**NEW GENERICS IN 2007**

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Amayeza Info Centre

A number of generic medicines were launched in 2007. There is some debate as to exactly what constitutes a generic. As far as most patients are concerned, a generic is a medicine that contains the same active ingredient, does the same as their original medicine and costs less. There has been some debate as to what constitutes the “same ingredient”, with some people saying that the ingredients must be identical and others saying that various salts of the same active ingredient are acceptable.

Products are considered to be pharmaceutical equivalents if they 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 to be administered by the same route.

Bioequivalent products are pharmaceutically equivalent and their bioavailabilities after administration of 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.

Two pharmaceutical products are considered therapeutically equivalent if they are pharmaceutically equivalent and after administration in the same molar dose, their effects, with respect to both efficacy and safety, will be essentially the same when administered by the same route under the conditions specified in the labelling.

Since differences in the excipients and in the manufacturing process may lead to differences in product performance, pharmaceutical equivalence does not necessarily imply bioequivalence or therapeutic equivalence. Thus, for pharmaceutically equivalent products to be considered therapeutically equivalent, a bioequivalence study and additional preclinical or clinical data may be required.

The policy on generic substitution requires the dispenser to inform the patient of any generic alternative where the originator brand has been prescribed, unless the prescriber has specified that no substitution should be made.

**Amlodipine besylate**

In 2007 a number of amlodipine besylate generics were launched. Previous amlodipine generics were not the besylate salt, which sparked the debate as to whether different salts of the same medicine may be considered generic equivalents.

Amlodipine besylate is a calcium channel blocker. The originator has proved to be effective in the treatment of mild to moderate hypertension and angina pectoris. Amlodipine besylate can be used alone or in combination with other antihypertensives in the treatment of hypertension.

**Dose:** The initial dose of amlodipine besylate is 5 mg once daily, which may be increased to 10 mg once daily depending on individual response after 10–14 days.
**Major adverse effects:** increased incidence of pulmonary oedema especially in patients with heart failure, palpitations, hypotension, syncope, vasculitis, myocardial infarction (MI), arrhythmias, chest pains, central nervous system (CNS) effects, peripheral neuropathy, gastrointestinal (GI) disturbances, paraesthesia and blood dyscrasias

**Contra-indications:** The safety of amldipine besylate has not been established in children, pregnancy and lactation or in patients with porphyria.

**Special precautions:** Special care is advised when using amldipine besylate in the elderly, patients with severe renal impairment or impaired hepatic function. An increased incidence of pulmonary oedema has been noted. Should the patient be intolerant or resistant to amldipine besylate the product should be withdrawn gradually.

See Table I for the products containing amldipine besylate that were introduced in 2007.

**Losartan (Zartan®)**

Losartan is an angiotensin-II receptor antagonist used for hypertension.

**Dose:** The usual dose is 50 mg once daily. It may take 3–6 weeks to reach maximum efficacy. The dose may be increased to 100 mg daily, if necessary. Losartan may be given alone or with other antihypertensives.

**Major adverse effects:** Hypotension, angioedema, GI disturbances, palpitations, tachycardia, muscle cramps and chest pain. Other effects that may be experienced are: headache, insomnia, migraine, cough, sinus disorders, impaired renal function and hyperkalaemia.

**Contra-indications:** Losartan is contra-indicated in pregnancy and lactation. Safety in children has not been established.

**Precautions:** Women of childbearing age should use adequate contraception while taking losartan. Use losartan with caution in patients with renal artery stenosis, aortic valve stenosis, cardiomyopathy, impaired liver and kidney function and in the elderly. Serum potassium levels should be monitored.

Pharma Dynamics produce Zartan®, and the cost is R85.50/30 (50 mg) tablets.

**Gabapentin (Epleptin®, Neurexal®)**

Two gabapentin generics were released in 2007: Epleptin® and Neurexal®. Both are indicated as adjunctive therapy (with other anticonvulsants), where adequate seizure control has not been achieved. Gabapentin can be used for simple and complex partial seizure control with or without secondary generalised tonic-clonic seizures.

**Dose:** Gabapentin is indicated only for adults and children over the age of 12 years. An initial dose of 300 mg three times a day may be gradually increased until a clinical response is achieved. Doses of 900–1800 mg per day in three divided doses, with intervals not greater than 12 hours between doses are usually effective.

**Major adverse effects:** Nystagmus, trembling, diplopia, ambylopia and dysarthria have been reported. GI disturbances, oedema, impotence, vasodilation, rhinitis, paraesthesia, psychiatric effects, skin effects and blood dyscrasias may also occur with gabapentin therapy.

**Contra-indications:** Safety and efficacy of gabapentin has not been established in children under the age of 12 years, in pregnancy or in lactation.

**Precautions:** Bioavailability may be impaired when administered with antacids. Care should be taken when using gabapentin in the elderly, patients with a history of psychotic illness or in those with impaired renal function. Therapy should be discontinued gradually to prevent possible seizures from occurring.

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**Table I: Products containing amlodipine besylate introduced in 2007**

<table>
<thead>
<tr>
<th>Name</th>
<th>Company</th>
<th>Dosage</th>
<th>Price</th>
<th>Dosage</th>
<th>Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amlodac®</td>
<td>Zydus</td>
<td>5 mg</td>
<td>R 51.30/30</td>
<td>10 mg</td>
<td>R 79.80/30</td>
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<td>Austell-Amlodipine®</td>
<td>Austell</td>
<td>5 mg</td>
<td>R 50.19/30</td>
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<td>Calbloc®</td>
<td>Be-Tabs</td>
<td>5 mg</td>
<td>R 72.95/30</td>
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<td>R103.01/30</td>
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<td>Ciplavasc®</td>
<td>Cipla Medpro</td>
<td>5 mg</td>
<td>R 51.30/30</td>
<td>10 mg</td>
<td>R 79.91/30</td>
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<td>CPL Alliance Amlodipine®</td>
<td>Alliance</td>
<td>5 mg</td>
<td>R 72.95/30</td>
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<td>Kloidip-S®</td>
<td>Dezzo Trading</td>
<td>5 mg</td>
<td>R 51.28/30</td>
<td>-</td>
<td>-</td>
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<td>Lomanor®</td>
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<td>R 81.28/30</td>
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**Torasemide (Torahexal®)**

Torasemide is a diuretic used in the treatment of essential hypertension, oedema of cardiac and hepatic origin and in pulmonary oedema due to acute cardiac insufficiency.

**Dose:** In essential hypertension the initial dose is 2.5 mg per day, which may be increased to 5 mg per day. For oedema, the usual dose is 5 mg per day, and may be up to 20 mg per day depending on severity.

**Major adverse effects:** Dizziness, confusion, hypotension, water and electrolyte disturbances, cardiac or cerebral ischaemia, thromboembolic complications, GI disturbances and altered blood glucose.

**Contra-indications:** Torasemide is contra-indicated in pregnancy, lactation and in children less than 12 years. It should not be used in patients with renal failure or anaemia, hepatic precoma or coma, sulphonamide sensitivity, hypovolaemia, hypernatraemia or hypokalaemia.

**Precautions:** Glucose, electrolyte levels, uric acid, creatinine and lipid levels must be monitored regularly. Use with caution in patients with hyperuricaemia, gout or diabetes mellitus.

Hexal manufacture Torahexal® and it is available in 3 strengths:

- 2.5 mg at R71.51/30
- 5 mg at R79.09/30
- 10 mg at R85.75/30

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**Note:**

These notes are intended for educational purposes only and should not replace the advice of a healthcare professional.
Mirtazapine (Adco-Mirteron®, Sandoz-Mirtazapine®)

Mirtazapine is an α2-antagonist and works by increasing central noradrenergic and serotonergic neurotransmitters. Two mirtazapine generics were launched in 2007 – Adco-Mirteron® and Sandoz-Mirtazapine®. Mirtazapine is indicated for the treatment of major depression.

Dose: Treatment may be initiated at a dose of 15 mg per day, as a single dose, at bedtime. The dose can be increased gradually until a clinical response is achieved. The effective range is 15–45 mg per day, which may be given as a single dose at bedtime or in two divided doses. Dosage changes should be made at intervals of not less than 1–2 weeks. Continuous therapy for six months is advised for the treatment of an acute depressive episode.

Major adverse effects: A flu-like syndrome, asthenia, increased sweating, sedation, paraesthesia, seizures,mania, restless legs syndrome, increased appetite, weight gain, GI disturbances, dry mouth with thirst and a bitter taste, oedema, jaundice, postural hypotension, arthralgia and myalgia.

Contra-indications: Treatment with mirtazapine is contra-indicated in pregnancy and lactation, in children and during concomitant monoamine oxidase inhibitor (MAOI) therapy, or within 14 days of stopping MAOI therapy.

Special precautions: Due to possible side effects, special precautions should be taken when using mirtazapine in epileptics. Caution must also be exercised when prescribing for patients with hepatic or renal insufficiencies. Therapy should be discontinued in cases of jaundice and if symptoms of infection occur. Blood counts should be performed.

Mirtazapine should be prescribed with care for patients with cardiac disturbances, including conduction disturbances, angina pectoris, recent MI and hypotension. Treatment with mirtazapine may worsen depression or cause suicidal ideation and behaviour to emerge. Patients at risk of these effects should be monitored closely during early therapy and during dosage changes. Changes in therapeutic regime or discontinuation of mirtazapine therapy should be considered if psychiatric symptoms occur which are severe or abrupt in onset or not part of the presenting symptoms. Mirtazapine therapy should be withdrawn gradually. Use mirtazapine with caution in the elderly, those with glaucoma and increased intraocular pressure.

Note: South African epilepsy guidelines recommend that patients taking anti-epileptics should not switch from the innovator to a generic or between generics themselves in order to avoid the occurrence of possible seizures.

See Table II for dosage and price for Epleptin® and Neurexal®.

Table II: Dosage and prices of Epleptin® and Neurexal®

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Company</th>
<th>Dose</th>
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<th>Price/100</th>
<th>Dose</th>
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<tr>
<td>Epleptin®</td>
<td>Pharmplan</td>
<td>100 mg</td>
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<td>300 mg</td>
<td>R241.40</td>
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<td>Neurexal®</td>
<td>Sandoz</td>
<td>100 mg</td>
<td>R96.62</td>
<td>300 mg</td>
<td>R241.19</td>
<td>400 mg</td>
<td>R241.19</td>
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Selegiline (Parkilyne®)

Selegiline is a monoamine oxidase B inhibitor used in conjunction with levodopa to reduce early morning and nocturnal akinesia or ‘end of dose’ deterioration in advanced Parkinson’s disease.

Dose: The initial dose is 5 mg given in the morning. It may be increased to 10 mg if necessary. Selegiline must always be given with existing levodopa therapy.

Major adverse effects: Selegiline may potentiate levodopa side effects and aggravate dyskinesia. Other side effects include hypotension, GI disturbances, muscle cramps, trembling, headache, confusion, agitation, psychosis, depression, hallucinations and insomnia.

Precautions: Care must be taken when prescribing selegiline for patients taking tricyclic antidepressants or selective serotonin reuptake inhibitors (SSRIs). Monitor use in patients with history of peptic ulceration, uncontrolled hypertension, angina, arrhythmia or psychosis.

Aspen Pharmacare produce Parkilyne®, which is priced at R197.09/30 (5 mg) tablets.

Sumatriptan (Migrex®)

Sumatriptan is a 5HT1 agonist that acts on serotonin receptors. It can be used in the established headache phase of a migraine attack and is the preferred treatment for those patients who fail to respond to conventional analgesics.

Dose: Sumatriptan is not used as a prophylactic for migraines. The tablets should be swallowed whole as soon as possible in the attack. The initial dose is 50 mg, which may be increased to 100 mg depending on response. A further dose may be taken if symptoms recur, provided that at least two hours separate the doses. A maximum dose of 300 mg may be taken in a 24-hour period.

Note: If no beneficial effects are experienced from the initial dose, a second dose is unlikely to produce relief.

Major adverse effects: Chest pain, flushing, increased blood pressure, bradycardia or tachycardia, hypotension, palpitations, MI, tingling, dizziness and fatigue. Hypersensitivity reactions may include anaphylaxis.

Contra-indications: Sumatriptan should not be used in patients sensitive to sulphonamides. Various cardiac condi-
tions including MI, ischaemic heart disease, Prinzmetal’s angina and uncontrolled hypertension contra-indicate the use of sumatriptan. This preparation should not be used with concomitant ergotamine or MAOI therapy. Safety in children under the age of 18 years, and patients over the age of 65 years has not been established. Safety is not established in pregnancy.

**Precautions:** Hypersensitivity reactions range from skin rash to anaphylaxis, including chest pain and tightness. Use sumatriptan with caution in patients with impaired hepatic function, cardiovascular disorders, SSRI therapy and history of epilepsy. Breast-feeding should be avoided for 24 hours after administration as sumatriptan is excreted in breast milk.

Topiramate (Sandoz Topiramate®, Toplep®)
Topiramate is used as adjunctive therapy for adults and children over 4 years of age for generalised tonic-clonic seizures. It can also be used for seizures associated with Lennox-Gastaut syndrome.

**Dose:** Topiramate should be initiated at a low dose and titrated to an effective dose. The tablets must not be broken.

- In adults the initial dose is 25–50 mg nightly for one week, increased at weekly intervals by 25–50 mg per day, with total dose given in two divided doses. The usual total dose is 200–400 mg per day in two divided doses. The maximum dose is 800 mg per day.
- Children of 4 years or older may start on 25 mg nightly for one week. This dose may be increased by increments of 1–3 mg/kg at 1–2 weekly intervals. If the total dose is more than 25 mg per day, it should be divided into two doses. The recommended dose is 5–9 mg/kg per day in two divided doses.

**Major adverse effects:** Acute myopia associated with secondary closed angle glaucoma has been reported, even in paediatric patients. Other side effects include CNS effects, paraesthesia, speech disorders, hyperkinesias and co-ordination problems, impaired memory and concentration, confusion, depression and mood problems, personality changes, psychosis and suicidal ideas. Other effects may include weight decrease, purpura, blood dyscrasias, anaemia, renal failure and urinary disorders, hepatitis and liver failure, skin reactions and increased sweating, hypersensitivity and hypotension.

**Contra-indications:** The safety of topiramate in pregnancy and in children under the age of 4 years is not established. It is unknown whether it is excreted in breast milk.

**Precautions:** Discontinue topiramate therapy if symptoms of acute myopia associated with secondary closed angle glaucoma occur. There is a risk of teratogenicity if used in pregnancy and oral contraceptive efficacy may be decreased. Oral contraceptives should contain at least 50 µg of oestrogen. Topiramate should be used with caution in patients with hepatic or renal impairment. Adequate hydration must be maintained especially prior to and during exercise and exposure to warm temperatures.

See Table IV for the two topiramate generics which were launched in 2007.

Levofloxacin (Sandoz Levofloxacin®)
Levofloxacin is a broad-spectrum fluoroquinolone antibiotic active against several Gram-positive and Gram-negative bacterial organisms. Levofloxacin is indicated for the treatment of respiratory tract infections (RTIs) such as acute exacerbations of chronic bronchitis, community-acquired pneumonia and sinusitis. Levofloxacin is also used in complicated urinary tract infection (UTI) and acute pyelonephritis and for uncomplicated UTI in women. This medicine may also be used for skin and soft tissue infections in adults caused by susceptible bacteria.

**Dose:** The dosage is determined by the type and severity of infection.

- **RTIs:** 500 mg once or twice daily for 5–14 days depending on complicating factors.
- **UTIs:** A dose of 250 mg daily for 10 days is used in complicated UTIs.
- In uncomplicated UTIs in women, a dose of 250 mg daily for 3 days is used.
- **Skin and soft tissue infections:** Uncomplicated cases are treated with 250-500 mg daily for 5–7 days. Complicated cases use 500 mg daily for 10–14 days.
- **Intra-abdominal infections:** 500 mg daily in combination with an antibiotic effective against anaerobes.

**Major adverse effects:** GI disturbances including severe or bloody diarrhoea may occur. Other side effects include CNS effects, visual disturbances, impaired hearing, taste and smell, convulsions, psychotic reactions, hepatitis, kidney failure, photosensitivity, hypoglycaemia and blood dyscrasias. Muscle weakness and rupture of the Achilles tendon has been reported. Use of levofloxacin may cause a superinfection, may trigger attacks in porphyria patients and may cause anaphylaxis.

**Precautions:** Use with caution in patients predisposed to seizures. Avoid unnecessary exposure to the sun. Use with care in patients with impaired renal function, diabetes, porphyria and myasthenia gravis. Discontinue levofloxacin if pseudomembranous colitis is suspected.

Sandoz produces Sandoz Levofloxacin® in two strengths: 250 mg at R69.79/5, 500 mg at R108.24/5, and 500 mg in a pack of 10 tablets for R216.49.

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**Table IV: Two topiramate generics launched in 2007**

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Company</th>
<th>Dose</th>
<th>Price</th>
<th>Dose</th>
<th>Price</th>
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<tbody>
<tr>
<td>Sandoz Topiramate®</td>
<td>Sandoz</td>
<td>25 mg</td>
<td>R143.33/60</td>
<td>50 mg</td>
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<td></td>
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<td>100 mg</td>
<td>R443.48/60</td>
<td>200 mg</td>
<td>R674.77/60</td>
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<tr>
<td>Toplep®</td>
<td>Ranbaxy</td>
<td>25 mg</td>
<td>R143.33/60</td>
<td>50 mg</td>
<td>R263.08/60</td>
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<tr>
<td></td>
<td></td>
<td>100 mg</td>
<td>R443.48/60</td>
<td>200 mg</td>
<td>R674.77/60</td>
</tr>
</tbody>
</table>
**Mometasone Cream (Aspen Mometasone® cream)**

Mometasone is a medium-potency corticosteroid. Aspen Mometasone® cream is indicated for the treatment of inflammatory manifestations of psoriasis and for skin conditions that respond to topical corticosteroid therapy.

*Dose:* Apply the cream in a thin layer once a day. Duration of therapy depends on clinical response but should be restricted to short courses of therapy only. Safety of use for longer than three weeks has not been established.

**Major adverse effects:** Allergic contact dermatitis, burning, dryness, itching, secondary infections and acne-like eruptions. Skin changes may occur with long-term use.

**Contra-indications:** Use of mometasone is contra-indicated in Herpes simplex, vaccinia and varicella. Mometasone is not recommended for use during pregnancy. Do not use mometasone topical cream in patients with an untreated fungal skin infection as an exacerbation of the fungal infection may occur.

**Precautions:** Mometasone cream is not for ophthalmic use. The safety and efficacy of this product for more than three weeks has not been established. Use is not recommended in children under the age of two years. Safety in lactation has not been established. Treatment must be discontinued if irritation or sensitisation occurs. Use in psoriasis may provoke a pustular form of the disease.

Aspen Mometasone® cream is produced by Aspen Pharmacare and is available in 20 g tubes at a price of R72.96.

**Pioglitazone (Cipla Pioglitazone®)**

Pioglitazone is a thiazolidinedione oral hypoglycaemic that reduces peripheral insulin resistance, leading to a decreased blood glucose concentration. Cipla Pioglitazone® is indicated as an adjunct to diet in Type 2 diabetes either as monotherapy, or in combination with metformin, a sulphonylurea or insulin when diet and exercise or single agents have failed to produce glycaemic control.

*Dose:* 

**Monotherapy:** The initial dose is 15–30 mg once daily, increased in increments to 45 mg once daily if necessary.

**Combination therapy:** The initial dose is 15–30 mg once daily in combination with the current dose of other medication. If hypoglycaemia is reported reduce dose of sulphonylurea, or if used with insulin; decrease either insulin or pioglitazone dose.

**Major adverse effects:** Anaemia, weight gain, insomnia, oedema, visual disturbances, elevated liver enzymes and heart failure may occur. When taken with metformin, arthralgia, haematuria, flatulence and erectile dysfunction may occur. Hypoglycaemia, sweating and vertigo have been reported when taken in combination with a sulphonylurea, as has dyspnoea when taken with insulin.

**Contra-indications:** Pioglitazone is contraindicated in patients with hepatic impairment, cardiac failure, type 1 diabetes mellitus and ketoacidosis. This product is not indicated for patients who are pregnant or lactating. Safety has not been established in children.

**Precautions:** Liver function should be monitored before and during therapy. Discontinue therapy if jaundice occurs.

Cipla produces Cipla Pioglitazone®. It is available at R57.00/30 (15 mg) and at R95.76/30 (30 mg).

**Major References:**

1. MIMS, October 2007
2. MIMS, November December 2007
3. MIMS January 2008

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