IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PA0405/054/001
Case No: 2056395

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

Transferred from PA1080/020/001.

Generics (UK) Limited

12 Station Close, **Potters Bar**, **Hertfordshire EN6 1TL**, **United Kingdom**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Topamat 25mg Film-coated Tablets

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **26/09/2008** until **24/01/2013**.

Signed on behalf of the Irish Medicines Board this

_____

A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Topamat 25 mg Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 25 mg of topiramate
For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet
White, round, biconvex, film-coated tablets debossed with “G” on one side and “TO” over “25” on the other

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Epilepsy:
Topiramate is indicated as monotherapy or adjunctive therapy for adults and children over 4 years of age for partial onset seizures with or without secondarily generalised seizures and primary generalised tonic-clonic seizures.

Topiramate is also indicated in adults and children as adjunctive therapy for seizures associated with Lennox Gastaut Syndrome.

Migraine:
Topiramate is indicated in adults for the prophylaxis of migraine headaches in patients intolerant of or unresponsive to other migraine treatments. Treatment should be initiated under the supervision of a consultant neurologist or a hospital based migraine specialist.

4.2 Posology and method of administration

General:
For optimal seizure control in both adults and children it is recommended that therapy be initiated at a low dose followed by titration to a clinically effective dose.

Topiramate Tablets should not be broken and can be taken without regard to meals.

Since topiramate is removed from plasma by haemodialysis, a supplemental dose of topiramate equal to approximately one-half the daily dose should be administered on haemodialysis days. The supplemental dose should be administered in divided doses at the beginning and completion of the haemodialysis procedure. The supplemental dose may differ based on the characteristics of the dialysis equipment being used.

The following dosing recommendations apply to children and all adults, including the elderly, in the absence of underlying renal disease (see section 4.4).

Epilepsy:
Monotherapy in adults and adolescents aged 16 years and over:
Titration should begin at 25 mg nightly for 7 days. The dosage should then be increased at 7 day or 14 day intervals by increments of 25 – 50 mg/day, administered in two divided doses. If the patient is unable to tolerate the titration regimen, smaller dose increments or longer intervals between dose increments may be used. Dose and titration should be guided by clinical outcome.

The recommended initial target dose for topiramate monotherapy in adults 100 to 200 mg/day. The recommended maximum daily dose is 500 mg. Some patients with refractory forms of epilepsy have tolerated doses of up to 1000 mg/day.

Monotherapy in children and adolescents aged 4 years and above:
Titration should begin at 1 to 3 mg/kg nightly for 7 days. The dosage should then be increased at 7 day or 14 day intervals by increments of 1 to 3 mg/kg, administered in two divided doses. If the child is unable to tolerate the titration regimen, smaller dose increments or longer intervals between dose increments may be used. Dose and titration should be guided by clinical outcome.

The recommended initial target dose range for topiramate monotherapy in children and adolescents aged 4 years and above is 3 -6 mg/kg/day. Higher doses have been tolerated and children over 50 kg with recently diagnosed partial onset seizures have received doses of up to 500 mg/day.

Topiramate Tablets are not suitable for children requiring doses of less than 25 mg/day.

Adjunctive therapy in adults and adolescents aged 16 years and over:
Titration should begin at 25 mg nightly for 7 days. The dosage should then be increased at 7 day or 14 day intervals by increments of 25 – 50 mg/day, administered in two divided doses. If the patient is unable to tolerate the titration regimen, smaller dose increments or longer intervals between dose increments may be used. Dose and titration should be guided by clinical outcome. Some patients may achieve efficacy with once-a-day dosing.

The minimal effective dose as adjunctive therapy is 200 mg/day. The usual total daily dose is 200 mg to 400 mg administered in two divided doses. Some patients may require higher doses. The maximum recommended daily dose is 1600 mg.

Adjunctive therapy in children and adolescents aged 4 – 16 years:
Titration should begin at 25 mg nightly for 7 days. The dosage should then be increased at 7 day or 14 day intervals by increments of 1 to 3 mg/kg, administered in two divided doses. Dose titration should be guided by clinical outcome.

The recommended total daily dose is 5 to 9 mg/kg/day, administered in two divided doses. Daily doses up to 30 mg/kg/day have been studied and were generally well tolerated.

Prophylaxis of migraine in adults:
Titration should begin at 25 mg nightly for 7 days. The dosage should then be increased at 7 day intervals by increments of 25 mg/day. If the patient is unable to tolerate the regimen, longer intervals between dose adjustments may be used.

The recommended total daily dose of topiramate for prophylaxis of migraine in adults is 100 mg/day administered in two divided doses. Higher doses do not result in increased benefit. Some patients may experience a benefit at a total daily dose of 50 mg/day. Dose and titration should be guided by clinical outcome.

Renal Impairment:
See section 4.4 Special Warnings and Precautions for Use.

Hepatic Impairment:
See section 4.4 Special Warnings and Precautions for Use.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients of the medicinal product.

Treatment for prophylaxis of migraine during pregnancy, and in women of child bearing potential if not using an effective method of contraception (see section 4.6).
In pregnancy, the occurrence of seizures forms a considerable risk for mother and child. Preventing seizures by topiramate, provided given for the right indication, therefore outweighs the risk of malformations. However, preventing migraine attack does not outweigh this risk. Consequently, topiramate for the indication of prophylaxis of migraine is contra-indicated in pregnancy and women with child bearing potential if not using an effective method of contraception.

4.4 Special warnings and precautions for use

General:
Topiramate, as with other antiepileptic drugs, should be withdrawn gradually to minimise the potential of increased seizure frequency. In clinical trials, dosages were decreased by 100 mg/day at weekly intervals. In some patients, withdrawal was accelerated without complications.

A dietary supplement or increased food intake should be considered if the patient is losing weight or has inadequate weight gain while on this medication.

Renal Impairment:
The major route of elimination of topiramate and its metabolites is via the kidney. Renal elimination is dependent on renal function and is independent of age. Caution should be exercised when treating patients with moderate to severe renal impairment.

As with all patients, the titration schedule should be guided by clinical outcome with the knowledge that subjects with known renal impairment may require longer to reach a steady-state at each dose.

Nephrolithiasis:
There is an increased risk of renal stone formation and associated signs and symptoms such as renal colic, renal pain or flank pain, especially in patients with a predisposition to nephrolithiasis. Adequate hydration whilst using topiramate is very important as it can reduce the risk of developing renal stones. In addition, it may also reduce the risk of heat-related adverse events during exercise and exposure to particularly warm environments (see section 4.8).

Risk factors for nephrolithiasis include prior stone formation, a family history of nephrolithiasis and hypercalciuria. However, none of these risk factors reliably predict stone formation during topiramate treatment. In addition, patients taking other medication associated with nephrolithiasis may be at increased risk.

Ketogenic diets should be avoided whilst on topiramate therapy since they may create a physiological environment that increases the risk of renal stone formation.

Hepatic Impairment:
In hepatically impaired patients, topiramate should be administered with caution as the clearance of topiramate may be decreased.

Acute Myopia and Secondary Angle Closure Formation:
Acute myopia associated with secondary angle closure glaucoma has been reported in both adults and children receiving topiramate. Symptoms typically occur within 1 month of the start of treatment and include decreased visual acuity and/or ocular pain. Ophthalmological findings include bilateral myopia, anterior chamber shallowing, hyperaemia and increased intra-ocular pressure with or without mydriasis. There may be supraciliary effusion resulting in anterior displacement of the lens and iris. Treatment with topiramate should be discontinued as rapidly as is clinically feasible and appropriate measures should be taken to reduce intraocular pressure. If increased intra-ocular pressure is suspected, immediate specialist advice should be sought.

Metabolic Acidosis:
Hyperchloraemic, non-anion gap, metabolic acidosis (i.e. decreased serum bicarbonate below the normal reference range in the absence of respiratory alkalosis) is associated with topiramate treatment. This decrease in serum bicarbonate is due to the inhibitory effect of topiramate on renal carbonic anhydrase. Generally, the decrease in bicarbonate occurs early in treatment although it can occur at any time during treatment. These decreases are usually mild to moderate (average decrease of 4 mmol/L at doses of 100 mg/day or above in adults and at approximately 6 mg/kg/day in paediatric patients). Rarely, patients have experienced decreases to values below 10 mmol/L. Conditions or therapies that predispose to acidosis (such as renal disease, severe respiratory disorders, status epilepticus, diarrhoea, surgery, ketogenic diet, or certain drugs) may be additive to the bicarbonate lowering effects of topiramate.

Chronic metabolic acidosis in paediatric patients can reduce growth rates and may cause osteomalacia (rickets). The effect of topiramate on growth and bone-related sequelae has not been systematically investigated in paediatric or adult populations.

Measurement of serum bicarbonate levels is recommended with topiramate therapy, especially in patients with conditions or therapies that predispose to metabolic acidosis. If metabolic acidosis develops and persists, consideration should be given to reducing the dose or discontinuing topiramate (using dose tapering).

4.5 Interaction with other medicinal products and other forms of interaction

Effects of Other Antiepileptic Drugs on Topiramate:
Phenytoin and carbamazepine decrease the plasma concentration of topiramate. The addition or withdrawal of phenytoin or carbamazepine to topiramate therapy may require an adjustment in dosage of topiramate. This should be done by titrating to clinical effect.

The addition or withdrawal of valproic acid or lamotrigine does not produce clinically significant changes in plasma concentrations of topiramate and, therefore, does not warrant dosage adjustment of topiramate.

The effects of phenobarbital and primidone on topiramate plasma concentrations have not been studied.

Effects of Topiramate on Other Antiepileptic Drugs:
The addition of topiramate to other antiepileptic drugs (carbamazepine, valproic acid, phenobarbital, primidone or lamotrigine) has no clinically significant effect on their steady-state plasma concentrations. In some patients, treatment with topiramate and phenytoin may result in an increase of plasma concentrations of phenytoin. Consequently, it is advised that any patient on phenytoin should have phenytoin levels monitored.

Other Drug Interactions:

Digoxin: In a single-dose study, serum digoxin area under plasma concentration curve (AUC) decreased 12% due to concomitant administration of topiramate. The clinical relevance of this observation has not been established. When topiramate is added or withdrawn in patients on digoxin therapy, serum digoxin should be carefully monitored.

Oral Contraceptives: In a pharmacokinetic interaction study with a combined oral contraceptive (1 mg norethisterone plus 35 mcg ethinyl estradiol) in healthy volunteers, topiramate monotherapy at doses of 50 to 200 mg/day did not affect exposure (AUC) of the oral contraceptive. However, in another study, exposure to ethinyl estradiol was significantly decreased at topiramate doses of 200, 400 and 800 mg/day when given as an adjunctive therapy in patients taking valproic acid. The levels of norethisterone exposure were not affected. The clinical significance of the changes observed is not known. The risk of decreased contraceptive efficacy and increased breakthrough bleeding should be considered in patients taking oestrogen containing contraceptive products in combination with topiramate.

Metformin: A drug-drug interaction study conducted in healthy volunteers evaluated in the steady-state pharmacokinetics of metformin 500 mg bd and topiramate 100 mg bd in plasma when metformin was given alone and when metformin and topiramate were given simultaneously. The results of this study indicated that metformin mean C_{max} and mean AUC_{0-12h} increased by 18% and 25%, respectively, while mean CL/F decreased 20% when metformin was co-administered with topiramate. Topiramate did not affect metformin t_{max}. The clinical significance of the effect of topiramate on metformin pharmacokinetics is unclear. Oral plasma clearance of topiramate appears to be reduced when administered with metformin. The extent of change in the clearance is unknown. The clinical significance of the effect of metformin on topiramate pharmacokinetics is unclear. When topiramate is added or withdrawn in patients on metformin therapy, careful attention should be given to the routine monitoring for adequate control of their diabetic disease state.

Pioglitazone: The steady-state pharmacokinetics of topiramate were not significantly influenced by the concomitant administration of pioglitazone. Topiramate causes a 15% decline in pioglitazone exposure and in the exposure of the active (but less potent) hydroxyl- and keto-metabolites of pioglitazone by 16% and 60%, respectively. The clinical significance of these findings is not known. When topiramate is added or withdrawn in patients on pioglitazone therapy, careful attention should be given to the routine monitoring for adequate control of their diabetic disease state.

Hydrochlorothiazide (HCTZ): HCTZ increases the topiramate exposure by approximately 30%. The clinical relevance of this change is unknown, but the addition of HCTZ to topiramate therapy may require an adjustment of the topiramate dose. The pharmacokinetics of HCTZ is not significantly influenced by the concomitant administration of topiramate. Clinical laboratory results indicate a decrease in serum potassium after topiramate or HCTZ administration, which was greater when HCTZ and topiramate were administered in combination.

Additional Pharmacokinetic Drug Interaction Studies: Topiramate does not change the exposure to amitriptyline. However, topiramate increases the exposure to the active amitriptyline metabolite, nortriptyline, by 20%. The clinical relevance of this is not known. Topiramate does not change the exposure to haloperidol. However, topiramate increases the exposure to the active reduced haloperidol metabolite by 31%. The clinical relevance of this is not known.

Others: Topiramate, when used concomitantly with other agents predisposing to nephrolithiasis, may increase the risk of nephrolithiasis. While using topiramate, agents like these should be avoided since they may create a physiological environment that increases the risk of renal stone formation.

Topiramate inhibits the enzyme CYP 2C19 and may influence other substances, which are metabolised via this enzyme, such as diazepam, imipramin, moklobemid, proguanil, omeprazole. However, this has not been studied.

4.6 Pregnancy and lactation

Pregnancy:
Topiramate, as with other antiepileptic drugs, was teratogenic in mice, rats and rabbits. In rats, topiramate has been shown to cross the placental barrier.

There are no studies of topiramate in pregnant women. Therefore topiramate should only be used during pregnancy if, in the opinion of the physician, the potential benefits outweigh the potential risks to the foetus.

In post marketing experience, hypospadias in male infants exposed *in utero* to topiramate, with or without other anticonvulsants, have been reported. However, a causal relationship with topiramate has not been established.

In pregnancy, if seizure prophylaxis is impaired or discontinued this may bring about a considerable risk for the mother as well as for the foetus, which is probably more severe than the risk of malformation. During pregnancy, antiepileptic drugs should consequently be prescribed with consideration of these risks.

Treatment for prophylaxis of migraine with topiramate is contraindicated in pregnancy and in women of childbearing potential if an effective method of contraception is not used (see Section 4.3).

Lactation:
Topiramate is excreted in human breast milk. Therefore topiramate should only be used during breast feeding if the potential benefits for the mother outweigh the potential risks to the child.

4.7 Effects on ability to drive and use machines

Topiramate, as with other antiepileptic drugs, may adversely affect the central nervous system causing drowsiness and sedation. Patients should be advised to exercise caution when driving or using machines until the individual patients experience with the drug is established.

4.8 Undesirable effects

Monotherapy:
Qualitatively, the types of adverse events observed in monotherapy trials were generally similar to those observed during adjunctive therapy trials (see below). With the exception of paraesthesia and fatigue in adults, these adverse events were reported at similar or lower incidence rates in monotherapy trials.

Adults:
In double-blind monotherapy clinical trials, the most common adverse events, i.e., those occurring in 10% or more of the topiramate-treated adults patients, were paraesthesia, headache, fatigue, dizziness, somnolence, weight decrease, nausea and anorexia.

Adverse events occurring at 5% or more but less than 10% included: insomnia, difficulty with memory, depression, difficulty with concentration/attention, abdominal pain, nervousness, hypoaesthesia, mood problems and anxiety.

Children and Adolescents:
In double-blind monotherapy clinical trials, the most common adverse events, i.e., those occurring in 10% or more of the topiramate-treated children, were headache, anorexia and somnolence.

Adverse events occurring at 5% or more but less than 10% included: difficulty with concentration/attention, fatigue, weight decrease, dizziness, paraesthesia, insomnia and nervousness.

Adjunctive Therapy

Adults:
Since topiramate has most frequently been co-administered with other antiepileptic agents, it is not possible to determine which agents, if any, are associated with adverse effects. In double blind clinical trials, some of which included a rapid titration period, adverse events which occurred with a frequency greater than or equal to 5% and with a higher incidence in the topiramate-treated adult patients than in placebo included: abdominal pain, ataxia, anorexia, asthenia, confusion, difficulty with concentration/attention, difficulty with memory, diplopia, dizziness, fatigue, language problems, nausea, nystagmus, paraesthesia, psychomotor slowing, somnolence, speech disorders/related speech problems, abnormal vision and weight decrease. Topiramate may cause agitation and emotional lability (which may manifest mood problems and nervousness) and depression. Other less common adverse effects include, gait abnormal, aggressive reaction, apathy, cognitive problems, co-ordination problems, leucopoenia, psychotic symptoms (such as hallucinations) and taste perversion.

Isolated cases of venous thromboembolic events have been reported. A causal association with the drug has not been established.

Reports of increases in liver enzymes in patients taking topiramate with and without other medications have been received. Isolated reports have been received of hepatitis and hepatic failure occurring in patients taking multiple medications while being treated with topiramate.

Children and Adolescents:
In double blind clinical trials, some of which included a rapid titration period, adverse events which occurred with a frequency greater than or equal to 5% and with a higher incidence in the topiramate-treated children/adolescents than in placebo included: somnolence, anorexia, fatigue, insomnia, nervousness, personality disorder (behaviour problems), difficulty with concentration/attention, aggressive reaction, weight decrease, gait abnormal, mood problems, ataxia, saliva increase, nausea, difficulty with memory, hyperkinesia, dizziness, speech disorders/related speech problems and paraesthesia.

Adverse events that occurred less frequently but were considered potentially medically relevant included: emotional lability, agitation, apathy, cognitive problems, psychomotor slowing, confusion, hallucination, depression and leucopoenia.

General:
Topiramate increases the risk of nephrolithiasis especially in those with a predisposition (see section 4.4). In the initial clinical trials none of the calculi required open surgery and three-quarters were passed spontaneously. Most of the patients opted to continue treatment despite nephrolithiasis.

Reduced sweating has been rarely reported. The majority of cases have been in children and some have been associated with flushing and raised temperature.

Acute myopia associated with secondary acute angle closure glaucoma has been reported rarely (See section 4.4).

Metabolic acidosis has been reported rarely (see Section 4.4).

Suicidal ideation or attempts have been reported rarely.

Very rarely, reports have been received for bullous skin and mucosal reactions (including erythema multiforme, pemphigus, Stevens-Johnson syndrome and toxic epidermal necrolysis). The majority of these reports have occurred in patients taking other medications also associated with bullous skin and mucosal reactions.

4.9 Overdose

Signs and Symptoms:
Ingestion of topiramate of between 6 g and 40 g has been reported in a few patients. Signs and symptoms reported include: headache, agitation, drowsiness, lethargy, metabolic acidosis and hypokalemia. However, the clinical consequences were generally not severe.

A patient who ingested a dose of topiramate calculated to be 96 – 110 g was admitted to hospital with coma lasting 20-24 hours but made a full recovery after 3 to 4 days.
Patient deaths have been reported following polydrug overdoses involving topiramate.

Treatment:
General supportive measures are indicated. In acute topiramate overdose where the ingestion is recent, the gastro-intestinal tract should be emptied by gastric lavage or induction of emesis. Activated charcoal has been shown to absorb topiramate *in vitro*. Haemodialysis has been shown to be an effective means of removing topiramate from the body. The patient should be well hydrated.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other antiepileptics, ATC code: N03 AX11

Topiramate is a novel antiepileptic agent classified as a sulphamate-substituted monosaccharide. Three pharmacological properties of topiramate have been identified that may contribute to its anticonvulsant activity.

Topiramate reduces the frequency at which action potentials are generated when neurones are subjected to a sustained depolarisation indicative of a state-dependent blockade of voltage-sensitive sodium channels.

Topiramate enhances the activity of GABA at some types of GABA receptors but has no apparent effect on the activity of N-methyl-D-aspartate (NMDA) at the NMDA receptor subtype.

Topiramate weakly antagonises the excitatory activity of the kainite/AMPA subtype of glutamate.

In addition, topiramate inhibits some isoenzymes of carbonic anhydrase. This effect is not thought to be a major component of topiramate antiepileptic activity.

5.2 Pharmacokinetic properties

Topiramate is rapidly and well absorbed. Recovery of radioactivity from urine indicates that the mean extent of absorption of a 100 mg dose of ^{14}C topiramate was at least 81%. There is no clinically significant effect of food on topiramate. The mean apparent volume of distribution has been measured as 0.55 – 0.81 l/kg for single doses up to 1200 mg. There is an effect of gender on the volume of distribution with the distribution volume in females being approximately 50% of that in males. Topiramate is known to bind to erythrocytes but the binding is likely to be saturated at 3 – 10 μg/mL. Generally, 13 – 17% of topiramate is bound to plasma proteins.

Topiramate is moderately metabolized (approximately 20%) in healthy volunteers. Topiramate metabolism may increase by up to 50% in patients receiving concomitant antiepileptic therapy with known inducers of drug metabolising enzymes. Six metabolites have been isolated, characterised and identified from plasma, urine and human faeces. Two metabolites, retaining most of the structure of topiramate, were tested and found to have little or no anticonvulsive activity.

In humans the major route of elimination of topiramate and its metabolites is via the kidney. Renal clearance is approximately 18 mL/min. This is less than expected and indicates a tubular reabsorption of topiramate. Overall, following oral administration in humans, plasma clearance is approximately 20 to 30 mL/min.

The pharmacokinetics of topiramate are linear with plasma clearance remaining constant and area under the plasma concentration curve increasing in a dose-proportional manner over a 100 mg to 400 mg single oral dose range in healthy subjects. Patients with normal renal function may take 4 to 8 days to reach steady-state plasma concentrations whilst patients with moderate to severe renal impairment may take 10 – 15 days. The mean maximal plasma concentration (C_{max}) in healthy volunteers following multiple, twice daily oral doses of 100 mg was approximately 7 μg/mL. Following administration of multiple doses of 50 mg and 100 mg topiramate twice daily, the mean plasma half-life was approximately 21 hours.

The plasma and renal clearance of topiramate are decreased in patients with impaired renal function. At a creatine clearance of less than 60 mL/min, the plasma clearance is 2 times lower and at a creatine clearance of less than 30 ml/min, 2 –4 times lower.

Plasma clearance of topiramate in elderly patients, in the absence of underlying renal disease, is unchanged.

Plasma clearance of topiramate is decreased in patients with moderate to severe hepatic impairment.

The pharmacokinetics of topiramate in children, as in adults receiving add-on therapy, are linear, with clearance independent of dose and steady-state plasma concentrations increasing in proportion to dose. Children, however, have a higher clearance and shorter elimination half-life. Consequently, the plasma concentrations of topiramate for the same mg/kg dose may be lower in children compared to adults. As in adults, hepatic enzyme inducing antiepileptic drugs decrease steady-state plasma concentrations.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of repeated dose toxicity and genotoxicity.

As with other antiepileptic drugs, topiramate was teratogenic in mice, rats and rabbits. Overall numbers of foetal malformations in mice were increased for all drug-treated groups, but no significant differences or dose-response relationships were observed for overall or specific malformations, suggesting that other factors such as maternal toxicity may be involved.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet Core:
Microcrystalline cellulose
Povidone K29-32
Silica, colloidal anhydrous
Sodium starch glycolate (type A)
Magnesium stearate
Film-coat:
Opadry White YS-1-7003 containing
Titanium dioxide E171
Hypromellose E464
Macrogol 400
Polysorbate 80

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

2 years

6.4 Special precautions for storage

Store in the original package

6.5 Nature and contents of container

Aluminium foil blisters in pack sizes of 60 tablets per pack

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Generics [UK] Limited
12 Station Close
Potters Bar
Hertfordshire EN6 1TL
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 405/54/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 25th January 2008

10 DATE OF REVISION OF THE TEXT

September 2008