: Innohep

Country	Effective Date	Description of action taken Grounds for decision
USA	2008	The US FDA has recommended the use of alternative treatments to tinzaparin sodium injection in elderly patients over 70 years of age with renal insufficiency and deep vein thrombosis, and/or pulmonary emboli due to the increased risk of death. **Reference:** 1. Communication about an Ongoing Safety Review, US FDA, 2 December 2008 (www.fda.gov). 2. WHO Pharmaceuticals Newsletter No. 1, 2009.

Product Name: **Tiotropium**

CAS Number: **186691-13-4**

Other Names: Spiriva

Country	Effective Date	Description of action taken Grounds for decision
Iraq	March 2009	Tiotropium solution for inhalation has been banned due to the lack of safety information. **Reference:** Communication from the Iraq National Pharmacovigilance Centre, May 2010.

Product Name: **Toremifene**

CAS Number: **89778-26-7**

Other Names: Fareston, Acapodene

Country	Effective Date	Description of action taken Grounds for decision
European Union	January 2009	Due to concerns over QT-prolongation caused by toremifene, the EMA has advised against the use of toremifene in patients at risk for prolonged QT intervals and other heart problems including electrolyte disturbances (particularly hypokalaemia), clinically relevant bradycardia, clinically relevant heart failure with reduced left-ventricular ejection fraction, and a history of symptomatic arrhythmia. Additionally, using toremifene with other medicines known to cause QT-prolongation is not recommended. **Reference:** 1. Press Release, EMA, 22 January 2009 (www.ema.europa.eu). 2. Alert No. 120, Information Exchange System, WHO, 23 January 2009 (www.who.int/medicines). 3. WHO Pharmaceuticals Newsletter No. 1, 2009.
Switzerland	12 February 2009	Due to the risk of QT-interval prolongation, toremifene is contraindicated in patients with an increased risk for this adverse event. **Reference:** Communication from Swissmedic, April 2010.

Product Name: **Tramadol**

CAS Number: **27203-92-5**

Other Names: Tramal, Tramundin

Country	Effective Date	Description of action taken Grounds for decision
Bahrain	2009	In Bahrain, tramadol is a controlled medicine dispensed only through special control drug prescription due to abuse problems. **Reference:** Communication from the Bahrain National Pharmacovigilance Centre, February 2009.

Product Name: **Triamcinolone**

CAS Number: **124-94-7**

Other Names: Kenalog, Aristocort, Nasacort

Country	Effective Date	Description of action taken Grounds for decision
Canada	July 2009	Intravitreal and intraocular injection of triamcinolone is not authorized in Canada due to ocular adverse reactions including retinal detachment and vitreous hemorrhage, which can later progress into cataracts, steroid-induced glaucoma, and endophthalmitis. Currently, only intramuscular and intra-articular administration, or injection into tendon sheaths or ganglia are approved for use. **Reference:** 1. Canadian Adverse Reaction Newsletter, Health Canada, Volume 19, Issue 3, July 2009 (www.hc-sc.gc.ca). 2. WHO Pharmaceuticals Newsletter No. 4, 2009.

Product Name: **Vincristine**

CAS Number: **57-22-7**

Other Names: Vincasar

Country	Effective Date	Description of action taken Grounds for decision
Iraq	May 2008	Vincristine should only be administered intravenously and not by any other route. **Reference:** Communication from the Iraq National Pharmacovigilance

Centre, May 2010.

Product Name: **Zinc-containing intranasal products**

CAS Number:

Other Names: Zicam Nasal Gel, Zicam Nasal Swab

Country	Effective Date	Description of action taken Grounds for decision
USA	2009	The US FDA has warned against the use of three zinc-containing intranasal products sold as over-the-counter cold remedies (Zicam Nasal Gel and Nasal Swab) due to their association with a long-lasting or permanent loss of sense of smell. These products have not been shown to be effective in reducing the duration or severity of cold symptoms. This advisory does not apply to oral zinc tablets and oral lozenges. **Reference:** 1. Safety Information, US FDA, 16 June 2009. 2. WHO Pharmaceuticals Newsletter No. 4, 2009.

Product Name: **Baithach**

CAS Number:

Other Names: Content: Desmodium, Adenosmatis, Scutellaria, Curcuma, Areca, Citrus, Magnolia, Imperata, Saussurea, Rheum

Country	Effective Date	Description of action taken Grounds for decision
Armenia	2009	The SCDMTE MoH did not approve the marketing authorization of Baithach (complex of herbal extracts recognized as a non-traditional herbal drug) because the description of plant properties and indications were not consistent with those described in the standard monographs. **Reference:** Communication from the Armenia National Pharmacovigilance Centre April, 2010.

Product Name: **Belly cut capsules**

CAS Number:

Other Names:

Country	Effective Date	Description of action taken Grounds for decision
Iraq	November 2008	Because of a high rate of adverse reactions and the fact that it is illegally distributed and not registered in Iraq, Belly Cut capsules have been withdrawn. **Reference:** Communication from the Iraq National Pharmacovigilance Centre, May 2010.

Product Name: **Chloral hydrate and triclofos**

CAS Number:

Other Names: Aquachloral, Somnos, Novo-Chlorhydrate, Welldorm

Country	Effective Date	Description of action taken Grounds for decision
UK	2009	The MHRA has advised health-care professionals that chloral hydrate (Welldorm) and triclofos are indicated as an adjunct to non-pharmacological therapies only for the short-term treatment of severe insomnia that interferes with normal daily life and where other therapies have failed. The product information for these medicines has recently been changed to reflect current clinical practice where they are not first-line

		options for insomnia. **Reference:** 1. Drug Safety Update, MHRA, Volume 2, Issue 11, June 2009 (www.mhra.gov.uk). 2. WHO Pharmaceuticals Newsletter No. 4, 2009.

Product Name: **Chloroproguanil and dapsone**

CAS Number:

Other Names: LapDap

Country	Effective Date	Description of action taken Grounds for decision
Ghana	2008	The anti-malarial combination chloroproguanil and dapsone has been withdrawn following demonstration of post-treatment haemolytic anaemia in G6PD deficient patients in a phase III clinical trial. **Reference:** Communication from the Ghana National Pharmacovigilance Centre, June 2010.

Product Name: **Clindamycin and miconazole**

CAS Number:

Other Names: Clindamed

Country	Effective Date	Description of action taken Grounds for decision
Armenia	2010	The SCDMTE MoH did not approve the marketing authorization of Rhinoil, a combination medication containing clindamycin and miconazole, used for the local treatment of nasal inflammation/infection because the combination was estimated as irrational and can cause serious adverse reactions. **Reference:** Communication from the Armenia National Pharmacovigilance Centre, April 2010.

Product Name: **Dietary supplements**

CAS Number:

Other Names: Hydroxycut

Country	Effective Date	Description of action taken Grounds for decision
USA	2009	The US FDA has alerted the public and health-care professionals about dietary supplement products named Hydroxycut that are associated with serious liver injuries, and warned consumers not to take these products. The Agency has received 23 reports of serious health problems ranging from jaundice and elevated liver enzymes, to liver damage requiring liver transplants. One death due to liver failure has been reported. Other health problems reported include seizures, cardiovascular disorders, and rhabdomyolysis. The products have been recalled by the company. **Reference:** 1. Media release, US FDA, 1 May 2009 (www.fda.gov). 2. WHO Pharmaceuticals Newsletter No. 3, 2009.

Product Name: **Dismectide**

CAS Number:

Other Names: Smecta sachets

Country	Effective Date	Description of action taken Grounds for decision
Iraq	January 2009	Dismectide sachets are to be used only in adults since there is not enough safety information related to their long term use. **Reference:** Communication from the Iraq National Pharmacovigilance Centre, May 2010.

Product Name: **Ephedrine and kava kava products**

CAS Number:

Other Names: Life Choice ephedrine hydrochloride, Life Cholice kava kava

Country	Effective Date	Description of action taken Grounds for decision
Canada	2008	Health Canada has advised consumers against using natural health products Life Choice ephedrine hydrochloride 30 mg capsules and Life Choice kava kava (kavain) 150 mg capsules. The advice came as the agency took steps to prevent these products, which have not been approved, from

		entering the Canadian market. According to Health Canada, Life Choice ephedrine contains an excessive amount of ephedrine, and when taken alone or in combination with caffeine or other stimulants may lead to serious, potentially life-threatening adverse events. Kava kava-containing products have been linked to liver dysfunction and associated with coordination disorders, muscle weakness, and kava dermopathy (a peculiar scaly eruption of the skin). **Reference:** 1. Media Release, Health Canada, 21 August 2008 (www.hc-sc.gc.ca). 2. WHO Pharmaceuticals Newsletter No. 4, 2008.

Product Name: **Levonorgestrel + Intra-uterine Contraceptive Devices (IUCDs)**

CAS Number:

Other Names:

Country	Effective Date	Description of action taken Grounds for decision
Iraq	November 2008	The combination should only be used in specialized centres, for uterine bleeding, where other treatments have failed. **Reference:** Communication from the Iraq National Pharmacovigilance Centre, May 2010.

Product Name: **Neomycin sulphate, polymyxine sulphate and nystatin**

CAS Number:

Other Names: Polygynax

Country	Effective Date	Description of action taken Grounds for decision
Cameroon		In Cameroon, Polygynax (Neomycine sulphate 35 000 IU, Polymyxine sulphate 35 000 IU, Nystatin 100 000 IU) is registered. Its use is not recommended during pregnancy and it must not be taken while breast-feeding. **Reference:** Communication from the Cameroon National Pharmacovigilance Centre, October 2009.

Product Name: **Paracetamol and pseudoephedrine**

CAS Number:

Other Names:

Country	Effective Date	Description of action taken Grounds for decision
Ghana	2009	The registration of oral paediatric formulations containing ibuprofen and paracetamol as a fixed-dose combination has been suspended as there is no scientific evidence to justify the use of the combination in children as compared to using the two components separately. **Reference:** Communication from the Ghana National Pharmacovigilance Centre, June 2010.
Iraq	May 2008	The combination should not contain less than 500 mg paracetamol to be effective as a therapeutic dose and not more than 30 mg of pseudoephedrine to decrease the risk of adverse reactions. **Reference:** Communication from the Iraq National Pharmacovigilance Centre, May 2010.

Product Name: **Rhinoil**

CAS Number:

Other Names: Vitamin A, Anise oil, Eucalipt oil, Mint oil, Camphor

Country	Effective Date	Description of action taken Grounds for decision
Armenia	2010	The SCDMTE MoH did not approve the marketing authorization of Rhinoil, a combination medication for the local treatment of nasal inflammation /infection because combination was estimated as irrational and can cause serious adverse reactions. **Reference:** Communication from the Armenia National Pharmacovigilance Centre, April 2010.

Product Name: **Tadimax**

CAS Number:

Other Names: Content: *Crinum sp., Anemarrhena, Phellodendron sp., Leonurus, Prunus, Alisma, Paeonia, Cinnamomum*

Country	Effective Date	Description of action taken Grounds for decision

Armenia	2009	The SCDMTE MoH did not approve the marketing authorization of Tadimax (complex of herbal extracts used as a non-traditional herbal drug), due to inconsistencies between the description of plant properties in monographs and indications for medicinal use. **Reference:** Communication from the Armenia National Pharmacovigilance Centre, April 2010.

Product Name: **Vitrum Beauty Elite**

CAS Number:

Other Names: Content: Vitamins, minerals, microelements, enzymes, amino acids, herbal extracts

Country	Effective Date	Description of action taken Grounds for decision
Armenia	2009	The SCDMTE MoH did not approve the marketing authorization of Vitrum Beauty Elite due to the lack of data on efficacy and safety. **Reference:** Communication from the Armenia National Pharmacovigilance Centre, April 2010.

Product Name: **Angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists**

CAS Number:

Other Names:

Country	Effective Date	Description of action taken Grounds for decision
Belarus	March 2009	Products containing angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor antagonists should not be initiated during pregnancy, and are not recommended during the first trimester of pregnancy. Patients planning pregnancy should be changed to alternative antihypertensive treatment and treatment should be stopped immediately when pregnancy is diagnosed. Products are not recommended during breastfeeding, especially while nursing a newborn or preterm infant. **Reference:** Communication from the Belarus National Pharmacovigilance Centre, April 2010.
UK	2009	ACE inhibitors (catopril, enalapril or quinapril) are not recommended in the first few weeks after delivery because of the possibility of profound neonatal hypotension; preterm babies may be at particular risk. ACE inhibitors and angiotensin II receptor antagonists should not be used at any stage of pregnancy unless absolutely necessary. Angiotensin II is essential for normal kidney development, and the use of ACE inhibitors and angiotensin II receptor antagonists in late pregnancy has been associated with adverse effects on the kidney and other congenital anomalies. **Reference:** 1. Drug Safety Update, MHRA, Volume 2, Issue 10, May 2009 (www.mhra.gov.uk). 2. WHO Pharmaceuticals Newsletter No. 3, 2009.

Product Name: **Nasal sprays**

CAS Number:

Other Names:

Country	Effective Date	Description of action taken Grounds for decision
Norway	19 November 2008	Nasal spray (oxymethazoline, xylomethazoline, ipratropiumbromide) use is restricted for children younger than 2 years of age. **Reference:** Communication from the Norway National Pharmacovigilance

Centre, April 2010.

Product Name: **Codeine and dihydrocodeine-containing medicines**

CAS Number:

Other Names:

Country	Effective Date	Description of action taken Grounds for decision
UK	2009	The MHRA announced a package of measures to minimize the risk of overuse and addiction associated with over-the-counter medicines containing codeine and dihydrocodeine (DHC). The Patient Information leaflet and labels will state that these products can cause addiction or overuse headache if used continuously for more than three days. All indications related to colds, flu, coughs and sore throats, and references to minor painful conditions will be removed. The package size and advertising will be also regulated. **Reference:** 1. Safety warnings and messages for medicines, MHRA, 2 September 2009 (www.mhra.gov.uk). 2. WHO Pharmaceuticals Newsletter No. 2, 2009.

Product Name: **Cough and cold medicines**

CAS Number:

Other Names:

Country	Effective Date	Description of action taken Grounds for decision
Barbados	April 2009	Prescription is needed for cold medicines for children under six years of age. **Reference:** Communication from the Barbados National Pharmacovigilance Centre, April 2008.
Belarus	September 2009	Use of cough and cold medicines is contraindicated in children under 6 years of age due to unfavourable risk/benefit ratio. For children aged 6 to 12 years, a strengthened warning and requirement for child resistant packaging were introduced. **Reference:** Communication from the Belarus National Pharmacovigilance Centre, April 2010.

Canada	2009	Health Canada has advised the public that certain over-the-counter cough and cold medicines should not be used in children under 6 years of age, following a review of available data. The Agency also says that cough and cold medicines marketed for use in children will require enhanced labeling and packaging. **Reference:** 1. Canadian Adverse Reaction Newsletter Volume 19, Issue 2, Health Canada, April 2009 (www.hc-sc.gc.ca). 2. WHO Pharmaceuticals Newsletter No. 3, 2009.
Kenya	2009	The Kenya Pharmacy and Poisons Board (PPB) stated that the following OTC cough and cold medicines are not recommended in children under 6 years of age: - antitussives (dextromethorphan and pholcodine) - expectorants (guaifenesin and ipecacuanha) - nasal decongestants (ephedrine, oxymetazoline, phenylephrine, pseudoephedrine and xylometazoline) - antihistamines (brompheniramine, chlorpheniramine, diphenhydramine, doxylamine, promethazine and tripolidine) Cough and cold medicines containing these ingredients will be available for children between ages 6 to 12 years, but only in pharmacies. **Reference:** 1. Statement on cough and cold medicines, Frequently Asked Questions, PPB, 13 March 2009. 2. WHO Pharmaceuticals Newsletter No. 2, 2009.
Malaysia	April 2009	Any oral liquid cough and cold preparations containing antihistamines, antitussives, expectorants and decongestants as a single ingredient or in combination should include the following warning in the label and package insert: - Not to be used in children less than 2 years old - To be used with caution and doctor's advice in children 2 to 6 years of age. **Reference:** Communication from the Malaysia National Pharmacovigilance Centre, May 2010.
New Zealand	2010	Cough and cold medicines containing the following substances are contraindicated for use in children under 6 years of age: brompheniramine, chlorpheniramine, dextromethorphan, diphenhydramine, doxylamine, guaifenesin, ipecacuanha, phenylephrine, pholcodine, promethazine, pseudoephedrine and triprolidine. This decision is based on the conclusion of the Cough and Cold Review Group (CCRG) that the risk-benefit balance of

		cough and cold medicines is unfavourable in children under 6 years of age. **Reference:** 1. Prescriber Update Volume. 31, No.1, February 2010 (www.medsafe.govt.nz). 2. WHO Pharmaceuticals Newsletter No. 2, 2010.
UK	2009	The MHRA has recommended that parents and carers should no longer use over-the-counter cough and cold medicines in children under 6 years of age, because there is no evidence that these medicines work and can cause side effects such as allergic reactions, effects on sleep or hallucinations. For 6 to 12 year-old children, these medicines will continue to be available but only in pharmacies. **Reference:** 1. Safety information, MHRA, 28 February 2009. 2. WHO Pharmaceuticals Newsletter No. 2, 2009.
USA	2008	The US FDA recommends that OTC cough and cold medicines should not be given to children under 4 years of age. Many pharmaceutical companies have voluntarily changed the labeling for OTC cough and cold medicines in order to minimize the risk of dosing errors and accidental ingestions. **Reference:** 1. Media Release, US FDA, 8 October 2008 (www.fda.gov). 2. WHO Pharmaceuticals Newsletters No. 5 & No. 6, 2008.

Product Name: **Ergot-derived dopamine agonists**

CAS Number:

Other Names:

Country	Effective Date	Description of action taken Grounds for decision
EU	2008	The EMA has recommended revising the product information for ergot-derived dopamine agonists with new warnings and contraindications relating to the risk of fibrosis. Although the development of fibrosis symptoms is a known adverse effect of ergot-derived dopamine agonists, new data have suggested that fibrosis may start long before the onset of symptoms. The EMA affirmed that marketing authorizations should be maintained, but that new warnings and contraindications should be added to the relevant product information - Bromocriptine and dihydroergocryptine is contraindicated for patients with pre-existing valve problems.

		- The maximum dose of bromocriptine is restricted to 30 mg per day. - Warning on the possible risk of fibrosis is required in patients taking bromocriptine, dihydroergocryptine and lisuride for long periods. **Reference:** 1. Media Release, EMA, 26 June 2008 (www.ema.europa.eu). 2. WHO Pharmaceuticals Newsletter No. 4, 2008.
Spain	March 2008	Ergot-derived dopamine agonists are contraindicated in patients with valvular heart diseases or fibrotic disorders. These warnings do not apply to short-term treatments for the inhibition/suppression of lactation or to treatment with lisuride. **Reference:** AEMPS, Alertas de Seguridad, 9 October 2008 (www.aemps.es/actividad/alertas/usoHumano/seguridad).

Product Name: Erythropoiesis-stimulating agents

CAS Number:

Other Names:

Country	Effective Date	Description of action taken Grounds for decision
USA	2008	The US FDA has informed health-care professionals of modifications to prescribing information for erythropoiesis-stimulating agents (ESAs). The changes clarify the US FDA-approved conditions for use of ESAs in patients with cancer and revise directions for dosing to state the haemoglobin level at which treatment with an ESA should be initiated. **Reference:** 1. Follow up to the 3 January 2008 communication, US FDA (www.fda.gov). 2. WHO Pharmaceuticals Newsletter No. 4, 2008.

Product Name: Herbal cold and flu products

CAS Number:

Other Names:

Country	Effective Date	Description of action taken Grounds for decision
Australia	December 2008	The Australia Therapeutic Goods Administration (TGA) has announced the voluntary recall of two herbal cold and flu medicines by the company, following reports of a number of allergic and anaphylactic reactions. Those products (Nyal Day

		& Night Cold & Flu Fighter tablets and Nyal Cold & Flu Fighter tablets) contain the herbs *Andrographis paniculata* (Andrographis), *Sambucus nigra* (Elderberry), *Salix alba* (White willow) and *Valeriana officinalis* (Valerian). **Reference:** 1. Health alert, TGA, 19 December 2008 (www.tga.gov.au). 2. WHO Pharmaceuticals Newsletter No. 1, 2009.

Product Name: **Inhalers with CFC propellants**

CAS Number:

Other Names:

Country	Effective Date	Description of action taken Grounds for decision
Iraq	November 2008	Chloroflourocarbon (CFC) propellants for inhalers must be replaced with other propellants, for example, 1,1,1,2,-tetrafluoroethane. **Reference:** Communication from the Iraq National Pharmacovigilance Centre, May 2010.

Product Name: **Long-acting beta-agonists**

CAS Number:

Other Names:

Country	Effective Date	Description of action taken Grounds for decision
USA	February 2010	A revised medication guide on the use of long-acting beta-agonists (LABAs) was issued based on studies showing an increased risk of severe exacerbation of asthma symptoms, leading to hospitalizations in paediatric and adult patients as well as death in some patients using LABAs for the treatment of asthma. The use of LABAs is contraindicated without the use of an asthma controller medication such as an inhaled corticosteroid. Due to insufficient data on whether using LABAs with an inhaled corticosteroid reduces or eliminates the risk of asthma-related death and hospitalizations, the Agency is requiring the manufacturers of LABAs to conduct studies evaluating the safety of LABAs when used in conjunction with an inhaled corticosteroids. **Reference:** 1. Safety Information, US FDA, 18 Feb 2010 (www.fda.gov). 2. WHO Pharmaceuticals Newsletter No. 2, 2010.

Product Name: **Oral preparations containing alcohol**

CAS Number:

Other Names:

Country	Effective Date	Description of action taken Grounds for decision
Iraq	April 2008	The use of alcohol in oral preparations has been restricted to no more than 10% in adults and up to 5% in children (preferable without alcohol). **Reference:** Communication from the Iraq National Pharmacovigilance Centre, May 2010.

Product Name: **Salicylates**

CAS Number:

Other Names:

Country	Effective Date	Description of action taken Grounds for decision
UK	23 April 2009	Topical oral (oral gel) pain relief products containing salicylate salts are contraindicated in children and young people under the age of 16 years. Substantial systemic level of salicylate could be reached from the overuse of salicylate-containing topical oral gels, which could lead to salicylate toxicity reactions that resemble Reye's syndrome. These products are therefore contraindicated in children and young people under the age of 16 years in line with other oral salicylate-containing preparations. **Reference:** 1. Safety warnings and messages for medicines, MHRA, 23 April 2009 (www.mhra.gov.uk). 2. WHO Pharmaceuticals Newsletter No. 3, 2009.

Product Name: **Short acting beta-agonists (SABAs)**

CAS Number:

Other Names:

Country	Effective Date	Description of action taken Grounds for decision
Belarus	February 2010	These products are contraindicated as tocolytic agents in patients with pre-existing ischaemic heart disease and in those with significant risk factors for ischaemic heart disease. For other patients who have undergone tocolytic therapy with

		SABAs, a strengthened recommendation for cardiorespiratory function supervision, including ECG monitoring, has been issued. Treatment should be discontinued if signs of myocardial ischaemia develop. Restrictions are based on the available evidence that SABAs can increase the risk of myocardial ischaemia. **Reference:** Communication from the Belarus National Pharmacovigilance Centre, April 2010.

Product Name: **Vitamins**

CAS Number:

Other Names:

Country	Effective Date	Description of action taken Grounds for decision
Iraq	September 2008	The use of vitamin B complex injection (i.m or slow i.v) has been banned because it is not effective in either therapeutic or preventive use. **Reference:** Communication from the Iraq National Pharmacovigilance Centre, May 2010.
Iraq	September 2008	Vitamin B12 is only to be used as hydroxycobalamine if used alone, and as cyanocobalamine if used in combination products. **Reference:** Communication from the Iraq National Pharmacovigilance Centre, May 2010.
Iraq	January 2010	Vitamin A is not to be used in the first three months of pregnancy because of its teratogenic potential, and preferably not to be given to nursing mothers unless there is vitamin A deficiency. **Reference:** Communication from the Iraq National Pharmacovigilance Centre, May 2010.

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