SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Glimepiride 1mg Tablets
Glimepiride 2mg Tablets
Glimepiride 3mg Tablets
Glimepiride 4mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Glimepiride 1mg
Excipient with known effect: Also contains lactose monohydrate 74.15mg

Each tablet contains Glimepiride 2mg
Excipient with known effect: Also contains lactose monohydrate 148.20mg

Each tablet contains Glimepiride 3mg
Excipient with known effect: Also contains lactose monohydrate 147.30mg

Each tablet contains Glimepiride 4mg
Excipient with known effect: Also contains lactose monohydrate 146.30mg

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Tablet.

Pink coloured, elongated with notch in centre, flat bevelled edged, uncoated tablets with “B” & “L” debossed on either side of breakline on one side & only breakline on other side.

Green coloured, elongated with notch in centre, flat bevelled edged, uncoated tablets with “B” & “L” debossed on either side of breakline on one side & only breakline on other side.

Light yellow coloured, elongated with notch in centre, flat bevelled edged, uncoated tablets with “B” & “L” debossed on either side of breakline on one side & only breakline on other side.

Blue coloured, elongated with notch in centre, flat bevelled edged, uncoated tablets with “B” & “L” debossed on either side of breakline on one side & only breakline on other side.

The breakline is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Glimepiride is indicated for the treatment of type 2 diabetes mellitus, when diet, physical exercise and weight reduction alone are not adequate.

4.2 Posology and Method of Administration

Posology

The basis for successful treatment of diabetes is a good diet, regular physical activity, as well as routine checks of blood and urine. Tablets or insulin cannot compensate if the patient does not keep to the recommended diet.

Dosage is determined by the results of blood and urinary glucose determinations.

The starting dose is 1 mg glimepiride per day. If good control is achieved this dosage should be used for maintenance therapy.

For the different dosage regimens appropriate strengths are available.

If control is unsatisfactory the dosage should be increased, based on the glycaemic control, in a stepwise manner with an interval of about 1 to 2 weeks between each step, to 2, 3 or 4 mg glimepiride per day.

A dosage of more than 4 mg glimepiride per day gives better results only in exceptional cases. The maximum recommended dose is 6 mg glimepiride per day.

In patients not adequately controlled with the maximum daily dose of metformin, concomitant glimepiride therapy can be initiated.

While maintaining the metformin dose, glimepiride therapy is started with a low dose, and is then titrated up depending on the desired level of metabolic control up to the maximum daily dose. The combination therapy should be initiated under close medical supervision.

In patients not adequately controlled with the maximum daily dose of Glimepiride, concomitant insulin therapy can be initiated if necessary. While maintaining the glimepiride dose, insulin treatment is started at low dose and titrated up depending on the desired level of metabolic control. The combination therapy should be initiated under close medical supervision.

Normally a single daily dose of glimepiride is sufficient. It is recommended that this dose be taken shortly before or during a substantial breakfast or – if none is taken - shortly before or during the first main meal.

If a dose is forgotten, this should not be corrected by increasing the next dose.

If a patient has a hypoglycaemic reaction on 1 mg glimepiride daily, this indicates that there is a possibility of diabetes control in the patient by diet alone.

During treatment, as an improvement in control of diabetes is associated with higher insulin sensitivity, glimepiride requirements may fall. To avoid hypoglycaemia timely dose reduction or cessation of therapy must therefore be considered. Change in dosage may also be necessary, if there are changes in weight or lifestyle of the patient, or other factors that increase the risk of hypoglycaemia or hyperglycaemia.

Switch over from other oral hypoglycaemic agents to Glimepiride:
A switch over from other oral hypoglycaemic agents to Glimepiride can generally be done. For the switch over to Glimepiride the strength and the half life of the previous medication has to be taken into account. In some cases, especially in antidiabetics that have a long half-life (e.g. chlorpropamide), a wash out period of a few days is advisable in order to minimise the risk of hypoglycaemic reactions due to the additive effect.

The recommended starting dose is 1 mg glimepiride per day. Based on the response the glimepiride dosage may be increased stepwise, as indicated earlier.

Switch over from Insulin to Glimepiride:
In exceptional cases, where type 2 diabetic mellitus patients are regulated on insulin, a changeover to Glimepiride may be indicated. The transition should be undertaken under close medical supervision.

Special Populations

Patients with renal or hepatic impairment:
See section 4.3

Paediatric population:
There are no data available on the use of glimepiride in patients under 8 years of age. For children aged 8 to 17 years, there are limited data on glimepiride as monotherapy (see sections 5.1 and 5.2).

The available data on safety and efficacy are insufficient in the paediatric population and therefore such use is not recommended.

Method of administration
For oral administration.

Tablets should be swallowed, without chewing, with some liquid.

4.3 Contraindications

Glimepiride is contraindicated in patients with the following conditions:

- Hypersensitivity to glimepiride, other sulphonylureas or sulphonamides or to any of the excipients listed in section 6.1
- insulin dependent diabetes
- diabetic coma
- ketoacidosis
- severe renal or hepatic function disorders. In case of severe impaired renal or hepatic function disorders, a change over to insulin is required.

4.4 Special Warnings and Special Precautions for Use

Glimepiride must be taken shortly before or during a meal.

When meals are taken at irregular hours or skipped altogether, treatment with Glimepiride may lead to hypoglycaemia. Possible symptoms of hypoglycaemia include: headache, severe hunger, nausea, vomiting, weakness, drowsiness, sleep disturbances, restlessness, aggression, impaired concentration, wakefulness and reaction time, depression, confusion, speech and visual disorders, aphasia, tremor, paresis, sensory disorders, dizziness, inability to care for oneself, loss of self-control, delirium, cerebral convulsions, nystagmus, somnolence and loss of consciousness up to and including coma, shallow breathing and bradycardia.

In addition, signs of adrenergic counter-regulation may be present such as sweating, clammy skin, anxiety, tachycardia, hypertension, palpitations, angina pectoris and cardiac arrhythmias.

The clinical picture of a severe hypoglycaemic attack may resemble that of a stroke.

Symptoms can almost always be promptly controlled by immediate intake of carbohydrates (sugar). Artificial sweeteners have no effect.

It is known, from other sulphonylureas that, despite initially successful countermeasures, hypoglycaemia may recur.

Severe hypoglycaemia or prolonged hypoglycaemia, only temporarily controlled by the usual amounts of sugar, require immediate medical treatment and occasionally hospitalisation.

Factors favouring hypoglycaemia include:

- unwillingness or (more commonly in elderly patients) inability of the patient to cooperate,
- malnutrition, irregular meal or incomplete meals or periods of fasting,
- alterations in diet,
- imbalance between physical exertion and carbohydrate intake,
- consumption of alcohol, especially in combination with skipped meals,
- impaired renal function,
- serious hepatic impairment,
- overdose with Glimepiride,
- specific unregulated endocrine system factors affecting carbohydrate metabolism or counter regulation of hypoglycaemia (such as, for example, in certain disorders of thyroid function and in insufficiency of the anterior pituitary or adrenal cortex),
- concurrent administration of certain other medicines (see section 4.5).

Treatment with Glimepiride requires regular monitoring of glucose levels in blood and urine. In addition, determination of the proportion of glycosylated haemoglobin is recommended.

Regular hepatic and haematological monitoring (especially leucocytes and thrombocytes) are required during treatment with Glimepiride.

In stress-situations (e.g. accidents, acute operations, infections with fever, etc.) a temporary switch to insulin may be indicated.

No experience has been gained concerning the use of Glimepiride in patients with severe impairment of liver function or dialysis patients. In patients with severe impairment of renal or liver function change over to insulin is indicated.

Treatment of patients with G6PD-deficiency with sulfonylurea agents can lead to hemolytic anaemia. Since glimepiride belongs to the class of sulfonylurea agents, caution should be used in patients with G6PD deficiency and a non-sulfonylurea alternative should be considered.

Important information regarding the excipient of this medicine

Lactose: This medicinal product contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Sodium: This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

If Glimepiride is taken simultaneously with certain other medicines, both undesired increases and decreases in the hypoglycaemic action of glimepiride can occur. For this reason, other medicines should only be taken with the knowledge (or at the prescription) of the doctor.

Glimepiride is metabolized by cytochrome P450 2C9 (CYP2C9). Its metabolism is known to be influenced by concomitant administration of CYP2C9 inducers (e.g. rifampicin) or CYP2C9 inhibitors (e.g. fluconazole).

Results from an in-vivo interactions study reported in literature show that glimepiride AUC is increased approximately 2-fold by fluconazole, one of the most potent CYP2C9 inhibitors.

Based on the experience with Glimepiride and with other sulphonylureas the following interactions have to be mentioned.

Potentiation of the blood-glucose-lowering effect and, thus, in some instances hypoglycaemia may occur when one of the following drugs is taken, for example:

- Phenylbutazone, azapropazone and oxyphenbutazone

- Insulin and other oral antidiabetic products, such as metformin,
- Salicylic and para-aminosalicylic acid,
- Anabolic steroids and male hormones,
- Chloramphenicol, certain long-acting sulfonamides, tetracyclines, quinolone antibiotics and clarithromycin,
- Coumarin-type anticoagulants,
- Fenfluramine,
- Disopyramide,
- Fibrates,
- ACE inhibitors,
- Fluoxetine, MAO-inhibitors,
- Allopurinol, probenecid, sulphinpyrazone,
- Sympatholytics,
- Cyclophosphamides, trophosphamides and ifosphamides,
- Miconazole, fluconazole,
- Tritoqualine,
- Pentoxifylline (high dose parenteral).

Decrease in hypoglycaemic activity and consequently increased blood sugar levels may occur when any of the following medicinal products are administered concomitantly, e.g.:

- Oestrogens and progestogens,
- Salt diuretics, thiazide diuretics,
- Thyroid hormones, glucocorticoids,
- Phenothiazine derivatives, chlorpromazine,
- Adrenaline and sympathomimetics,
- Nicotinic acid (in high doses) and nicotinic acid derivatives,
- Laxatives (long term use),
- Phenytoin, diazooxides,
- Glucagon, barbiturates and rifampicin,
- Acetazolamide.

H_2 antagonists, beta-receptors blockers, clonidine and reserpine may cause an increase or decrease in hypoglycaemic activity.

Under the influence of sympatholytic medicinal products, such as beta-receptor blockers, clonidine, guanethidine and reserpine, the signs of adrenergic counter regulation to hypoglycaemia may be reduced or absent.

Alcohol intake may potentiate or weaken the hypoglycaemic effect of glimepiride in an unpredictable fashion.

Glimepiride may either potentiate or weaken the effects of coumarin derivatives.

Colesevelam binds to glimepiride and reduces glimepiride absorption from the gastro-intestinal tract. No interaction was observed when glimepiride was taken at least 4 hours before colesevelam. Therefore, glimepiride should be administered at least 4 hours prior to colesevelam.

4.6 Fertility, pregnancy and lactation

Pregnancy

Risk associated with diabetes

Abnormal blood glucose levels during pregnancy are associated with a higher incidence of congenital abnormalities and perinatal mortality. So, the blood glucose level must be closely monitored during pregnancy in order to avoid the teratogenic risk. The use of insulin is required under such circumstances. Patients who consider pregnancy should inform their physician.

Risk associated with glimepiride

There are no adequate data from the use of glimepiride in pregnant women. Animal studies have shown reproductive toxicity which likely was related to the pharmacologic action (hypoglycaemia) of glimepiride (see section 5.3).

Consequently, glimepiride should not be used during the whole pregnancy. In case of treatment by glimepiride, if the patient plans to become pregnant or if a pregnancy is discovered, the treatment should be switched as soon as possible to insulin therapy.

Breast-feeding

Excretion in breastmilk is not known. Glimepiride is excreted in rat milk. As other sulfonylureas are excreted in breast milk and because there is a risk of hypoglycaemia in nursing infants, breast-feeding is advised against during treatment with glimepiride.

4.7. Effects on Ability to Drive and Use Machines

No studies on the effects on the ability to drive and use machines have been performed.

The patient's ability to concentrate and react may be impaired as a result of hypoglycaemia or hyperglycaemia or, for example, as a result of visual impairment. This may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or operating machinery).

Patients should be advised to take precautions to avoid hypoglycaemia whilst driving. This is particularly important in those who have reduced or absent awareness of the warning symptoms of hypoglycaemia or have frequent episodes of hypoglycaemia. It should be considered whether it is advisable to drive or operate machinery in these circumstances.

4.8 Undesirable effects

The following convention has been used for classification of the frequency of undesirable effects:

Very common	≥1/10
Common	≥1/100 to <1/10
Uncommon	≥1/1000 to <1/100
Rare	≥1/10,000 to <1/1000
Very rare	<1/10,000

Not known (cannot be estimated from the available data)

The following undesirable effects are based on experience with Glimepiride and other sulfonylureas.

Blood and lymphatic system disorders
Rare: thrombocytopenia, leukopenia, granulocytopenia, agranulocytosis, erythropenia, haemolytic anaemia and pancytopenia, which are in general reversible upon discontinuation of medication.

Not known: severe thrombocytopenia with platelet count less than 10,000/µl and thrombocytopenic purpura

Immune system disorders
Very rare: leukocytoclastic vasculitis, mild hypersensitivity reactions that may progress to serious reactions with dyspnoea, drop in blood pressure and sometimes shock.

Not known: A Cross-allergic reaction is possible wit sulfonylureas, sulfonamides or related substances is possible.

Metabolism and nutrition disorders
Rare: hypoglycaemia.

These hypoglycaemic reactions mostly occur immediately, may be severe and are not always easy to correct. The occurrence of such reactions depends, as with other hypoglycaemic therapies, on individual factors such as dietary habits and dosage (see further under section 4.4).

Eye disorders
Not known: Visual disturbances, transient, may occur especially on initiation of treatment, due to changes in blood glucose levels.

Gastrointestinal disorders
Very rare: nausea, vomiting, diarrhoea, abdominal distension, abdominal discomfort and abdominal pain, which seldom lead to discontinuation of therapy.
Rare: dysgeusia.

Hepato-biliary disorders
Not known: Hepatic enzymes increased.
Very rare: hepatic function abnormal (e.g. with cholestasis and jaundice), hepatitis and hepatic failure.

Skin and subcutaneous tissue disorders
Not known: Hypersensitivity reactions of the skin may occur as pruritus, rash, urticaria and photosensitivity.
Rare: alopecia.

Investigations
Very rare: blood sodium decrease.
Rare: weight gain.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms
After ingestion of an overdosage hypoglycaemia may occur, lasting from 12 to 72 hours, and may recur after initial recovery. Symptoms may not be present for up to 24 hours after ingestion. In general observation in hospital is recommended. Nausea, vomiting and epigastric pain may occur. The

hypoglycaemia may in general be accompanied by neurological symptoms like restlessness, tremor, visual disturbances, co-ordination problems, sleepiness, coma and convulsions.
Acute overdose as well as long-term treatment with very high dose glimepiride can lead to severe, life-threatening hypoglycaemia.

Confrontation
Once an overdose with Glimepiride is detected, a doctor should be notified without delay. The patient should immediately take sugar, if possible, in the form of glucose, unless the doctor has already taken responsibility for treating the overdose. Careful monitoring is necessary until the doctor is sure that the patient is out of danger. It must be remembered that hypoglycemia may recur after initial recovery.

In case of a mild episode of hypoglycaemia, treatment initially consists of taking glucose by mouth. Severe hypoglycemic reactions require immediate treatment.

Major overdoses with Glimepiride and severe reactions with symptoms such as loss of consciousness or other serious neurological disorders are medical emergencies and require immediate treatment. It is recommended to be admitted to hospital in an intensive care unit.

Management
Treatment primarily consists of preventing absorption by inducing vomiting and then drinking water or lemonade with activated charcoal (adsorbent) and sodium-sulphate (laxative). If large quantities have been ingested, gastric lavage is indicated, followed by activated charcoal and sodium-sulphate. In case of (severe) overdosage hospitalisation in an intensive care department is indicated. Start the administration of glucose as soon as possible, if necessary by a bolus intravenous injection of 50 ml of a 50% solution, followed by an infusion of a 10% solution with strict monitoring of blood glucose. Further treatment should be symptomatic.

In severe cases with a prolonged course, hypoglycemia, or the risk of return to hypoglycemia, may persist for several days.

In particular when treating hypoglycaemia due to accidental intake of Glimepiride in infants and young children, the dose of glucose given must be carefully controlled to avoid the possibility of producing dangerous hyperglycaemia. Blood glucose should be closely monitored.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Blood sugar lowering drugs, excluding insulins:Sulphonylureas.
ATC Code: A10B B12.

Glimepiride is an oral, active hypoglycaemic substance belonging to the sulphonylurea group. It may be used in cases of non-insulin dependent diabetes mellitus.
Mechanism of action
Glimepiride acts mainly by stimulating insulin release from pancreatic beta cells.

As with other sulphonylureas, this action is based on an increase of responsiveness of the pancreatic beta cells to the physiological glucose stimulus. In addition, glimepiride seems to have pronounced extrapancreatic effects, which also postulated for other sulphonylureas.

Insulin release:
Sulfonylureas regulate insulin secretion by closing the ATP-sensitive potassium channel in the beta cell membrane. Closing the potassium channel induces depolarisation of the beta cell and results through the opening of calcium channels in an increased influx of calcium into the cell.

This leads to insulin release through exocytosis.

Glimepiride binds with a high exchange rate to a beta cell membrane protein, which is associated with the ATP-sensitive potassium channel, but which is different from the usual sulfonylurea binding site.

Extrapancreatic activity:
The extrapancreatic effects are for example an improvement of the sensitivity of the peripheral tissue for insulin and a decrease of the insulin uptake by the liver.

The uptake of glucose from blood into peripheral muscle and adipose tissues occurs via special transport proteins, located in the cells membrane. The transport of glucose in these tissues is the rate limiting step in the use of glucose. Glimepiride increases very rapidly the number of active glucose

transport molecules in the plasma membranes of muscle cells and adipose tissue cells, resulting in stimulated glucose uptake.

Glimepiride increases the activity of the glycosyl-phosphatidylinositol-specific phospholipase C, which may be correlated with the drug-induced lipogenesis and glycogenesis in isolated fat cells and muscle cells.

Glimepiride inhibits the glucose production in the liver by increasing the intracellular concentration of fructose-2,6‑disphosphate, which in its turn inhibits the neoglycogenesis.

Generally

In healthy persons, the minimum effective oral dose is approximately 0.6 mg. The effect of glimepiride is dose-dependent and reproducible. The physiological response to acute physical exercise, reduction of insulin secretion, is still present under glimepiride.

There was no significant difference in effect regardless of whether the drug was given 30 minutes or immediately before a meal. In diabetic patients, good metabolic control over 24 hours can be achieved with a single daily dose.

Although the hydroxy metabolite of glimepiride caused a small but significant decrease in serum glucose in healthy persons, it accounts for only a minor part of the total drug effect.

Combination therapy with metformin

Improved metabolic control for concomitant glimepiride therapy compared to metformin alone in patients not adequately controlled with the maximum daily dosage of metformin has been shown in one study.

Combination therapy with insulin

Data from combination therapy with insulin are limited. In patients not adequately controlled with the maximum dosage of glimepiride, concomitant insulin therapy can be initiated. In two studies, the combination achieved the same improvement in metabolic control as insulin alone; however, a lower average dose of insulin was required in combination therapy.

Special populations

Paediatric population

An active controlled clinical trial (glimepiride up to 8 mg daily or metformin up to 2,000 mg daily) lasting 24 weeks was performed in 285 children (8-17 years of age) with type 2 diabetes.

Both glimepiride and metformin exhibited a significant decrease from baseline in HbA_{1c} (glimepiride -0.95 (se 0.41); metformin -1.39 (se 0.40)). However, glimepiride did not achieve the criteria of non-inferiority to metformin in mean change from baseline of $HbA_{1c.}$

The difference between treatments was 0.44% in favour of metformin. The upper limit (1.05) of the 95% confidence interval for the difference was not below the 0.3% non-inferiority margin.

Following glimepiride treatment, there were no new safety concerns noted in children compared to adult patients with type 2 diabetes mellitus. No long-term efficacy and safety data are available in paediatric patients.

5.2. Pharmacokinetic Properties

Absorption
The bioavailability of glimepiride after oral administration is complete. Food intake has no relevant influence on absorption, only absorption rate is slightly diminished. Maximum serum concentrations (C_{max}) are reached approx. 2.5 hours after oral intake (mean 0.3 µg/ml during multiple dosing of 4 mg daily) and there is a linear relationship between dose and both C_{max} and AUC (area under the time/concentration curve).

Distribution
Glimepiride has a very low distribution volume (approx. 8.8 litres) which is roughly equal to the albumin distribution space, high protein binding (>99%), and a low clearance (approx. 48 ml/min).

In animals, glimepiride is excreted in milk. Glimepiride is transferred to the placenta. Passage of the blood brain barrier is low.

Biotransformation and elimination
Mean dominant serum half-life, which is of relevance for the serum concentrations under multiple-dose conditions, is about 5 to 8 hours. After high doses, slightly longer half-lives were noted.

After a single dose of radiolabelled glimepiride, 58% of the radioactivity was recovered in the urine, and 35% in the faeces. No unchanged substance was detected in the urine. Two metabolites ‑most probably resulting from hepatic metabolism - (the main enzyme being CYP2C9) were identified both in urine and faeces: the hydroxy derivative and the carboxy derivative. After oral

administration of glimepiride, the terminal half-lives of these metabolites were 3 to 6 and 5 to 6 hours respectively.

Comparison of single and multiple once-daily dosing revealed no significant differences in pharmacokinetics, and the intraindividual variability was very low. There was no relevant accumulation.

Special Population

Pharmacokinetics were similar in males and females, as well as in young and elderly (above 65 years) patients. In patients with low creatinine clearance, there was a tendency for glimepiride clearance to increase and for average serum concentrations to decrease, most probably resulting from a more rapid elimination because of lower protein binding. Renal elimination of the two metabolites was impaired. Overall no additional risk of accumulation is to be assumed in such patients.

Pharmacokinetics in five non-diabetic patients after bile duct surgery were similar to those in healthy persons.

Paediatric population
A non-fasting study investigating the pharmacokinetics, safety, and tolerability of a 1 mg single dose of glimepiride in 30 paediatric patients (4 children aged 10-12 years and 26 children aged 12-17 years) with type 2 diabetes showed mean $AUC_{(0\text{-last})}$, Cmax and $t_{1/2}$ similar to that previously observed in adults.

5.3 Preclinical safety data

Preclinical effects observed occurred at exposures sufficiently in excess of the maximum human exposure as to indicate little relevance to clinical use, or were due to the pharmacodynamic action (hypoglycaemia) of the compound. This finding is based on conventional safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenicity, and reproduction toxicity studies. In the latter (covering embryotoxicity, teratogenicity and developmental toxicity), adverse effects observed were considered to be secondary to the hypoglycaemic effects induced by the compound in dams and in offspring.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Lactose monohydrate,

Sodium starch glycollate,
Povidone K 30
Microcrystalline cellulose
Colloidal silicon dioxide
Magnesium stearate

(For PL 17907-0106)
Red ferric oxide (E172)

(For PL 17907-0107)
Yellow ferric oxide (E172)
Indigo carmine lake (E132)

(For PL 17907-0108)
Yellow ferric oxide (E172)

(For PL 17907-0109)
Indigo carmine lake (E132)

6.2 Incompatibilities
Not applicable.

6.3. Shelf Life
3 years

6.4 Special precautions for storage
Do not store above 25ºC. Store in the original package

6.5 Nature and contents of container
Aluminium / PVC blister. Pack sizes of 10, 20, 30, 60 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal
No special requirements

7 MARKETING AUTHORISATION HOLDER

Bristol Laboratories Limited
Unit 3, Canalside,
Northbridge, Berkhamsted,
Hertfordshire HP4 1EG,
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 17907/0106
PL 17907/0107
PL 17907/0108
PL 17907/0109

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

22/11/2007

10 DATE OF REVISION OF THE TEXT

09/07/2025