New Generics in 2008

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Abstract
The existence of generic medicines promotes the availability of medicines at a price lower than the original product. Pharmacological studies have only to prove that the generic product is bio-equivalent to the original medicine before registration and no clinical trials to prove efficacy and safety are required. Once a generic medicine is registered, the price will be determined by market forces, which may drive down the price of similar products, including the innovator medicine.

Several new generics were launched in 2008, some of which were the first generic for the original product. The policy on generic substitution requires the dispenser to inform the patient of the availability of a generic alternative where the originator product has been prescribed, thus all dispensers must be aware of the existence of these new generics. This review looks at the first generics for originator products launched in 2008. Prices quoted are the single exit price inclusive of VAT, taken from Mims October 2008.

Introduction
From a patient’s perspective, a generic medicine “does the same, for less”. While this is true to some extent, it is somewhat more involved than that. A generic medicine is an off-patent and licensed ‘copy’ of an original medicine. Generic companies identify certain products that fit within their target market and, once the patent of the originator product has expired, produce, register and sell their generic.

Generic manufacture requires that the same standards as for the originator be upheld with regard to quality, safety and efficacy. Generic products must undergo pharmacological studies to prove they are bio-equivalent to the originator product. Bio-equivalent products are pharmaceutically equivalent and their bioavailabilities after administration in the same molar dose under the same conditions are similar to such a degree that their effects can be expected to be essentially the same. Pharmaceutical equivalence means that the products contain the same molar amount of the same active pharmaceutical ingredients in the same dosage form that meet the same or comparable standards and are intended for administration by the same route.

Efavirenz
In 2008, three efavirenz generics were launched: Adco-Efavirenz®, Aspen-Efavirenz® and Cipla-Efavirenz®.

Efavirenz is a non-nucleoside reverse transcriptase inhibitor with activity against human immunodeficiency virus (HIV). It is used with other antiretrovirals for combination therapy of HIV infection.

Dose: The recommended dose for adults is 600 mg once daily. For adolescents and children under the age of 17 years the recommendation is 600 mg efavirenz at bedtime. The generic products do not recommend use in children weighing less than 40 kg.

Major Adverse Effects: Efavirenz may cause palpitations, tachycardia, convulsions, gastrointestinal (GI) disturbances, malaise, pain, hepatic failure, redistribution or accumulation of body fat, central nervous system (CNS) effects, syncope, speech disorders, changes in libido, skin reactions and allergic reactions.

Contra-Indications: Efavirenz is contra-indicated with concomitant terfenadine, astemizole, cisapride, midazolam, triazolam or ergot derivatives as potentially life-threatening adverse effects are possible. Concomitant use of St John’s Wort is also contra-indicated. Efavirenz has shown teratogenic effects in animal studies, use in pregnancy is contra-indicated. Breast-feeding while taking efavirenz is not recommended. Use in children under the age of 3 years or under 13 kg is contra-indicated.

Special Precautions: Women of childbearing age should use barrier contraceptives in combination with other contraceptive methods, as well as performing a pregnancy test before commencing efavirenz therapy. Efavirenz should not be used as monotherapy. Monitor liver enzymes and cholesterol levels.
Desloratadine (Dazit®)
Desloratadine, the major active metabolite of loratadine, is a non-sedating antihistamine. It is a long-acting, selective, peripheral histamine-1 (H1)-receptor antagonist. Desloratadine is used in the symptomatic relief of allergic conditions including rhinitis and chronic urticaria.

**Dose:** The recommended dose for adults and children over the age of 12 years is one tablet (5 mg) once daily.

**Major Adverse Effects:** Headache, fatigue, sedation, blurred vision, confusion, nightmares, GI disturbances, abnormal hepatic function and allergic reactions, including anaphylaxis.

**Contra-Indications:** Dazit® is contra-indicated in patients sensitive to other antihistamines, and in patients with porphyria. Safety in pregnancy and lactation has not been established.

**Special Precautions:** Dazit® should be used with caution in patients with severe liver impairment, renal impairment, emphysema, prostatic hypertrophy, narrow angle glaucoma, cardiovascular disorders and epilepsy. Safety in elderly patients or children under the age of 2 years has not been established.

Dazit® is manufactured by Pharmaplan.

**Price:** R124.01/30 5 mg tablets.

Sibutramine (Ectiva®)
Sibutramine is a serotonin and noradrenaline reuptake inhibitor. It is used in the management of obesity, and may also be used in overweight patients if other risk factors such as hypertension, diabetes mellitus or hyperlipidaemias are present.

Pharmacotherapy for obesity, when combined with lifestyle and behavioural changes to improve diet and increase physical activity, helps some obese patients to maintain weight loss.

**Dose:** Ectiva® is recommended in a dose of 10 mg once daily in the morning. It should not be used for longer than three months if weight loss is not equal to or more than 5% of the initial weight. The dose may be increased to 15 mg once daily if the response is inadequate (i.e. less than 2 kg in 4 weeks). Therapy with Ectiva® should not be continued if the weight loss is not maintained.

**Major Adverse Effects:** Chills, GI disturbances, psychiatric effects, sweating, taste perversion, increased pulse rate and cardiovascular effects.

**Contra-Indications:** Ectiva® is contra-indicated in patients whose obesity is caused by organic factors, patients with hyperthyroidism, patients with a history of or presenting with an eating disorder or patients with a history of drug, medicine or alcohol abuse. Ectiva® is also contra-indicated in patients with psychiatric illness, on concomitant mono-amine oxidase inhibitors (MAOIs) or other centrally acting medications for mental disorders, sleep disturbances, or other weight reducing agents, as well as other medications that raise serotonin levels. Patients with uncontrolled hypertension, severe renal or hepatic impairment, coronary artery disease, tachycardia, arrhythmias and cerebrovascular disease should not take Ectiva®. The product is not recommended for children under the age of 18 years and is contra-indicated in pregnancy and lactation.

**Special Precautions:** Ectiva® should only be used in the elderly as part of an integrated approach to weight management, including modifications to diet and lifestyle, and should be administered only by a physician experienced in the treatment of obesity.

Ectiva® should be used with caution in patients with primary pulmonary hypertension symptoms, mild to moderate renal or hepatic impairment, and in patients with family history of epilepsy. Women of childbearing age should use adequate contraceptive measures while taking this product. Use Ectiva® with caution in patients taking concomitant medications affecting blood pressure or heart rate.

Ectiva® is manufactured by Aspen Pharmacare.

**Price:** R523.01/30 10 mg capsules
R634.91/30 15 mg capsules

Escitalopram (Lexamil®)
Escitalopram is a selective serotonin reuptake inhibitor (SSRI). These agents are considered medicines of choice in the treatment of depression. Lexamil® is indicated for the...
treatment of major depressive episodes.

Dose: Lexamil® is given as a single daily dose of 10 mg in the treatment of major depressive episodes. The dose may be increased to 20 mg daily depending on individual response. Two to four weeks of treatment are necessary for an antidepressant response.

In the treatment of panic disorder, 5 mg is given as a single daily dose for the first week, before increasing to 10 mg once daily, with a possible increase to 20 mg once daily depending on response.

Major Adverse Effects: Paradoxical anxiety may be demonstrated at the start of panic disorder treatment. Other adverse effects include cutaneous bleeding abnormalities, CNS effects, sleep disturbances, taste changes, sinusitis, nose bleeds, GI effects, sexual dysfunction, movement disorders, seizures, sweating and fever. Lexamil® may also precipitate hostility, suicide ideation and self-harm, especially in children.

Contra-Indications: Lexamil® is contra-indicated in children under the age of 18 years. Escitalopram should not be taken with concomitant MAOIs. Safety in pregnancy and lactation has not been established. There is no information on use of Lexamil® in patients with severe renal impairment.

Special Precautions: Lexamil® should be used with caution in patients with a history of mania or hypomania. Treatment with escitalopram should be discontinued if a manic phase is entered. Lexamil® should be avoided in patients with unstable epilepsy. Patients should be monitored during early therapy with respect to dosage changes for worsening symptoms and for suicidal behaviour. Dose should be tapered on discontinuation of therapy.

Lexamil® is manufactured by Cipla Medpro.
Price: R119.70/30 5 mg tablets
R153.90/30 10 mg tablets
R188.10/30 20 mg tablets

Sodium warfarin (Cipla-Warfarin®)
Warfarin is a coumarin anticoagulant used in the treatment and prevention of thromboembolic disorders. It acts on the synthesis of coagulation factors. Therefore, because warfarin acts indirectly, it has no effect on existing clots. The coagulation factors have long half-lives, and therefore the therapeutic effect of warfarin is usually only apparent after several hours. If an immediate effect is required heparin will normally be co-administered for the first few days.

Cipla-Warfarin® is indicated for the prevention and treatment of deep-vein thrombosis (DVT) and pulmonary embolism, for the prevention of thromboembolism in atrial fibrillation, prosthetic heart valves and after myocardial infarction (MI) and for the treatment of transient ischaemic attacks.

Dose: The dose of warfarin depends on individual prothrombin time (PT) or International Normalised Ratio (INR) levels, which must be monitored before and during therapy. The initial dose usually ranges from 10–15 mg per day for 3 days. The maintenance level of warfarin is usually between 2.5–10 mg per day. This medicine should be taken at the same time each day.

Major Adverse Effects: The side effects include haemorrhage with possible anaemia and haematoma, GI disturbances including nausea and vomiting, alopecia, fever, hypersensitivity and skin reactions, purple toe syndrome, skin necrosis, renal damage and hepatotoxicity.

Contra-Indications: Cipla-Warfarin® should not be used in patients sensitive to other coumarins or in patients with bleeding disorders including haemophilia, leukaemia and peptic ulcers. Patients undergoing surgery or with large open wounds should not use warfarin. Use of Cipla-Warfarin® is contra-indicated in patients with infective endocarditis, pericarditis, hypertension, cerebral or aortic aneurysm, and patients with a vitamin C deficiency. Warfarin should not be used in pregnancy as it is a recognised teratogen, nor should it be used in breastfeeding mothers. Safety and efficacy has not been established for patients under the age of 18 years.

Special Precautions: Cipla-Warfarin® therapy should not be stopped abruptly. The dose is individualised and prothrombin time must be monitored. If the prothrombin time changes, other factors must be considered (Prothrombin time is increased by factors including carcinoma, fever, diarrhoea, liver problems and congestive heart failure. Prothrombin time may be decreased by diabetes, hypothyroidism or hyperlipidaemias). Cipla-warfarin® should be used with caution in patients with hyperthyroidism, intestinal disturbances and in those on antibiotic therapy.

Cipla-Warfarin® is manufactured by Cipla Medpro.
Price: R88.27/100 1mg tablets
R97.13/100 5mg tablets

Risperidone (Risperidone Hexal®)
Risperidone is a benzisoxazole derivative. It is indicated for treatment of schizophrenia, psychoses and psychoses with manic or mixed episodes. Risperidone is also indicated for patients with dementia when aggressiveness, disturbed behaviour or psychotic symptoms are present. It may also be used for behavioural disorders in children aged 5 to 12 years with mental deficiencies where destructive behaviour is prominent.

Dose: Dosages of Risperidone Hexal® depend on the indication and for some indications must be individualised.
• Schizophrenia: If the patient is being switched from another antipsychotic to Risperidone Hexal®, the previous treatment must be withdrawn gradually. The dose must be individualised. The initial dose is 2 mg per day and may be increased to 4 mg on the second day. Usual dose
range is 4–8 mg per day. Maximum daily dose is 16 mg.

• **Behavioural disturbances in patients with dementia:**
  initial dose is 0.25 mg twice a day. Dose may be increased by 0.25 mg twice daily every second day as required by the individual patient. Optimum dose is usually 0.5 mg to 1 mg twice daily.

• **Behavioural disturbances in children ages 5 to 12 years:**
  In children under 50 kg the initial dose is 0.01 mg/kg once daily. Dose may be increased according to individual requirements by 0.01 mg/kg every second day. The recommended daily dose is 0.02–0.04 mg/kg once daily. The need for this medication should be regularly evaluated.

**Major Adverse Effects:** Side effects of risperidone include altered blood counts, rash and allergic reactions, hyperglycaemia and exacerbation of diabetes and body temperature irregularities. Galactorrhoea, gynecomastia and menstrual irregularities may result from dose-dependent increases in plasma prolactin. Other side effects reported are extrapyramidal symptoms, seizures, blurred vision, blood pressure disturbances, urinary incontinence and erectile dysfunction.

**Contra-Indications:** The safety and efficacy of Risperidone Hexal® has not been established for children under the age of 5 years for behavioural disturbances. Safety and efficacy have not been established in pregnancy and lactation, and for children under the age of 15 years for schizophrenia.

**Special Precautions:** Risperidone should be used with caution in patients with renal and hepatic impairment, epilepsy and Parkinson’s disease.

Risperidone Hexal® is manufactured by Sandoz.

Price: R254.47/30 1 mg tablets
  R428.56/30 2 mg tablets
  R626.60/30 3 mg tablets

**Moxonidine (Moxotens®)**

Moxonidine is a centrally-acting antihypertensive, structurally related to clonidine. It appears to act through stimulation of central imidazoline receptors to reduce sympathomimetic tone, and also has alpha-(2)-adrenoceptor agonist activity. Moxotens® is indicated for the treatment of mild to moderate hypertension.

**Dose:** The initial dose of Moxotens® is 0.2 mg in the morning. This may be increased after 3 weeks to 0.4 mg administered once daily or in divided doses. The maximum recommended dose is 0.4 mg daily, in a single or as 2 divided doses.

**Major Adverse Effects:** CNS effects, asthenia, vasodilation, nausea and dry mouth.

**Contra-Indications:** Moxotens® is contra-indicated in patients with a history of angioneurotic oedema, in patients with sick sinus syndrome, in sino-atrial block or 2nd or 3rd degree atrioventricular block. Moxonidine should not be used in patients with malignant arrhythmias, with severe renal or hepatic dysfunction, in patients with bradycardia, in severe coronary artery disease or unstable angina. Patients with either Raynaud’s disease or Parkinson’s disease should not use Moxotens®.

Moxonidine is contra-indicated in patients with epilepsy, glaucoma, depression, in pregnancy and lactation, and in patients under the age of 16 years.

**Special Precautions:** If Moxotens® is used in combination with a beta-blocker, and if the treatment has to be discontinued, then discontinue the beta-blocker first, and withdraw Moxotens® a few days later. Moxotens® therapy should not be discontinued abruptly, but should be withdrawn gradually over a period of one to two weeks. Moxotens® should be used with caution in patients with moderate renal dysfunction.

Moxotens® is manufactured by Sandoz.

Price: R135.04/28 0.2 mg tablets
  R135.04/28 0.3 mg tablets
  R153.04/28 0.4 mg tablets

References: