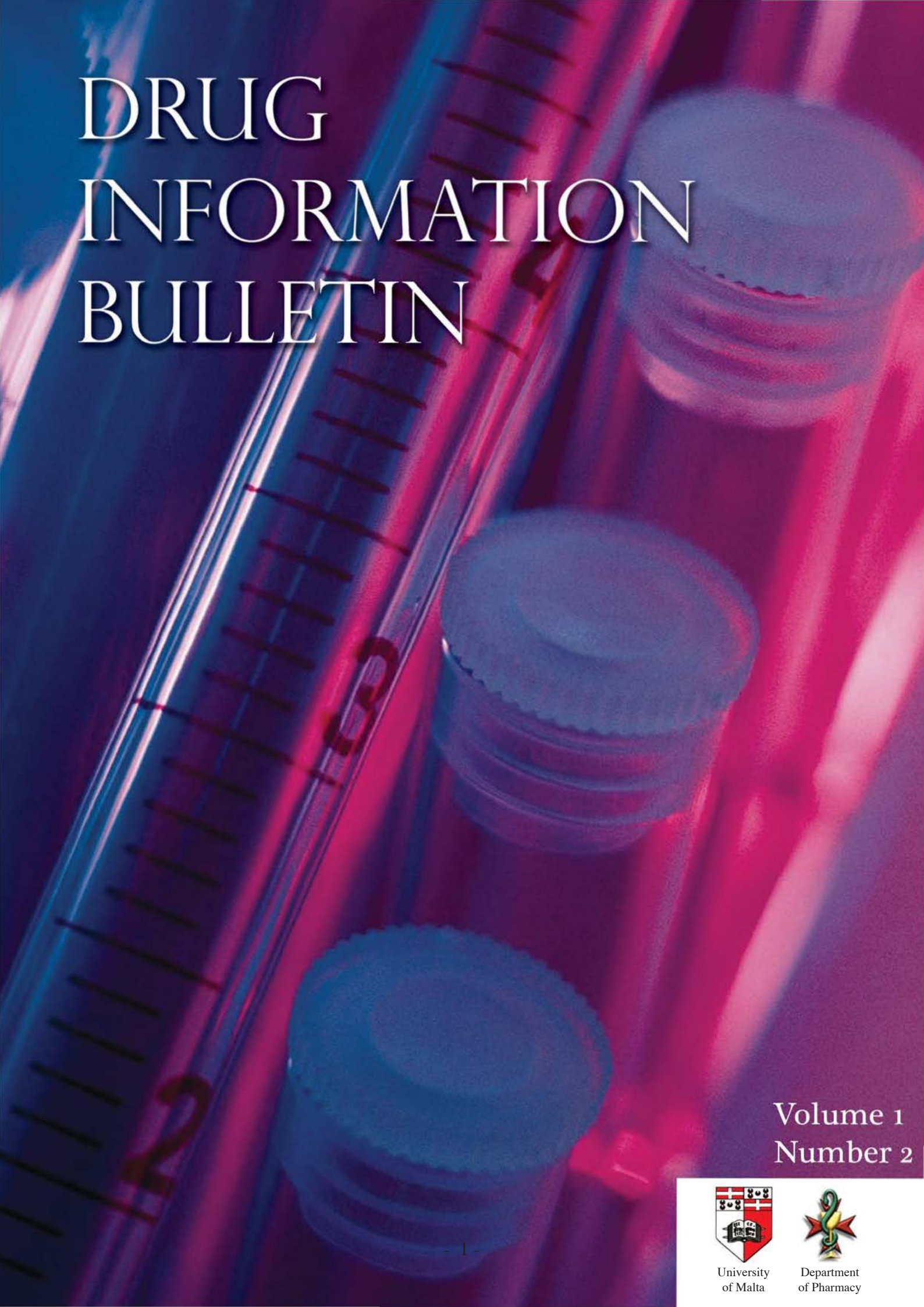
DRUG INFORMATION BULLETIN



Volume 1
Number 2

University of Malta
Department of Pharmacy

Contents

New medicinal products available on the local market

Variations in Summary of Product Characteristics of medicinal products available locally

Drug Information Bulletin

Volume 1 Number 2

Editorial

Over the past sixty years the focus of pharmacist practitioners changed; from compounding and distribution of medicinal products to new activities and responsibilities that highlight the rational, safe and cost-effective use of drugs. The ultimate goal is always the well-being of the patient. Improvements in technology such as dispensing machines aid the pharmacist in the dispensing and distribution process thus enhancing the pharmacist's clinical role.

Improvements in drug therapy require health professionals to filter and assimilate to update their practice. Being an expert in medicines, the patient looks at the pharmacist as an accessible and trusted source of advice and treatment. This involves a life-long commitment to keep abreast with the current innovations in treatment and also in the growth and changes in the profession.

This bulletin is a student project undertaken in partial fulfilment for the requirements leading to the Bachelor of Pharmacy (Hons.) degree under the supervision of Professor Lilian M. Azzopardi B.Pharm.(Hons.), M.Phil., Ph.D., Head of Department of Pharmacy, University of Malta.

Published by the Department of Pharmacy, University of Malta, Msida MSD 2080 Malta
Tel: +356 21343764/5
Fax: +356 21340427
E-mail: phcy@um.edu.mt

New medicinal products available on the local market

From June 2008 till November 2008, the following new medicinal products have been included to our vast range of pharmaceutical products used locally both in the private and hospital pharmacies. They have been granted a marketing authorisation either by the centralised procedure or by the mutual recognition procedure or by the decentralised procedure. Inovelon®, Janumet™ and Tyverb® have been granted their marketing authorisation by the centralised procedure whilst ACWY Vax®, Arcoxia®, Cozaar®-COMP, Donecept, Lendrate, Luvinsta SR, Magnevist®, Nodiril, Panrazol, Propofol®-Lipuro, Sindaxel, Valsotens and Yaz® have been registered via a national procedure. The other medicinal products have been registered via a simplified procedure in line with article 4(2) of the Medicines (Marketing Authorisations) Regulations in accordance with article 126(a) of Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community Code relating to medicinal products for human use, as amended by Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004.

ACWY Vax® (SmithKline Beecham)

***Neisseria meningitidis* groups A, C, Y, W_{135}**

Pharmaceutical form: Powder and solvent for solution for injection
Available in: Private Sector

ACWY Vax® is indicated for active immunisation of children older than 2 years, adolescents and adults against invasive meningococcal disease caused by meningococci of groups A,C,W_{135} and Y. It is contraindicated in cases of hypersensitivity to active substances or excipients or after previous administration of ACWY Vax®. The administration of such vaccine should be postponed in subjects suffering from severe febrile illness. Mostly reported adverse effects in recent clinical studies occurred within 48 hours following vaccination with the most common being headache, fatigue, nausea, pain and redness at the injection site.[1]

Reference

1. Medicines Authority [online]. 2009 [cited 2009 August 1]; Available from: URL: http://www.medicinesauthority.gov.mt/products/SPC_MA172%2000601_ACWY%20Vax%C2%AE%20Pdr+Solv%20for%20Soln%20for%20Inj%20NA%20glass%20syringe_Powder%20and%20Solvent%20for%20Solution%20for%20Injection_Refer%20to%20SmPC_SmithKline%20Beecham%20PLC_United%20Kingdom_PoM_J07AH04_30.09.08.pdf

Alendronic Acid Tablets (Arrow Generics)

Alendronic acid

Pharmaceutical form: 70mg tablets
Available in: Private Sector

Alendronic acid is a bisphosphonate which inhibits osteoclastic bone resorption. It reduces the risk of vertebral and hip fractures. Thus it is indicated for the treatment of post-menopausal osteoporosis. It is contraindicated in patients who have abnormalities of the oesophagus and other factors which can delay oesophageal emptying such as stricture, inability to stand or sit upright for at least 30 minutes, hypocalcaemia and hypersensitivity to bisphosphonates or excipients. Some common adverse effects are headache, musculoskeletal pain and gastro-intestinal disorders such as constipation.[1]

Reference

1. Lakemedelsverket. Medical products agency. [online]. 2009 August 10 [cited 2009 August 10]; Available from: URL: http://www.lakemedelsverket.se/SPC_PILPdf/enhumspc/Alendronat%20Arrow%20Veckotablett%2070mg%20tabl%20ENG.pdf

Amlodipine Tablets (Arrow Generics)

Amlodipine

Pharmaceutical form: 5mg, 10mg tablets
Available in: Hospital and Private Sector

The calcium antagonist, amlodipine is indicated for arterial hypertension and stable angina pectoris. It is contraindicated in cases of severe hypotension, shock,

heart failure after acute myocardial infarction (during first 28 days), obstruction of the outflow tract of the left ventricle and instable angina pectoris. Patients with known hypersensitivity to dihydropyridines or any excipients should not be administered amlodipine. Common adverse reactions include ankle swelling, facial flushing with heat sensation, dizziness and headache especially on initiation of treatment. [1]

Reference

1. Lakemedelsverket. Medical products agency. [online]. 2009 August 10 [cited 2009 August 10]; Available from: URL: http://www.lakemedelsverket.se/SPC_PILPdf/enhumspc/Alendronat%20Arrow%20Veckotablett%2070mg%20tabl%20ENG.pdf

Arcoxia® (Merck Sharp & Dohme)

Etoricoxib

Pharmaceutical form: 30mg tablets
Available in: Private Sector

Etoricoxib is a selective cyclo-oxygenase-2 inhibitor which is indicated for the symptomatic relief of osteoarthritis, rheumatoid arthritis, pain and signs of inflammation associated with acute gouty arthritis. Some cases when Arcoxia® is contraindicated include active peptic ulceration, active gastrointestinal bleeding, severe hepatic dysfunction, estimated renal creatinine clearance <30mL/min, patients under 16 years and cardiovascular problems. Common undesirable effects include dizziness, headache, oedema, gastrointestinal disorders, hypertension and palpitations.[1]

Reference

1. Medicines Authority [online]. 2009 [cited 2009 July 7]; Available from: URL: http://www.medicinesauthority.gov.mt/products/SPC_MA058%2001504_Arcoxia%20Tablets%2030mg_Tablets_Etoricoxib%2030mg_Merck%20Sharp%20&%20Dohme%20Ltd_United%20Kingdom_PoM_M01AH05_06.10.08.pdf

Chloromycetin Opthalmic Ointment 1% w/w (Goldshield Pharmaceuticals)

Chloramphenicol

Pharmaceutical form: 1% w/w eye ointment
Available in: Hospital Sector

Chloramphenicol is indicated for treatment of bacterial conjunctivitis caused by susceptible organisms including *Escherichia coli*, *Staphylococcus aureus* and *Haemophilus influenzae*. It is contraindicated in cases of hypersensitivity. Undesirable effects include transient burning or stinging sensations. When more serious side effects such as bone marrow depression occur, it should be discontinued. [1]

Reference

1. Goldshield Group Plc. Goldshield caring for your health [online]. 2007 [cited 2009 July 8]; Available from: URL: http://www.goldshieldpharmaceuticals.com/csp/gsh/pharma/pdf/spc/6/3.pdf

Cozaar®-COMP (Merck Sharp & Dohme)

Losartan, Hydrochlorothiazide

Pharmaceutical form: 100/25mg tablets

Losartan is an oral, specific angiotensin-II receptor antagonist whilst hydrochlorothiazide is a diuretic and antihypertensive. It is indicated for the treatment of hypertension in patients whose blood pressure is not adequately controlled on hydrochlorothiazide or losartan monotherapy. In hypertensive patients with left ventricular hypertrophy a reduced risk of stroke was demonstrated with losartan administered usually in combination with hydrochlorothiazide. The data does not support the use of losartan for this indication in black patients. It is contraindicated in pregnancy, patients who are hypersensitive to any component of this product or to other sulphonamide-derived drugs and in patients with anuria. In clinical trials with the combination tablet of losartan and hydrochlorothiazide, no adverse experiences peculiar to this combination drug have been observed. [1]

Reference

1. Medicines Authority [online]. 2009 [cited 2009 July 7];Available from: URL: http://www.medicinesauthority.gov.mt/products/SPC_MA058%2001201_Cozaar%C2%AE-COMP%20100 %20Film%20Coated%20Tablets_Filmcoated%20Tablets_Losartan%2091.6mg%20Hydrochlorothiazide%2025mg_Merck%20Sharp%20&%20Dohme%20Ltd._United%20Kingdom_PoM_.pdf

Derbac M Cutaneous Emulsion (SSL International)

Malathion

Pharmaceutical form: 0.5% w/w cutaneous emulsion
Available in: Private Sector

Malathion is indicated for the eradication of head lice, pubic lice, their eggs and also for the treatment of scabies. It is contraindicated in cases of known sensitivity to malathion. It should not be used in infants less than 6 months except on medical advice. Reported adverse effects include skin irritation, hypersensitivity

reactions such as anaphylaxis, angioedema, swollen eyes and chemical burns. [1]

Reference

1. Datapharm Communications Ltd. eMC. [online]. 2008 August 29 [cited 2009 August 1]; Available from: URL: http://emc.medicines.org.uk/medicine/18995/SPC/Derbac+M+Liquid/

Diamox® SR (Goldshield Pharmaceuticals)

Acetazolamide

Pharmaceutical form: 250mg capsule

Acetazolamide is indicated in glaucoma. It is a potent inhibitor of carbonic anhydrase which catalyses the reversible reaction involving the hydration of carbon dioxide and dehydration of carbonic acid. Its use is contraindicated in marked renal and liver disease, suprarenal gland failure, hyperchloremic acidosis, hypokalaemia, hyponatraemia and hypersensitivity to sulphonamides, its derivatives or its excipients. Long term administration is contraindicated in patients with chronic non-congestive angle-closure glaucoma. During short-term use, adverse reactions include loss of appetite, taste disturbance, polyuria and headache. In long term therapy use, metabolic acidosis and electrolyte imbalance may occur. [1]

Reference

1. Goldshield Group Plc. Goldshield caring for your health [online]. 2007 [cited 2009 July 8]; Available from: URL: http://www.goldshieldpharmaceuticals.com/csp/gsh/pharma/pdf/spc/11/1.pdf

Diazepam Tablets BP (Actavis UK Limited)

Diazepam

Pharmaceutical form: 2mg, 5mg tablets
Available in: Private Sector

The benzodiazepine, diazepam is indicated for cerebral palsy, muscle spasm and short term relief of anxiety. It can also be administered as an adjunct to certain types of epilepsy, symptomatic treatment of acute alcohol withdrawal and as oral premedication for the nervous dental patient or before surgery. In children, it is indicated as an adjunct to control muscle spasm in tetanus, control of tension and irritability in cerebral spasticity in selected cases and as oral premedication. Its contraindications include phobic or obsessional states, chronic psychosis, acute pulmonary insufficiency, respiratory depression, sleep apnoea and as monotherapy in patients with depression with or without anxiety. The latter is due to a risk of precipitating suicide in such patients. Common adverse effects are dose-related include drowsiness, sedation, unsteadiness and ataxia. [1]

Reference

1. Actavis [online]. 2009 [cited 2009 July 10]; Available from: URL: http://www.actavis.com.mt/NR/rdonlyres/7B0266ED-59C5-44AE-9A6C-AE67DFA0F247/0/Diazepam2mg5mg.pdf

Donecept (Actavis Group PTC ehf)

Donepezil hydrochloride

Pharmaceutical form: 5mg, 10 mg tablets
Available in: Private Sector

Donepezil, being a specific and reversible inhibitor of acetylcholinesterase is indicated for the symptomatic treatment of mild to moderately severe Alzheimer's dementia. It is contraindicated in cases of hypersensitivity to donepezil, piperidine derivatives or any excipients and in pregnancy. The most common adverse events include diarrhoea, muscle cramps, fatigue, nausea, vomiting and insomnia. [1]

Reference

1. Actavis [online]. 2009 [cited 2009 July 10]; Available from: URL: http://www.actavis.com.mt/NR/rdonlyres/2D3BF4B0-29C2-4328-B1DB-56ABD31A890/0/Donecept5mg10mgSPC.pdf

Elitan (Medochemie)

Metoclopramide hydrochloride

Pharmaceutical form: 10mg/2ml solution for injection
Available in: Private sector

Elitan is indicated in duodenal intubation, post-operative conditions, to relieve the symptoms of nausea and vomiting in migraine and other conditions such as heart failure. It is also indicated to relieve the symptoms of gastroduodenal dysfunction including dyspepsia. In cases of patients under 20 years, its use is restricted to severe intractable vomiting of known cause; vomiting associated with radiotherapy and intolerance to cytotoxic drugs; as an aid to gastro-intestinal intubation and as part of the premedication before surgical procedure. It is contraindicated in pregnancy, lactation and concomitant use of anticholinergics. Extrapyramidal symptoms usually dystonic reactions

and raised serum prolactin has been reported as undesirable effects. [1]

Reference

1. Elitan [package insert]. Limassol (Cyprus): Medochemie; 2009

Epilim® Liquid (Sanofi-Aventis)

Sodium valproate

Pharmaceutical form: 200mg/5mL oral solution
Available in: Hospital and Private sector

Sodium valproate is indicated in the treatment of generalised partial or other epilepsy. It is contra-indicated in active liver disease, personal or family history of severe hepatic dysfunction especially drug related cases, porphyria and in cases of hypersensitivity. At start of treatment nausea, gastralgia and diarrhoea usually occur as undesirable effects but usually disappear after few days without discontinuing treatment. It should be taken with or after food or using the enteric coated. Isolated and moderate hyperammonemia without change in liver function and thrombocytopenia may also occur frequently. The former is usually transient and does not require discontinuation. However the latter would return to normal upon discontinuation. [1]

Reference

1. Medicines Authority [online]. 2009 [cited 2009 July 7]; Available from: URL: http://www.medicinesauthority.gov.mt/ products/SPC_MA082%2004311_Epilim%20Liquid%20Oral%20Solution%20_Oral%20Solution_Valproate%20Sodium%20200mg5ml_SanofiAventis%20Malta%20Ltd._Malta_PoM_N03AG01_01.07.08.pdf

Folic Acid Tablets (Actavis UK Limited)

Folic acid

Pharmaceutical form: 5mg tablets
Available in: Private Sector

Since folic acid is necessary for the production and maturation of red blood cells, it is indicated for the treatment of folate-deficient megaloblastic anaemia, for prophylaxis of drug-induced folate deficiency and folate deficiency in chronic haemolytic states or in renal dialysis. It is also used in prevention of neural tube defects for women at risk or planning a pregnancy. Long-term folate therapy is contraindicated in any patient with untreated cobalamin deficiency as it has precipitated cobalamin neuropathy when given for 3 months or longer. It is also contraindicated in cases of hypersensitivity, malignant disease unless megaloblastic anaemia and when used as monotherapy in the treatment of Addisonian pernicious anaemia and other vitamin B_{12} deficiency state. Rare adverse effects include hypersensitivity reactions, anorexia, nausea, abdominal distension and flatulence. [1]

Reference

1. Actavis [online]. 2009 [cited 2009 July 15]; Available from: URL: http://www.actavis.com.mt/NR/rdonlyres/83E81177-0C80-4CBC-9B61-7409A195D309/0/FolicAcid5mg.pdf

Gadovist® (vial) (Bayer)

Gadobutrol

Pharmaceutical form: 1mmol/mL solution for injection
Available in: Hospital Sector

Gadobutrol is a paramagnetic contrast media which is used only for diagnostic purposes as a contrast enhancement in cranial, spinal magnetic resonance imaging (MRI) and magnetic resonance angiography. It is also used as a contrast enhanced MRI of liver or kidneys in patients with high suspicion or evidence of having focal lesions to classify them as benign or malignant. In cases of hypersensitivity to any of its ingredients, Gadovist® use is contraindicated. Its adverse reactions are uncommon or rare in occurrence such as headache, dizziness and nausea. [1]

Reference

1. Datapharm Communications Ltd. eMC. [online]. 2009 February 26 [cited 2009 July 16]; Available from: URL: http://emc.medicines.org.uk/medicine/9553/SPC/Gadovist+1.0++mmol+ml/

Glyceryl trinitrate Tablets (Actavis UK Limited)

Glyceryl trinitrate

Pharmaceutical form: 500mcg tablets
Available in: Hospital Sector

The vasodilator glyceryl trinitrate is indicated for the relief of angina pectoris, acute spontaneous coronary artery spasm and for prophylaxis of angina pectoris. Its contraindications include patients with rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption, marked anaemia, closed angle glaucoma, obstructive heart failure and patients taking phosphodiesterase type-5

inhibitors. The undesirable effects include throbbing headache, facial flushing, localised burning sensation, dizziness, weakness, tachycardia and postural hypotension. [1]

Reference

1. Actavis [online]. 2009 [cited 2009 July 13]; Available from: URL: http://www.actavis.co.uk/NR/rdonlyres/9FC5C8C0-789D-4C3D-990B-45477E14C159/0/Glyceryltrinitratetablet500mcgT3955SPC.pdf

Guastil® (J. Uriach & Cia)

Sulpiride

Pharmaceutical form: 50mg capsules, 25mg/5mL children oral suspension
Available: Private and Public Sector

Guastil® is indicated for psychic behaviour disturbances such as neurosis and anxiety states; digestive system such as gastroduodenal ulcers, irritable colon and cardio-circulatory system such as palpitations. Guastil® children is indicated for alteration of behaviour and conduct of children, low school performance, nervous tics, neurovegetative dystonias and insomnia amongst others. It is contraindicated in cases of paradoxical reaction in epileptic patients. No adverse events were reported at the usual dosage but on higher dosage, some cases of galactorrhea were reported that disappear upon stopping the treatment or reduce the dose. [1]

Reference

1. Guastil® capsule [package insert]. Barcelona (Spain): J. Uriach&Cia; 2009
2. Guastil® children [package insert] Barcelona (Spain): J. Uriach&Cia; 2009

Inovelon® (Eisai)

Rufinamide

Pharmaceutical form: 400mg tablets
Available in: Hospital Sector

Rufinamide is indicated as an adjunctive therapy in the treatment of seizures associated with Lennox-Gastaut syndrome in patients over 4 years. Patients who suffer from hypersensitivity to the active substance, triazole derivatives or any of its excipients should not use Inovelon®. Very common adverse effects during clinical studies include headache, dizziness, nausea, vomiting, fatigue and somnolence. Carers should be advised to exercise caution due to risk of falls which could be caused by somnolence and dizziness. [1]

Reference

1. European Medicines Agency. EPARs for authorised medicinal products for human use. [online]. 2009 March 23 [cited 2009 July 8]; Available from: URL: http://www.emea.europa.eu/humandocs/Humans/EPAR/inovelon/inovelon.htm

Janumet™ (Merck Sharp & Dohme)

Sitagliptin, metformin

Pharmaceutical form: 50mg/ 850mg, 50mg/1000mg tablets
Available in: Private Sector

Janumet™ combines two antihyperglycaemic agents with complementary mechanisms of action to improve glycaemic control. It is indicated in patients with type 2 diabetes as an adjunct to diet and exercise to improve glycaemic control when treatment with both active ingredients is appropriate. Janumet™ can also be used in combination with a sulphonylurea or a PPARγ agonist as a triple combination therapy. It is contraindicated in cases of hepatic and moderate to severe renal impairment, diabetic ketoacidosis, diabetic pre-coma and history of serious hypersensitivity reactions amongst others. In post-marketing experience of Janumet™ or sitagliptin additional adverse reactions reported included hypersensitivity reactions including anaphylaxis, angioedema, rash, urticaria and exfoliative skin conditions including Stevens-Johnson syndrome. [1]

Reference

1. European Medicines Agency. EPARs for authorised medicinal products for human use. [online]. 2009 July 6 [cited 2009 July 10]; Available from: URL: http://www.emea.europa.eu/humandocs/Humans/EPAR/janumet/janumet.htm

Lamotrigine Tablets (Arrow Generics)

Lamotrigine

Pharmaceutical form: 25mg conventional tablets
Available in: Hospital Sector

Lamotrigine is indicated as monotherapy in primary generalized epilepsy and partial epilepsy with or without generalisation in adults and children over 12 years. It is also indicated as an add-on therapy in these cases and Lennox-Gastaut Syndrome both in adults and children over 2 years. It is contraindicated in individuals with known hypersensitivity to the active ingredient and excipients. Very common adverse effects that may occur include skin rash, headache, dizziness and diplopia. [1]

Reference

1. Medicines Authority [online]. 2009 [cited 2009 July 29]; Available from: URL: http://www.medicinesauthority.gov.mt/products/SPC_MA574%2000103_Lamotrigine%2025mg%20Tablets_Tablet_Lamotrigine%2025mg_Arrow%20Generics%20Ltd._United%20Kingdom_PoM_N03AX09_31.07.06.pdf

Lendrate (Actavis Group PTC ehf)

Alendronic Acid

Pharmaceutical form: 70mg tablets
Available in: Private Sector

Alendronic acid is a bisphosphonate which inhibits osteoclastic bone resorption. It reduces the risk of vertebral and hip fractures. Thus it is indicated for the treatment of post-menopausal osteoporosis. It is contraindicated in patients who have abnormalities of the oesophagus and other factors which can delay oesophageal emptying such as stricture, inability to stand or sit upright for at least 30 minutes, hypocalcaemia and hypersensitivity to bisphosphonates or excipients. Some common adverse effects are headache, musculoskeletal pain and gastro-intestinal disorders such as constipation and dyspepsia.[1]

Reference

1. Actavis [online]. 2009 [cited 2009 July 13]; Available from: URL: http://www.actavis.com.mt/NR/rdonlyres/6B820D85-5F99-4F79-AA00-8C19803B4BC4/0/Lendrate70mgSPC.pdf

Levothyroxine BP Tablets (Actavis UK Limited)

Levothyroxine

Pharmaceutical form: 50mcg, 100mcg tablets
Available in: Private sector and sometimes Hospital sector

Levothyroxine is indicated for hypothyroidism. It is contraindicated in cases of hypersensitivity to any of its components, thyrotoxicosis and cases of adrenal insufficiency without adequate corticosteroid cover. Hypersensitivity reactions include rash, pruritus and oedema. The side effects usually indicate an excessive dosage which on reduction of dose or withdrawal of treatment, they would disappear. These include anginal pain, cardiac arrhythmias, insomnia and headache. These are similar to symptoms of hyperthyroidism. [1]

Reference

1. Actavis [online]. 2009 [cited 2009 July 10]; Available from: URL: http://www.actavis.com.mt/NR/rdonlyres/FB00BE98-31CB-4491-ABF8-8D0AECB88CF1/0/Levothyroxine50mcg100mcg.pdf

Luvinsta SR (Actavis Group PTC ehf)

Fluvastatin

Pharmaceutical form: 80mg prolonged-release tablets
Available in: Private Sector

Fluvastatin is a synthetic cholesterol-lowering agent which competitively inhibits HMG-CoA reductase. It is responsible for the conversion of HMG-CoA to the precursor of sterols, mevalonate. It is used to treat primary hypercholesterolaemia and mixed hyperlipidaemia as an adjunct to diet. It is also indicated for secondary prevention of coronary events after percutaneous coronary interventions in patients with coronary heart disease. Fluvastatin is contraindicated in cases of hypersensitivity to any of its ingredients, pregnancy, lactation and active liver disease or unexplained persistent elevations in serum transaminases. Some of the most commonly reported undesirable effects include minor gastrointestinal symptoms, insomnia and headache. [1]

Reference

1. Actavis [online]. 2009 [cited 2009 July 13]; Available from: URL: http://www.actavis.com.mt/NR/rdonlyres/FEF6BFAF-D38E-450E-9BDC-CF08C2F057AC/0/LuvinstaSR80mg.pdf

Magne B6® (Sanofi-Aventis)

Magnesium, Pyridoxine

Pharmaceutical form: 100mg/10mg coated tablets
Available in: Private Sector

Magne B6® is indicated in number of symptoms which may be evocative of a magnesium deficiency such as nervousness, irritability, signs of anxiety, muscle cramps and tingling sensation. It is contraindicated in kidney failure, congenital galactosemia, glucose or galactose malabsorption syndrome or lactase deficiency, lactation and hypersensitivity to active ingredients and excipients. Adverse effects include allergic reactions and gastrointestinal disorders such as diarrhea and abdominal pain. [1, 2]

References

1. Magne B6® [package insert] France: Sanofi Aventis; 2005
2. CharlesdeGiorgio.com [online]. 2009 [cited 2009 August 1]; Available from: URL: http://www.charlesdegiorgio.com/news/09b.html

Magnevist® (Bayer)

Gadopentetic acid

Pharmaceutical form: 0.5mmol/l solution for injection
Available in: Hospital and Private Sector

Magnevist® is indicated as a paramagnetic contrast medium in cranial, spinal and whole body MRI and for the evaluation of renal function. It is contraindicated in patients with severe renal impairment (GFR<30mL/min/1.73m^2). Some frequent adverse reactions include nausea, vomiting, headache, dizziness, sensation of pain, general feeling of warmth and injection site warmth or coldness. [1]

Reference

1. Medicines Authority [online]. 2009 [cited 2009 July 28]; Available from: URL: http://www.medicinesauthority.gov.mt/products/SPC_MA185%2001001_Magnevist%20Solution%20for%20InjInf%20_Solution%20for%20InjectionInfusion_Gadopentate%20Dimeglumine%20469.01mg_Bayer%20PLC_United%20Kingdom_PoM_V08CA_15.09.08.pdf

Metformin Tablets (Actavis UK Limited)

Metformin

Pharmaceutical form: 500mg coated tablets
Available in: Private Sector

The biguanide, metformin produces antihyperglycaemic effects by lowering both basal and post-prandial plasma glucose. Since it does not stimulate insulin secretion therefore it does not cause hypoglycaemia. It is indicated for the treatment of type 2 diabetes mellitus in adults when dietary management and exercise do not provide adequate glycaemic control. It can be used both as monotherapy and in combination with other antidiabetic agents or insulin. The use of metformin is contraindicated in diabetic ketoacidosis, diabetic pre-coma, renal failure and acute conditions with the potential to alter renal function. Other contraindications include lactation and hepatic insufficiency, acute alcohol intoxication, acute or chronic conditions which may cause tissue hypoxia. Very common undesirable effects caused by metformin are gastrointestinal disorders such as nausea, diarrhoea, abdominal pain and loss of appetite. These occur mostly on initiation of therapy and in most cases resolve spontaneously. [1]

Reference

1. Actavis [online]. 2009 [cited 2009 July 13]; Available from: URL: http://www.actavis.com.mt/NR/rdonlyres/F2DE7D94-143A-423A-A9F3-F31D15217B40/0/Metformin500mgSPC.pdf

Metronidazole BP Tablets (Actavis UK Limited)

Metronidazole

Pharmaceutical form: 200mg, 400mg tablets
Available in: Private Sector

Metronidazole has antiprotozoan and antibacterial effects, notably against species of *Bacteroids*, *Fusobacteria, Clostridia, Eubacteria,* anaerobic cocci*, Gardnerella vaginalis, Trichomonas vaginalis, Entamoeba histolytica, Gardia lamblia, Balantidium coli and Helicobacter pylori*. Its indications include prevention of post-operative infection, treatment of urogenital trichomoniasis, septicaemia, peritonitis and acute dental infections. It is contraindicated in hypersensitivity, pregnancy and breast feeding. Breast feeding should be discontinued for 12-24 hours when single high dose therapy is used. Unwanted effects that occasionally occur include unpleasant taste, furred tongue, oral mucositis, anorexia and gastro-intestinal disturbances. Other serious adverse effects occur very rarely with standard recommended regimens. [1, 2]

Reference

1. Actavis [online]. 2009 [cited 2009 July 13]; Available from: URL: http://www.actavis.com.mt/NR/rdonlyres/FE842333-A648-4CC0-B66B-3C694A3B7520/0/Metronidazole200mgSPC.pdf
2. Actavis [online]. 2009 [cited 2009 July 14]; Available from: URL: http://www.actavis.com.mt/NR/rdonlyres/C2D47B95-E7F4-4FE6-8606-8B3393CD826E/0/Metronidazole400mgSPC.pdf

Nodiril (Actavis Group PTC ehf)

Risperidone

Pharmaceutical form: 1mg, 2mg coated tablet
Available in: Hospital and Private Sector

Risperidone is a selective monoaminergic antagonist indicated for the treatment of acute and chronic schizophrenic psychoses and other psychotic conditions where positive and/or negative symptoms are prominent. The affective symptoms associated with schizophrenia are also alleviated. Risperidone is also effective in maintaining the clinical improvement during continuation therapy in patients who have shown an initial treatment response. It is contraindicated in cases of hypersensitivity. The common adverse effects

include agitation, sleeplessness, sedation and weight gain. Sedation which is generally mild and transient has been reported more frequently in children and adolescents than in adults. In such case it is difficult to differentiate between symptoms of the disease and adverse effects. [1]

Reference

1. Actavis [online]. 2009 [cited 2009 July 13]; Available from: URL: http://www.actavis.com.mt/NR/rdonlyres/C2F495C9-B861-41C9-9B62-473C6C3C8E46/11967/NodirilSPC.pdf

No-spa® (Sanofi-Aventis)

Drotaverine Hydrochloride

Pharmaceutical form: 40mg, 80mg tablets
Available in: Private Sector

The antispasmodic agent drotaverine is indicated in smooth muscle spasm in connection with biliary tract disease, urinary tract disease and as an adjuvant treatment in smooth muscle spasm of gastrointestinal origin, tension type headache and dysmenorrhoea. It is contraindicated in hepatic, nephritic and cardiac insufficiency and in childhood. Rarely its side-effects include headache, nausea, hypotension, vertigo and heart palpitations. [1, 2, 3]

Reference

1. No-spa® 40mg [package insert] Hungary: Sanofi Aventis; 2006
2. No-spa® 80mg [package insert] Hungary: Sanofi Aventis; 2006
3. CharlesdeGiorgio.com [online]. 2009 [cited 2009 August 8]; Available from: URL: http://www.charlesdegiorgio.com/news/09i.html

Omesar® (Menarini International Operations)

Olmesartan Medoxomil

Pharmaceutical form: 10mg, 20mg, 40mg tablets

Olmesartan is a potent, orally active, selective angiotensin II receptor antagonist that is expected to block all actions of angiotensin II mediated by the AT_1 receptor. It is indicated in essential hypertension. It is contraindicated in second and third trimester of pregnancy, lactation, biliary obstruction and hypersensitivity to any of its components. In clinical trials, common adverse reactions reported include dizziness, cough, urinary tract infections, chest pain, peripheral oedema and musculoskeletal disorders such as arthritis and skeletal pain. [1]

Reference

1. Medicines Authority [online]. 2009 [cited 2009 July 28]; Available from: URL: http://www.medicinesauthority.gov.mt/products/SPC_MA204%2000303_Omesar%C2%AE_Filmcoated%20tablets_Olmesartan%20Medoxomil%2040mg_Menarini%20International%20Operations%20Luxembourg%20S.A._Luxembourg_PoM_C09CA08_11.10.05.pdf

Panrazol (Actavis Group PTC ehf)

Pantoprazole

Pharmaceutical form: 20mg, 40mg gastro-resistant tablets
Available in: Private Sector

The proton pump inhibitor, pantoprazole is a substituted benzimidazoles that inhibits the secretion of hydrochloric acid in the stomach. Thus it is indicated for the symptomatic improvement and healing of gastrointestinal diseases which require a reduction in acid secretion such as duodenal and gastric ulcer, reflux oesophagitis. Whilst, the 20mg dose is indicated for prevention of gastroduodenal ulcers induced by NSAIDs. The 40mg dose is also indicated for the eradication of *H.pylori*, in combination with antibiotics. It is contraindicated in the case of hypersensitivity and in patients taking atazanavir treatment. The 40mg preparation should not be used in moderate or severe hepatic or renal impairment when used in combination therapy for eradication of *H. pylori* since no data is available. Common adverse effects include headache, upper abdominal pain, diarrhoea, constipation and flatulence. [1, 2]

Reference

1. Actavis [online]. 2009 [cited 2009 July 13]; Available from: URL: http://www.actavis.com.mt/NR/rdonlyres/C4CEF221-AE67-403D-BEEF-713A91914763/0/Panrazol20mgSPC.pdf
2. Actavis [online]. 2009 [cited 2009 July 13]; Available from: URL: http://www.actavis.com.mt/NR/rdonlyres/1C0145AB-498E-47DE-948F-374D5590E501/0/Panrazol40mgSPC.pdf

Prednisolone Tablets (Actavis UK Limited)

Prednisolone

Pharmaceutical form: 5mg enteric coated tablets
Available in: Private Sector

Prednisolone is indicated for a number of conditions both for long and short term such as systemic lupus erythematosus, nephritic syndrome, various blood dyscrasias, lymphomas in adults and as an adjunct therapy during acute episode of rheumatoid arthritis. In patients suffering from systemic fungal, viral and acute

bacterial infection unless specific anti-infective therapy is administered, ocular herpes simplex and hypersensitisation, the medicinal product is contraindicated. Some adverse effects include cushingoid faces, hirsutism, peptic ulceration with perforation and haemorrhage, skin atrophy and impaired wound healing. The incidence of predictable undesirable effects including hypothalamic-pituitary-adrenal suppression correlates with the relative potency of the drug, dosage, timing of administration and duration of treatment. [1]

Reference

1. Actavis [online]. 2009 [cited 2009 July 10]; Available from: URL: http://www.actavis.com.mt/NR/rdonlyres/C3D343DE-EB29-4C67-8E58-63CF88625F60/0/Prednisolone5mgECSPC.pdf

Propofol® - Lipuro 1% (B.Braun Melsungen AG)

Propofol

Pharmaceutical form: 10mg/mL emulsion for injection or infusion

Available in: Hospital Sector

Propofol, being a short acting intravenous general anaesthetic indicated for induction and maintenance of general anaesthesia, sedation of ventilated patients in intensive care unit and sedation for diagnostic and surgical procedures, alone or in combination with local or regional anaesthesia. Its use is contraindicated in patients allergic to soya, peanut or propofol or any of its excipients and in children under one month for induction or maintenance of anaesthesia. In case of sedation in intensive care, propofol is contraindicated for use in patients of 16 years of age or younger. Very common adverse effects are hypotension and respiratory depression depending on the dose administered and other medications administered. [1]

Reference

1. Medicines Authority [online]. 2009 [cited 2009 July 28]; Available from: URL: http://www.medicinesauthority.gov.mt/products/SPC_MA223%2000601_Propofol-% C2%AELipuro%201%%20Emulsion%20for%20InjInf%2010mgml_Emulsion%20for%20Injection%20or%20Infusion_Propofol%2050mg5ml_B.%20Braun%20Melsungen%20AG_Germany_PoM_N01AX10_01.07.08.pdf

Pulmicort Respules® (Associated Drug)

Budesonide

Pharmaceutical form: 0.5mg/ml pressurised inhalation suspension

Available in: Hospital and Private Hospitals Sectors

The anti-inflammatory corticosteroid, budesonide is indicated for the maintenance and prophylactic therapy of asthma for children between 12 months to 8 years. It exhibits potent glucocorticoid activity and weak mineralocorticoid activity. In cases of hypersensitivity and primary treatment of status asthmaticus or other acute episodes of asthma where intensive measures are required, the use of Pulmicort Respules® is contraindicated. Some common adverse reactions with the treatment include respiratory system disorders such as rhinitis, coughing and gastrointestinal disorders. [1]

Reference

1. Astrazeneca.Pulmicort Respules®.[online]. 2009 [cited 2009 July 28]; Available from: URL: http://www1.astrazeneca-us.com/pi/pulmicortrespules.pdf

Reminyl™ (Janssen-Cilag International)

Galantamine

Pharmaceutical form: 4mg/mL oral solution

The tertiary alkaloid galantamine is indicated for the symptomatic treatment of mild to moderately severe Alzheimer's disease. It is a selective, competitive and reversible inhibitor of acetylcholinesterase. Reminyl™ is contraindicated in cases of hypersensitivity to any of its components and also in patients having significant renal and hepatic dysfunction. This is due to lack of data available in these populations. Very common adverse effects are nausea and vomiting. [1]

Reference

1. Medicines Authority [online]. 2009 [cited 2009 July 28]; Available from: URL: http://www.medicinesauthority.gov.mt /products/SPC_MA018%2000104_Reminyl%E2%84%A2_Oral%20solution_Galantamine%204mg%20per%20ml_JanssenCilag%20International%20NV_Belgium_PoM_N06DA04_29.12.06.pdf

Salbutamol Tablets (Actavis UK Limited)

Salbutamol

Pharmaceutical form: 4mg tablets

Available in: Hospital Sector

Salbutamol is a selective beta-2-adrenergic agonist indicated for the relief of bronchospasm in all types of bronchial asthma, chronic bronchitis, emphysema and

also for inhibition of premature labour in selected patients where a definite benefit is likely to occur. Its use is contraindicated in case of hypersensitivity, co-administration with beta-blocking drugs and in threatened abortion during the first and second trimester of pregnancy. The prime significant side effect is a fine tremor of skeletal muscle usually hands. This occurs in some patients and it is dose related. Its effect on the skeletal muscle can also cause tension in few patients. [1]

Reference

1. Actavis [online]. 2009 [cited 2009 July 10]; Available from: URL: http://www.actavis.co.uk/NR/rdonlyres/08675E78-749C-43F0-BD90-DCDC3E6B3F16/0/Salbutamoltablet4mgt6754spc.pdf

Seretide™ Evohaler™ (GlaxoSmithKline)

Salmeterol, fluticasone propionate

Pharmaceutical form: 25mcg/50mcg/dose pressurised inhalation suspension

Seretide™ Evohaler™ is indicated for regular treatment of asthma in cases where its use as a combination product consisting of a long-acting beta-2 agonist and inhaled corticosteroid is appropriate in patients who are not adequately controlled. It must not be used in cases of hypersensitivity to any of its components. No adverse effects specific to the concurrent administration of the two active ingredients have been reported but they have been limited to those associated with each of the compound. The side effects of beta-2-agonist treatment such as tremor, palpitations and headache have been reported but tend to be transient and reduce with regular therapy. Due to the fluticasone propionate component, hoarseness and candidiasis can occur in some patients. These may be relieved by gargling with water after using it. [1]

Reference

1. Datapharm Communications Ltd. eMC. [online]. 2008 January 15 [cited 2009 July 16]; Available from: URL:http://emc.medicines.org.uk/medicine/2914/SPC/Seretide+50%2c+125%2c+250+Evohaler/

Simvastatin Tablets (Arrow Generics)

Simvastatin

Pharmaceutical form: 10mg, 20mg, 40mg, 80mg tablets
Available in: Hospital Sector

Simvastatin is an HMG-CoA reductase inhibitors which is indicated in hypercholesterolaemia and for cardiovascular prevention in patients who manifest atherosclerotic cardiovascular disease or diabetes mellitus. Simvastatin is contraindicated in active liver disease or unexplained persistent elevations of serum transaminase, concomitant administration of potent CYP3A4 inhibitors, pregnancy, lactation and hypersensitivity to any of its components. Undesirable effects occurring rarely include jaundice, myalgia, muscle cramps and rash. [1]

Reference

1. Ministry of Health Manatu Hauora, newzealend.govt.nz. Medsafe. Information for consumers. [online]. 2009 February 3 [cited 2009 August 10]; Available from: URL: http://www.medsafe.govt.nz/consumers/cmi/a/Arrow-Simva.htm

Sindaxel (Actavis Group PTC ehf)

Paclitaxel

Pharmaceutical form: 6mg/mL concentrate for solution for infusion
Available in: Hospital Sector

The antimicrotubule agent, paclitaxel is indicated for ovarian carcinoma, breast carcinoma, advanced non-small cell lung carcinoma and AIDS-related Kaposi's sarcoma. Paclitaxel promotes the assembly of microtubules from tubulin dimers and stabilizes microtubules by preventing depolymerisation. It is contraindicated in pregnancy, lactation, baseline neutrophils $<1500/mm^3$, patients with concurrent serious uncontrolled infections and cases of hypersensitivity to any of its ingredients especially macrogolglycerol ricinoleate. Very common side effects include infections mainly urinary tract and upper respiratory tract infections, myelosuppression, neutropenia, anaemia, bleeding, minor hypersensitivity reaction, myalgia and gastrointestinal disorders. [1]

Reference

1. Medicines Authority [online]. 2009 [cited 2009 July 28]; Available from: URL: http://www.medicinesauthority.gov.mt/products/SPC_MA628%2004001_Sindaxel%20Concentrate%20for%20Soln%20for%20Inf%206mgml_Concentrate%20for%20Solution%20for%20Infusion_Paclitaxel%206mg%20per%20ml_Actavis%20Group%20PTC%20ehf_Iceland_PoM_L01CD01_08.10.08.pdf

Singulair® Paediatric (Merck Sharp & Dohme)

Montelukast

Pharmaceutical form: 4mg chewable tablets

The leukotriene receptor antagonist, montelukast is indicated for the treatment of asthma as an add-on therapy in patients suffering from mild to moderate persistent asthma who are inadequately controlled on inhaled corticosteroids and in whom 'as-needed' short-acting β-agonists provide inadequate clinical control of asthma. It may also be used as an alternative treatment option to low-dose inhaled corticosteroids for patients with mild persistent asthma who do not have a recent history of serious asthma attacks that require oral corticosteroid use and who have demonstrated that they are not capable of using inhaled corticosteroids. It is also indicated in the prophylaxis of asthma in which the predominant component is exercise-induced bronchoconstriction. In cases of hypersensitivity to any of the components, the product is contraindicated. The adverse reactions commonly reported in clinical studies include headache in adults to paediatric patients of 6 years, abdominal pain in adults and 2 to 5 year old patient group and thirst in patients of 2 to 5 years. [1]

Reference

1. Medicines Authority [online]. 2009 [cited 2009 July 28]; Available from: URL: http://www.medicinesauthority.gov.mt/products /SPC_MA058%2000601_Singulair%20Paediatric%204mg_Chewable%20tablets_Montelukast%204mg_Merck%20Sharp%20&%20Dohme%20Ltd._United%20Kingdom_PoM_R03DC03_30.06.05.pdf

Sivacor (Actavis Group PTC ehf)

Simvastatin

Pharmaceutical form: 40mg, 80mg tablets
Available in: Private Sector

Simvastatin is an HMG-CoA reductase inhibitors which is indicated in hypercholesterolaemia and for cardiovascular prevention in patients who manifest atherosclerotic cardiovascular disease or diabetes mellitus. Simvastatin is contraindicated in active liver disease or unexplained persistent elevations of serum transaminase, concomitant administration of potent CYP3A4 inhibitors, pregnancy, lactation and hypersensitivity to any of its components. Undesirable effects occurring rarely includes, jaundice, myalgia, muscle cramps and rash. [1]

Reference

1. Medicines Authority [online]. 2009 [cited 2009 July 28]; Available from: URL: http://www.medicinesauthority.gov.mt/ products/ SPC_MA628%2000703_Sivacor_Film-coated% 20tablets_ Simvastatin%2020mg_Actavis%20Group%20PTC%20ehf_Iceland_ PoM_C10AA01_26.02.08.pdf

Tramadol Hydrochloride Capsules (Actavis UK Limited)

Tramadol

Pharmaceutical form: 50mg capsules
Available in: Private Sector

Tramadol is a centrally acting synthetic analgesic which is indicated for the treatment of moderate to severe pain. According to the severity of the pain and clinical response of the individual, the dose is adjusted. Its use is contraindicated in cases of acute intoxication with central nervous system depressants, severe hepatic, renal and respiratory impairment, uncontrolled epilepsy and hypersensitivity. It must not be administered to lactating mothers when treatment for more than 3 days is necessary and in patients receiving monoamine oxidase inhibitors or within two weeks of their withdrawal. Very common adverse reactions include dizziness, nausea and vomiting. Tramadol has the potential to cause withdrawal symptoms such as agitation, tremor and insomnia at therapeutic doses. Reports of drug dependence and abuse are rare and less frequent than withdrawal reactions. [1]

Reference

1. Medicines Authority [online]. 2009 [cited 2009 July 28]; Available from: URL: http://www.medicinesauthority.gov.mt /products /SPC_MA628%2000701_Sivacor_Filmcoated%20tablets_Simvastatin%2080mg_Actavis%20Group%20PTC%20ehf_Iceland_PoM_C10AA01_02.10.07.pdf

Tyverb® (Glaxo Group)

Lapatinib ditosylate monohydrate

Pharmaceutical form: 250 mg tablets
Available in: Private Sector

Lapatinib is a protein kinase inhibitor that is indicated for treatment of patients with advanced or metastatic breast cancer whose tumours overexpress ErbB2 (HER2) in combination with capecitabine. Patients should have progressive disease following prior therapy which must include anthracyclines and taxanes and

therapy with trastuzumab in the metastatic setting. Orally administered lapatinib inhibits the intracellular tyrosine kinase domain of ErbB1 and ErbB2 receptors which are responsible for tumour growth. It is contraindicated in cases of hypersensitivity to any of its components. Some very common adverse effects include nausea, diarrhoea, rash and fatigue. [1]

Reference

1. European Medicines Agency. EPARs for authorised medicinal products for human use. European [online]. 2009 June 23 [cited 2008 September 8]; Available from: URL: http://www.emea.europa.eu/humandocs/Humans/EPAR/tyverb/tyverb.htm

Valsotens (Actavis Group PTC ehf)

Valsartan

Pharmaceutical form: 80mg, 160mg coated tablets
Available in: Private Sector

Valsartan is an orally active specific angiotensin II receptor antagonist. It is indicated for essential hypertension and to improve survival following recent myocardial infarction in clinically stable patients with signs, symptoms or radiological evidence of left ventricular failure and/or with left ventricular systolic dysfunction. It is contraindicated in cases of hypersensitivity, severe hepatic and renal impairment, biliary cirrhosis and cholestasis, patients undergoing dialysis, second and third trimester of pregnancy and lactation. Common adverse effects include viral infections, postural dizziness and orthostatic hypotension. The latter two adverse effects were reported when used in heart failure indication. [1]

Reference

1. Medicines Authority [online]. 2009 [cited 2009 July 28]; Available from: URL: http://www.medicinesauthority.gov.mt/products/SPC_MA628%2002403_Valsotens%20Coated%20Tablets%20160mg_Coated%20Tablets_Valsartan%20160mg_Actavis%20Group%20PTC%20ehf_Iceland_PoM_C09CA03_19.11.08.pdf

Varivax® (MSD-SP)

Varicella virus Oka/Merck strain (live, attenuated)

Pharmaceutical form: powder and solvent for suspension for injection.

Varivax® is indicated for vaccination against varicella in individuals from 12 months of age. It may also be administered to individuals who have been exposed to varicella. If the vaccination is carried out within 3 days of exposure, it may prevent a clinically apparent infection or modify its cause. It is contraindicated in blood dyscrasias, leukaemia, lymphomas, other malignant neoplasms affecting the hemic and lymphatic systems, pregnancy, immunosuppressed patients, persons with humoral or cellular immunodeficiency or family history of congenital or hereditary immunodeficiency. It is also contraindicated in active untreated tuberculosis and any illness with fever >38.5^{o}C. Some common adverse effects reported in temporal association with vaccination include upper respiratory tract infection, rash, irritability, injection site erythema and very commonly fever. [1]

Reference

1. Medicines Authority [online]. 2009 [cited 2009 July 28]; Available from:URL: http://www.medicinesauthority.gov.mt/products/SPC_MA499%2000201_Varivax%C2%AE_Pdr%20&%20solvent%20for%20suspension%20for%20injection_Varicella%20Virus%20-%20Oka%20Merck%20Strain%201350PFU%20per%200.5ml_MSD-SP%20Limited_United%20Kingdom_PoM_J07BK01_07.10.05.pdf

Yaz® (Bayer)

Drospirenone, ethinylestradiol

Pharmaceutical form: 3mg/0.02mg coated tablets
Available in: Private Sector

Yaz® is indicated for oral contraception. It is contraindicated in the presence or history of venous thrombosis, arterial thrombosis, cerebrovascular accident, severe renal insufficiency or acute renal failure and presence or history of liver tumours amongst others. Common undesirable effects that have been associated with the use of Yaz® include emotional lability, headache, nausea, breast pain, amenorrhea and metrorrhagia. The latter bleeding irregularities usually subside during continued treatment. [1]

Reference

1. Irish pharmaceutical health care association. Medicines.ie. [online]. 2009 January 12 [cited 2009 July 8]; Available from: URL: http://www.medicines.ie/medicine/13973/spc/yaz

Variations in summary of product characteristics of medicinal products available locally

From June 2008 till November 2008, the following variations (Type II variations) have been included in the summary of products characteristics (SPC) of medicinal products available locally as accepted by the European Medicines Agency.

Cialis®

Active Ingredient: Tadalafil

Available in: Private Sector

Variation: Four clinical pharmacology studies which evaluated the interaction between tadalafil and three α-adrenergic antagonists (doxazosin, tamsulosin and alfuzosin) were reviewed by Committee for Medicinal Products for Human Use (CHMP). The effect of doxazosin on blood pressure in combination with tadalafil was evaluated using 3 different dosing regimens of a single dose of 20mg tadalafil and doxazosin 4mg or 8mg daily in one study and 5mg tadalafil and concomitant increasing doses of doxazosin up to 4mg daily in another study. In these studies, hypotension occurred in some patients which last at least twelve hours including syncope. Thus concomitant administration of tadalafil with doxazosin is not recommended.

The third study evaluated the effects on blood pressure with coadministration of alfuzosin 10mg and single dose of 20mg tadalafil. The fourth study evaluated the effects on blood pressure of a single dose of tamsusolin 0.4mg and 5mg tadalafil daily. In these latter two studies, hypotension was not reported. Caution should still be exercised in patients, especially the elderly taking both tadalafil and any alpha-adrenergic receptor blocking agent. [1]

Reference

1. European Medicines Agency. EPARs for authorised medicinal products for human use. [online]. 2009 April 28 [cited 2009 July 15]; Available from: URL: http://www.emea.europa.eu/humandocs/ Humans/EPAR/cialis/cialis.htm

Combivir™

Active Ingredients: Lamivudine, Zidovudine

Available in: Hospital Sector

Variation: Studies relating to the administration of crushed tablets with a small amount of semi-solid food or liquid showed that it does not have any pharmaceutical quality impact. This is useful for the treatment of paediatric patients who are unable to swallow tablets and also for adults with swallowing difficulties. It should be consumed immediately. [1]

Reference

1. European Medicines Agency. EPARs for authorised medicinal products for human use. [online]. 2009 April 28 [cited 2009 July 15]; Available from: URL: http://www.emea.europa.eu/humandocs/ Humans/ EPAR/ combivir/combivir.htm

Crixivan®

Active Ingredient: Indinavir

Available in: Hospital Sector

Variation: The current recommended dosage of indinavir is 800mg every 8 hours. Data from published studies suggested an alternative dosage regimen of indinavir 400mg in combination with ritonavir 100mg both administered twice daily. Besides the contraindications of indinavir and ritonavir respectively, ritonavir should not be given to patients with decompensated liver disease and not administered with alfuzosin, meperidine and piroxicam amongst others. In a pharmacokinetic study, concomitant use of indinavir with lopinavir/ ritonavir (400mg/100mg) and rosuvastatin (20mg) in healthy volunteers resulted in a 2.1 and 4.7 fold increase in rosuvastatin AUC and C_{max} respectively. The exact mechanism of this interaction is unknown. Thus the

concomitant use of rosuvastatin with protease inhibitor is not recommended. Due to limited pharmacokinetic data available on the interaction between protease inhibitors (PI) and HMG-CoA reductase inhibitors that are not metabolised by cytochrome CYP3A4 do not allow for predictions to be made. The exact mechanism of interaction behind this significant increase of rosuvastatin exposure is unknown so concomitant use of rosuvastatin with PI is not recommended. The limited pharmacokinetic data that is available on the interactions between PIs and the statins that are not metabolised by CYP3A4 do not allow for predictions to be made as to the effects of a given individual PI on an individual statin.

Combination of rifampicin with indinavir given with low dose ritonavir is contraindicated. In 2005 an interaction study on saquinavir boosted with ritonavir together with rifampicin in healthy volunteers had to be prematurely discontinued due to an increased risk of hepatotoxicity associated with this co-administration.

Rifampicin is a strong CYP3A4 inducer and has been shown to cause a 92% decrease in indinavir area under the curve (AUC) which can result in virological failure and resistance development. The mechanism of this interaction is not fully elucidated but it has been hypothesised that the predominant effect between the inducer effect of rifampicin and the inhibitor effect of the boosted protease inhibitors might depend on the boosted protease inhibitor involved.[1]

Reference

1. European Medicines Agency. EPARs for authorised medicinal products for human use. [online]. 2009 April 28 [cited 2009 July 15]; Available from: URL: http://www.emea.europa.eu/humandocs/ Humans/ EPAR /crixivan/crixivan.htm

Epivir®

Active Ingredient: Lamivudine

Available in: Hospital Sector

Variation: Studies relating to the administration of crushed tablets with a small amount of semi-solid food or liquid show that it does not have any pharmaceutical quality impact. This is useful for the treatment of paediatric patients who are unable to swallow tablets and also for adults with swallowing difficulties.[1]

Reference

1. European Medicines Agency. EPARs for authorised medicinal products for human use. [online]. 2008 September 25 [cited 2009 July 8]; Available from: URL: http://www.emea.europa.eu/humandocs/Humans/EPAR/epivir/epivir.htm

Fosavance®

Active Ingredient: Alendronic acid

Available in: Private Sector

Variation: Alopecia was included in the list of undesirable effects after the Marketing Authorisation Holder (MAH) has received a total of 1720 spontaneous adverse reaction reports of alopecia in association with alendronate from its introduction on the market till 31 January 2008. It was generally characterised by a diffuse loss of scalp hair 1-2 months after initiation of alendronate therapy. 224 reports showed evidence of recovery upon discontinuation of alendronate therapy including 23 reports where the condition recurred after restarting alendronate therapy. Since an improvement or full recovery was observed in some cases upon discontinuation of alendronate therapy, the CHMP considered that a causal relationship between alopecia and alendronate therapy cannot be excluded.[1]

Reference

1. European Medicines Agency. EPARs for authorised medicinal products for human use. [online]. 2009 May 18 [cited 2009 July 8]; Available from: URL: http://www.emea.europa.eu/humandocs /Humans/EPAR/fosavance/fosavance.htm

Infanrix hexa®

Active Ingredient: Diphtheria toxoid adsorbed, tetanus toxoid adsorbed, pertussis toxoid adsorbed, filamentous haemagglutinin adsorbed, pertactin adsorbed, recombinant Hepatitis B surface antigen adsorbed, inactivated poliovirus types 1, 2, 3, conjugate of *Haemophilus influenzae* type b capsular polysaccharide and tetanus toxoid adsorbed.

Available in: Private Sector

Variation: The effectiveness of the Hib component of Infanrix hexa® has been and continues to be investigated

via an extensive post-marketing surveillance study conducted in Germany. Over a five year follow-up period, the effectiveness of the Hib components of two hexavalent vaccines, of which one was Infanrix hexa®, was 90.4% for a full primary series and 100% for a booster dose (regardless of priming). These results confirmed the high effectiveness of hexavalent vaccines against invasive Hib diseases.

The effectiveness of several acellular pertussis-based combined vaccines was assessed via a long-term surveillance study in Sweden. Results over eight years of follow-up (1997-2005) showed that acellular pertussis vaccines are effective in infants vaccinated according to the 3-5-12 month vaccination schedule. However, protection against pertussis may be waning at 7-8 years of age. Therefore, a second booster dose of pertussis vaccine may be needed in children aged 5-7 years who have previously been vaccinated according to this schedule.

The product information was updated according to data from clinical trials and post-marketing setting to clarify the prescribing information and extend the advice. Premature infants might be vaccinated but a lower response may be observed and the level of clinical protection remains currently unknown. The adverse events added as reported in the post-marketing setting include apnoea, injection site vesicles, lymphadenopathy and angioedema. The potential risk of apnoea and the need for respiratory monitoring for 48-72 hours should be considered when administering the primary immunisation series to very premature infants (born ≤28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity. As the benefit of the vaccination is high in this group of infants, vaccination should not be withheld or delayed. Protective antibodies against hepatitis B have been shown to persist for at least 3.5 years in more than 90% of children administered four doses of Infanrix hexa®. Antibody levels were not different from what was observed in a parallel cohort administered 4 doses of monovalent hepatitis B vaccine.[1]

Reference

1. European Medicines Agency. EPARs for authorised medicinal products for human use. [online]. 2008 December 23 [cited 2009 August 7]; Available from: URL: http://www.emea.europa.eu /humandocs/Humans/EPAR/infanrixhexa/infanrixhexa.htm

Lantus®

Active Ingredient: Insulin glargine

Available in: Private and Hospital Sectors

Variation: An open-label 5-year NPH-controlled study (NPH given bid) was conducted in 1024 type 2 diabetic patients where the effects of Lantus® (once daily) on diabetic retinopathy were evaluated. The progression of retinopathy by 3 or more steps on the Early Treatment Diabetic Retinopathy scale (ETDRS) was investigated by fundus photography. No significant difference was observed in the progression of diabetic retinopathy when Lantus® was compared to NPH insulin as basal insulin for a 5 year treatment. [1]

Reference

1. European Medicines Agency. EPARs for authorised medicinal products for human use. [online]. 2009 May 11 [cited 2009 August 6]; Available from: URL: http://www.emea.europa.eu/humandocs/ Humans/EPAR/lantus/lantus.htm

Levitra®

Active Ingredient: Vardenafil

Available in: Private Sector

Variation: Coadministration of erythromycin (500mg three times a day) with vardenafil (5mg) caused a 4 fold and 3 fold increase in vardenafil AUC and C_{max} respectively. Although a specific interaction study has not been conducted, the in vivo studies submitted for erythromycin are supportive of the in vivo extrapolation for clarithromycin, considering the similar inhibitory potency view in other in vivo studies, the co-administration of clarithromycin can be expected to result in similar effects on vardenafil AUC and C_{max}. It was found that the dose of vardenafil should not exceed 5mg when administered in combination with CYP3A4 inhibitors such as erythromycin and clarithromycin.

Single oral doses of 10mg and 80mg vardenafil have shown to prolong the QTc interval by a mean of 8msec and 10msec. A post-marketing study was conducted on 44 healthy volunteers who were co-administered 10mg vardenafil or 50mg sildenafil with 400mg gatifloxacin, a drug with comparable QT effect. Both showed an additive Frederica QTc effect of 4msec vardenafil and 5msec sildenafil when compared to either drug alone. The actual clinical impact of these QT changes is unknown. [1]

Reference

1. European Medicines Agency. EPARs for authorised medicinal products for human use. [online]. 2009 April 29 [cited 2009 July 8]; Available from: URL: http://www.emea.europa.eu/humandocs/Humans/EPAR/levitra/levitra.htm

Nexavar®

Active Ingredient: Sorafenib

Available in: Private Sector

Variation: A three-way, single dose cross-over study was conducted on healthy male volunteers to evaluate the effect of moderate fat meal and the effect of concomitant omeprazole treatment on the bioavailability of sorafenib. Results showed that daily treatment with a 40mg omeprazole led to a mean increase in gastric pH from 1 to 4 but this had no effect on sorafenib availability. Therefore it was concluded that anti-acidic treatment would not be expected to have a clinically meaningful effect on sorafenib exposure. Thus information on SPC regarding the potential risk of decreased sorafenib exposure when co-administered with substances that increase gastric pH was deleted. For patients at risk of renal dysfunction, it was recommended to monitor fluid balance and electrolytes. Renal failure was also included in the adverse drug reaction list.

On the basis of a review of sorafenib relevant to renal dysfunction, it was considered that there is little evidence to support a primary nephrotoxic potential of sorafenib. However, due to the possible indirect action through the induction of diarrhoea, vomiting, dehydration with subsequent possible volume depletion and hypotension that is associated with sorafenib, it is considered that sorafenib may have the potential to contribute to the development of renal dysfunction through pre-renal mechanisms. [1]

Reference

1. European Medicines Agency. EPARs for authorised medicinal products for human use. [online]. 2009 May 20 [cited 2009 July 27]; Available from: URL: http://www.emea.europa.eu/humandocs/Humans/EPAR/nexavar/nexavar.htm

PegIntron™

Active Ingredient: Interferon alfa-2b

Available in: Hospital Sector

Variation: Following a cumulative search for overdose cases that occurred in patients taking pegInterferon alfa-2b until 24 January 2008, 3 important cases to note out of the 68 cases reported included one which was with a potential overdose of 10.5 times the intended dose (about 500 mcg), one of 7.5 times the dose (1200 mcg) and one of 5 times the dose (600 mcg, taken over a 5-day period). The majority of reported reactions were generally reactions that are part of the known spectrum of pharmacologic effects of alfa interferons but perhaps were of greater severity than the adverse reactions reported during therapeutic use. Standard methods to promote elimination such as dialysis, have not shown to be useful and also, no specific antidote for PegIntron® is available. Therefore, symptomatic treatment and close observation of the patient are recommended in cases of overdose.

Following a cumulative review till 31 December 2007 and also data from the literature, a causal relationship could not be excluded between pegylated interferon alfa 2b and the adverse effect pericarditis. The latter is a serious and fatal reaction if diagnosis is delayed. Moreover, treatment with interferon alpha 2b may induce mania and bipolar disorders especially in patients with predisposing factors. Thus, pericardial effusion, pericarditis, bipolar disorders and mania were included in the undesirable effects section.[1]

Reference

1. European Medicines Agency. EPARs for authorised medicinal products for human use. [online]. 2008 December 22 [cited 2009 July 8]; Available from: URL: http://www.emea.europa.eu/humandocs/Humans/EPAR/pegintron/pegintron.htm

Rebetol®

Active Ingredient: Ribavirin

Available in: Hospital Sector

Variation: The undesirable list was reviewed to include the adverse events reported in post-marketing in combination with interferon alfa 2b containing products. Some cases reported in post-marketing with either pegylated interferon alfa 2b or interferon alfa 2b has also been included in the list such as pure red cell aplasia, seizure and pancreatitis. However, those generally attributed to interferon therapy but that had been reported in the context of hepatitis C therapy were unlisted. [1]

Reference

1. European Medicines Agency. EPARs for authorised medicinal products for human use. [online]. 2008 December 22 [cited 2009 July 10]; Available from: URL: http://www.emea.europa.eu/humandocs/Humans/EPAR/rebetol/rebetol.htm

Revlimid®

Active Ingredient: Lenalidomide

Available in: Private Sector

Variation: Lenalidomide induced in monkeys malformations were similar to those described with thalidomide. Based on this data, the CHMP considered that lenalidomide is teratogenic in animals and thus it is expected to be teratogenic in humans. An embryo foetal development study has been conducted in monkeys that were administered lenalidomide at doses up to 4 mg/kg/day. Preliminary findings from the ongoing study showed that lenalidomide produced malformations (short limbs, bent digits, wrist and/or tail, supernumerary or absent digits) in the offspring whose mother received the drug during pregnancy. Therefore, it is advisable that patients taking lenalidomide should use effective method of contraception.

An *in vitro* study with human hepatocytes suggested that lenalidomide did not induce CYP1A2, CYP2B6, CYP2C9, CYP2C19 and CYP3A4/5 at various concentrations. Therefore, reduced efficacy of drugs including hormone contraceptives due to induction is not expected with the use of lenalidomide alone. From the results of human in vitro metabolism studies showed that lenalidomide is not metabolised by CYP450 enzymes. Thus inferring that administration of lenalidomide with inhibitors of CYP450 enzymes is not likely to cause any metabolic drug interactions. In vitro studies indicated no inhibitory effect on CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP2E1 or CYP3A. [1]

Reference

1. European Medicines Agency. EPARs for authorised medicinal products for human use. [online]. 2009 April 23 [cited 2009 July 27]; Available from: URL: http://www.emea.europa.eu/humandocs/Humans/EPAR/revlimid/revlimid.htm

Rotarix®

Active Ingredient: Human rotavirus, live attenuated

Available in: Private Sector

Variation: On the basis of a clinical study evaluating the concomitant use of Rotarix® with other vaccines including oral polio vaccine, it was shown that concomitant administration of oral polio vaccine may slightly reduce the immune response to Rotarix®. However, it was shown that the protection against severe rotavirus gastroenteritis was still maintained, in a clinical trial involving more than 4200 subjects.

A clinical study performed in Europe evaluated the efficacy, immunogenicity, reactogenicity and safety of two doses of Rotarix® in healthy infants when co-administered with specific childhood vaccinations. The efficacy results showed that sufficient protection against gastroenteritis caused by the serotypes G1P 8, G2P 4, G3P 8, G4P 8 and G9P 8 continues in the second year of life, although the data for some of the serotypes indicate a certain waning immunity over time. However no interference of Rotarix® on immune response to antigens contained in coadministered childhood vaccines (Infanrix Hexa®, Infanrix Polio Hib, Prevenar® or Meningitec™) was observed in the study. The safety

data for both the first and second year of the study were comparable and no further concerns were raised.

A new pharmaceutical form, an oral suspension has been added. It is intended for the same population like Rotarix® powder and solvent for oral suspension.[1]

Reference

1. European Medicines Agency. EPARs for authorised medicinal products for human use. [online]. 2008 November 17 [cited 2009 July 8]; Available from: URL: http://www.emea.europa.eu/humandocs/Humans/EPAR/rotarix/rotarix.htm

Silgard®

Active Ingredient: human papillomavirus (HPV) [types 6, 11, 16, 18] (recombinant, adsorbed)

Available in: Private Sector

Variation: Silgard® is indicated for the prevention of premalignant genital lesions (cervical, vulvar and veginal), cervical cancer and external genital warts causally related to HPV types 6, 11, 16 and 18. A warning was updated that Silgard® will only protect against diseases that are caused by the above HPV types and to a limited extent against diseases caused by certain related HPV types.

The following adverse reactions: arthralgia, myalgia, asthenia, fatigue and malaise were included after a cumulative review of the New Worldwide Adverse Event System Database was performed by the MAH from its introduction on the market till 28 September 2007. A warning was also added regarding syncope as it may occur after vaccination so patients should be carefully observed for about 15 minutes following its administration. [1]

Reference

1. European Medicines Agency. EPARs for authorised medicinal products for human use. European [online]. 2009 June 15 [cited 2009 July 8]; Available from: URL: http://www.emea.europa.eu/humandocs/Humans/EPAR/silgard/silgard.htm

Tamiflu®

Active Ingredient: Oseltamivir phosphate

Available in: Private and Hospital Sectors

Variation: The SPC was updated with data concerning viral resistance to oseltamivir. No evidence for emergence of drug resistance associated with the use of oseltamivir was present in clinical studies conducted to date in post-exposure, post-exposure within household groups and seasonal prevention of influenza. The risk of emergence of influenza viruses with reduced susceptibility or frank resistance to oseltamivir has been examined during Roche-sponsored clinical studies. All patients who were found to carry oseltamivir-resistant virus did so transiently, cleared the virus normally and showed no clinical deterioration. The rate of emergence of resistance may be higher in the youngest children and in immunosuppressed patients. Naturally occurring mutations in influenza A/H1N1 virus associated with reduced susceptibility to oseltamivir *in vitro* have been detected in patients who, based on the reported information, have not been exposed to oseltamivir. The extent of reduction in susceptibility to oseltamivir and the prevalence of such viruses appear to vary seasonally and geographically. The therapeutic indication section of SPC was also updated with general statements on the appropriate use of antiviral agents that should be determined according to the official guidance.

Following the assessment of a follow-up measure on the review of the MAH's safety database, visual disturbances and cardiac arrhythmia were included as undesirable effects.

Analysis of neuropsychiatric adverse events reported the occurrence of convulsions and delirium in patients with influenza who were receiving oseltamivir. Very few cases resulted in accidental injury or fatal outcomes. These events were reported more frequently among paediatrics and adolescents after a rapid onset and rapid resolution. Since neuropsychiatric events have also been reported in patients with influenza who were not taking oseltamivir, the contribution of oseltamivir to these events is not known. [1]

Reference

1. European Medicines Agency. EPARs for authorised medicinal products for human use. [online]. 2009 June 9 [cited 2009 July 10]; Available from: URL: http://www.emea.europa.eu/humandocs/Humans/EPAR/tamiflu/tamiflu.htm

Temodal®

Active Ingredient: Temozolomide

Available in: Hospital Sector

Variation: After the assessment of the 11th European periodic safety update report (PSUR), the Special Warning and Precaution for use section was updated to include very rare cases of myelodysplastic syndrome and secondary malignancies including myeloid leukaemia. Cases of interstitial pneumonitis / pneumonitis and related disorders have also been reported very rarely and were included in the undesirable effects section. [1]

Reference

1. European Medicines Agency. EPARs for authorised medicinal products for human use. [online]. 2009 March 10 [cited 2009 July 27]; Available from: URL: http://www.emea.europa.eu/humandocs/Humans/EPAR/temodal/temodal.htm

Twinrix Adult®

Active Ingredient: Inactivated hepatitis A, hepatitis B recombinant, adsorbed vaccine

Available in: Private Sector

Variation: In a non clinical study in rats, Twinrix® was not associated with any adverse effects on embryo-fetal, pre-natal and post-natal development. No findings of direct or indirect harmful effects were found on the parental females or on reproduction. Likewise, no safety concern has been identified based on the limited clinical and post-marketing data of pregnant women exposed to vaccination with Twinrix®. However, these limited data should be interpreted with caution and is recommended that vaccination should be delayed until after delivery unless there is an urgent need to protect the mother against Hepatitis B infection.

The effect of risk factors likely to influence the immunogenicity of Twinrix® in adults aged 41 years or older was evaluated in an open, randomised, multi-centre and multi-country study where Twinrix Adult® was compared to separately administered monovalent hepatitis A and hepatitis B vaccines. Analysis of anti-HAV seropositivity rates up to 24 months after the first vaccine dose showed that the anti-HAV antibody response was influenced mostly by body mass index (BMI), followed by age, gender and the vaccine received. Obese patients (BMI>30kg/m^2) achieved significantly lower anti-HAV seropositivity rates compared to patients with lower BMI. [1]

Reference

1. European Medicines Agency. EPARs for authorised medicinal products for human use. [online]. 2008 July 9 [cited 2009 July 8]; Available from: URL: http://www.emea.europa.eu/humandocs/Humans/EPAR/twinrixadult/twinrixadult.htm

Twinrix Paediatric®

Active Ingredient: Inactivated hepatitis A, hepatitis B recombinant, adsorbed vaccine

Available in: Private Sector

Variation: In a non clinical study in rats, Twinrix® was not associated with any adverse effects on embryo-fetal, pre-natal and post-natal development. No findings of direct or indirect harmful effects were found on the parental females or on reproduction. Likewise, no safety concern has been identified based on the limited clinical and post-marketing data of pregnant women exposed to vaccination with Twinrix®. However, these limited data should be interpreted with caution and is recommended that vaccination should be delayed until after delivery unless there is an urgent need to protect the mother against Hepatitis B infection. [1]

Reference

1. European Medicines Agency. EPARs for authorised medicinal products for human use. [online]. 2008 July 9 [cited 2009 July 8]; Available from: URL: http://www.emea.europa.eu/humandocs/Humans/EPAR/twinrixpaediatric/twinrixpaediatric.htm

Velcade®

Active Ingredient: Bortezomib

Available in: Private Sector and Hospital Named Patient

Variation: In order to study the effect of renal impairment, patients with various degrees of renal impairment were enrolled and exposed to Velcade®. In patients with mild to moderate renal impairment (CCL >20 mL/min/1.73m^2) the pharmacokinetics of Velcade® are not influenced and therefore, dosing adjustments are not necessary. However, the available data are very limited to demonstrate that Velcade® total body clearance is not modified when the medicinal product is

administered at therapeutic doses to patients with creatinine clearance below 20 mL/min/1.73m^2 not undergoing dialysis. It should be administered after the dialysis procedure since the latter may reduce bortezomib concentrations. Septic shock was included in the adverse drug reaction list.

Its indication was extended to include treatment of patients with previously untreated multiple myeloma who are not eligible for high-dose chemotherapy with bone marrow transplant in combination with melphalan and prednisone.[1]

Reference

1. European Medicines Agency. EPARs for authorised medicinal products for human use. [online]. 2009 June 25 [cited 2009 July 10]; Available from: URL: http://www.emea.europa.eu/humandocs /Humans/EPAR/velcade/velcade.htm

Zyprexa®

Active Ingredient: Olanzapine

Available in: Hospital and Private Sectors

Variation: Long-term results from studies conducted on a population comprising of adolescents and adults showed that weight gain ≥7% of baseline body weight (kg) as very common adverse effects. Elevations in total /LDL/HDL cholesterol and triglyceride levels were observed commonly in both populations. Adults suffered also from an elevated glucose level. The magnitude of weight gain and the ratio of adolescents having clinically significant weight gain were greater with long-term exposure (at least 24 weeks) than with short-term exposure. [1]

Reference

1. European Medicines Agency. EPARs for authorised medicinal products for human use. [online]. 2009 June 12 [cited 2009 August 8]; Available from: URL: http://www.emea.europa.eu/humandocs/ Humans/EPAR/zyprexa/zyprexa.htm

Contributors

Arrowpharm (Malta) Ltd
HF62, Qasam Industrijali
Hal-Far, B'Bugia BBG3000
Tel: 22298000

Associated Drug Company Ltd
Triq L-Esportaturi
Imriehel BKR 3000
Tel: 22778000
Fax: 22778120
E-mail: info@associateddrug.com

BestPrint Co. Ltd
Zurrieq Road
Qrendi ZRQ 09
Tel: 21680789
Fax: 21649012
E-mail: bestprint@maltanet.net

Charles de Giorgio Ltd.
Triq il-Kan. Karmenu Pirotta
B'Kara, BKR1114
Tel: 25600500
Fax: 25600200
E-mail: admin@charlesdegiorgio.com