AUSTRALIAN PRODUCT INFORMATION

GLICLAZIDE MR VIATRIS

(gliclazide) 30 mg modified release tablets

1 NAME OF THE MEDICINE

Gliclazide

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each modified release tablet contains 30 mg of gliclazide as the active ingredient.

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

Gliclazide 30 mg modified release tablets: A white to off-white, oblong, biconvex tablet debossed with '**M**' on one side of the tablet and '**GL 30**' on the other side.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Type II diabetes in association with dietary measures when dietary measures alone are inadequate to control blood glucose.

During controlled clinical trials in patients with type II diabetes, a modified release formulation of gliclazide (30 mg - 120 mg), taken as a single daily dose, was shown to be effective long term in controlling blood glucose levels, based on monitoring of HbA1c.

4.2 DOSE AND METHOD OF ADMINISTRATION

For adult use only.

GLICLAZIDE MR VIATRIS 30 mg tablets do not have a break bar and therefore should not be broken.

So that the modified release properties of the product can be maintained, GLICLAZIDE MR VIATRIS tablets should not be chewed or crushed.

GLICLAZIDE MR VIATRIS should be taken with food because there is an increased risk of hypoglycaemia if a meal is taken late, if an inadequate amount of food is consumed or if the food is low in carbohydrate. It is recommended that the medication be taken at breakfast time. If a dose is forgotten, the dose taken on the next day should not be increased.

A single daily dose provides an effective blood glucose control. The daily dose may vary from 30 mg to 120 mg taken orally, once daily. The initial recommended dose is 30 mg daily, even in elderly patients (≥ 65 years). It should not exceed 120 mg.

As with all hypoglycaemic agents, the dose should be titrated according to the individual patient's response. Titration should be carried out in steps of 30 mg, according to the fasting blood glucose response. Each step should last for at least two weeks.

Previously untreated patients should commence with a dose of 30 mg and will benefit from dose titration until the appropriate dose is reached.

GLICLAZIDE MR VIATRIS 30 mg tablets can replace gliclazide 80 mg tablets, tablet for tablet, for doses of one to four tablets per day.

GLICLAZIDE MR VIATRIS tablets may be used to replace other antidiabetic treatments without any transitional period. If a patient is switched from a hypoglycaemic sulfonylurea with a prolonged half-life he/she should be carefully monitored (for one to two weeks) in order to avoid hypoglycaemia due to possible residual effects of the previous therapy.

GLICLAZIDE MR VIATRIS tablets may be given in combination with biguanides, alpha glucosidase inhibitors or insulin.

Elderly patients

The efficacy and tolerance of the modified release formulation of gliclazide (30 mg - 120 mg) has been confirmed in clinical trials in patients over 65 years who were given the same dosage regimen as the general population. The dosage is therefore identical to that recommended for adults under the age of 65 years.

Renal impairment

The efficacy and tolerance of the modified release formulation of gliclazide (30 mg - 120 mg) has been confirmed in clinical trials of patients with mild to moderate renal failure (creatinine clearance of between 15 and 80 mL/min) who were given the same dosage regimen as the general population. No dosage adjustment is therefore required in patients with mild to moderate renal impairment.

Use of GLICLAZIDE MR VIATRIS tablets in patients with severe renal impairment is contraindicated (see **Section 4.3 CONTRAINDICATIONS**).

4.3 CONTRAINDICATIONS

- hypersensitivity to gliclazide, other sulfonylureas, sulfonamides, or to any of the excipients.
- Type I diabetes, diabetic keto-acidosis, diabetic pre-coma and coma.
- severe renal or hepatic impairment: in these cases the use of insulin is recommended.
- treatment with miconazole (see **Section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS**)
- pregnancy and lactation (see **Section 4.6 FERTILITY, PREGNANCY AND LACTATION** – **Use in pregnancy** and **Use in lactation**).

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

The risks of hypoglycaemia, together with its symptoms, treatment and conditions that predispose to its development, should be explained to the patient and to family members. The patient should be informed of the importance of following dietary advice, of taking regular exercise, and of regular monitoring of blood glucose levels.

Hypoglycaemia

Hypoglycaemia may occur following administration of sulfonylureas. Rarely cases may be severe and prolonged. This may involve hospitalisation and glucose infusion may need to be continued for several days.

Careful selection of patients and of the dose used, as well as provision of adequate information to the patient are necessary to avoid hypoglycaemic episodes.

The following factors may increase the risk of hypoglycaemia:

- patient does not follow the doctor’s treatment advice (particularly elderly patients)
- malnutrition or debilitated patients

- irregular mealtimes, skipping meals, periods of fasting or dietary changes
- imbalance between physical exercise and carbohydrate intake
- renal impairment
- severe hepatic impairment
- overdose of anti-diabetic agents
- certain endocrine disorders: thyroid disorders, hypopituitarism and adrenal impairment, concomitant administration of certain other medicines (see **Section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS**).

Gliclazide should only be prescribed if the patient is likely to have a regular food intake (including breakfast). It is important to have a regular carbohydrate intake due to the increased risk of hypoglycaemia if a meal is delayed, an inadequate amount of food is consumed or the food is low in carbohydrate. Hypoglycaemia is more likely to occur during periods of low-calorie diet, following prolonged or strenuous exercise, following alcohol intake or during treatment with a combination of hypoglycaemic agents.

Since the effects of oral hypoglycaemic agents on the vascular changes and other long-term sequelae of diabetes mellitus are not fully known, patients receiving such medicinal products must be closely observed for both short and long-term complications. Periodic assessment of cardiovascular, ophthalmic, renal, and hepatic status is advisable.

Poor blood glucose control

Blood glucose control in treated patients may be affected by St. John's Wort (Hypericum perforatum) preparations (see **Section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS**), fever, trauma, infection or surgical intervention. It may be necessary to discontinue treatment and to administer insulin in these cases.

The efficacy of oral antidiabetic agents often decreases in the long term. This may be due to progression in the severity of the diabetes, or to a reduced response to treatment. This phenomenon is known as secondary failure and should be distinguished from primary failure, when the drug is ineffective as first-line treatment. However, before classifying the patient as a secondary failure, dose adjustment and reinforcement of dietary measures should be considered.

If a loss of adequate blood glucose-lowering response to gliclazide is detected, the medicine should be discontinued.

Unstable blood glucose level (Dysglycaemia)

Disturbances in blood glucose, including hypoglycaemia and hyperglycaemia have been reported, in diabetic patients receiving concomitant treatment with fluoroquinolones, especially in elderly patients. Indeed, careful monitoring of blood glucose is recommended in all patients receiving gliclazide and a fluoroquinolone at the same time.

Glucose-6-phosphate dehydrogenase deficiency (G6PD)

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

Use in renal and hepatic impairment

Severe renal or hepatic impairment may affect the distribution of gliclazide and hepatic impairment may also reduce the capacity for neoglucogenesis. These two effects increase the risk of severe hypoglycaemic reactions. A hypoglycaemic episode in these patients may be prolonged and appropriate management should be initiated.

Hepatic and renal functions should be assessed before initiating therapy and periodically in patients with mild to moderately impaired hepatic and renal function.

Patients with porphyria

Cases of acute porphyria (which can cause severe abdominal pain, gastrointestinal symptoms, unspecified neurologic symptoms along with chronic, blistering lesions on sun-exposed skin) have been described with the class of sulfonylurea drugs, in patients who have porphyria. Therefore, caution should be taken in the administration of gliclazide, as it may precipitate attacks of acute porphyria.

Use in the Elderly

See **Section 4.2 DOSE AND METHOD OF ADMINISTRATION** and **Section 5.2 PHARMACOKINETIC PROPERTIES**.

Paediatric Use

Not recommended for paediatric use, see **Section 4.2 DOSE AND METHOD OF ADMINISTRATION**.

Effects on Laboratory Tests

Glycated haemoglobin should be monitored regularly. Blood glucose measurement may also be useful.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Blood glucose monitoring during and after treatment is necessary when GLICLAZIDE MR VIATRIS is used with medicines which can interact with gliclazide. It may also be necessary to adjust the dose of GLICLAZIDE MR VIATRIS during and after treatment with such medicines.

1) The following medications are likely to increase the risk of hypoglycaemia

Concomitant use which is contraindicated:

Miconazole (systemic route, oromucosal gel)

Increases the hypoglycaemic effect with possible onset of hypoglycaemia symptoms, or even coma.

Concomitant use which is not recommended:

Phenylbutazone (systemic route)

Increases the hypoglycaemic effect of sulfonylureas (displaces their binding to plasma proteins and/or reduces their elimination).

It is preferable to use a different anti-inflammatory agent, or else to warn the patient and emphasise the importance of self-monitoring. Where necessary, adjust the dose during and after treatment with the anti-inflammatory agent.

Alcohol

Acute alcohol intoxication potentiates the hypoglycaemic action of all sulfonylurea agents by inhibiting compensatory reactions. This can lead to the onset of hypoglycaemic coma. Ingestion of alcohol may also cause a disulfiram-like reaction with characteristic flushing of the face, sensation of warmth, throbbing headache, giddiness, nausea, tachypnoea, tachycardia or angina pectoris. Chronic alcohol abuse may, as a result of liver enzyme induction, increase the metabolism of sulfonylurea drugs, shortening the plasma half-life and duration of action.

Avoid alcohol or medicines containing alcohol.

Concomitant use which requires special care:

Potentiation of the blood glucose lowering effect and therefore in some instances, hypoglycaemia may occur when one of the following medications is taken:

Other antidiabetic agents (insulins, acarbose, biguanides, metformin, thiazolidinediones, dipeptidyl peptidase-4 inhibitors, GLP-1 receptor agonists), sulfonamides, clarithromycin, clofibrate, salicylates (high doses), fibrates, chloramphenicol, MAOIs, probenecid, beta-blockers, azole antifungal agents (oral and parenteral preparations), H2-receptor antagonists, ACE inhibitors, fluconazole, tuberculostatics and nonsteroidal anti-inflammatory agents.

2) The following medications may cause an increase in blood glucose levels

Advise the patient and emphasise the importance of glucose monitoring.

Concomitant use which is not recommended:

Danazol

Combination is not recommended because of diabetogenic effect of danazol. If the use of danazol cannot be avoided, warn the patient and emphasise the importance of urine and blood glucose monitoring. It may be necessary to adjust the dose of GLICLAZIDE MR VIATRIS during and after treatment with danazol.

Concomitant use which requires special care:

Chlorpromazine

High doses (>100 mg per day of chlorpromazine) can increase blood glucose levels (reduced insulin release). Advise the patient and emphasise the importance of glucose monitoring. It may be necessary to adjust the dose of GLICLAZIDE MR VIATRIS during and after treatment with chlorpromazine.

Glucocorticoids (systemic and local route: intra-articular, cutaneous and rectal preparations) and tetracosactide.

Concomitant use may increase blood glucose levels with possible ketosis (glucocorticoids cause reduced tolerance to carbohydrates). Emphasise the importance of blood glucose monitoring, particularly at the start of treatment. It may be necessary to adjust the dose of GLICLAZIDE MR VIATRIS during and after treatment with glucocorticoids.

Salbutamol, terbutaline (intravenous)

May cause increased blood glucose levels due to beta-2 agonist effects. If necessary, switch to insulin.

Barbiturates, Oestrogens and progestogens (oral contraceptives)

May adversely affect blood sugar control with hypoglycaemic agents in some patients by causing increased blood glucose levels.

St John's Wort (Hypericum perforatum) preparations:

Gliclazide exposure is decreased by St John's Wort (Hypericum perforatum).

Certain drugs tend to induce hyperglycaemia and may lead to loss of blood sugar control. These include diuretics (thiazides, furosemide), ritodrine and nicotinic acid in pharmacological doses.

3) The following products may cause unstable blood glucose

Concomitant use which requires special care:

Fluoroquinolones

In case of a concomitant use of gliclazide and a fluoroquinolone, the patient should be warned of the risk of unstable blood glucose, and the importance of blood glucose monitoring should be emphasised.

Concomitant use to be taken into consideration:

Anticoagulant therapy (Warfarin)

Sulfonylureas may lead to potentiation of anticoagulation during concurrent treatment. Adjustment of warfarin may be necessary.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on Fertility

No data available.

Use in Pregnancy

Pregnancy Category: C

In animal studies embryo-toxicity and/or birth defects have been demonstrated with some sulfonylureas.

Gliclazide should not be used in pregnant women. From a clinical point of view, there are limited data (less than 300 pregnancies) to allow evaluation of the possible malformative or foetotoxic effects of gliclazide, when administered during pregnancy. Animal studies of gliclazide have not shown any teratogenic effect.

Gliclazide is contra-indicated during pregnancy and insulin is the drug of first choice for treatment of diabetes during pregnancy. Treatment should be changed from gliclazide to insulin therapy before pregnancy is attempted, or as soon as pregnancy is discovered. Control of diabetes should be achieved before the time of conception to reduce the risk of congenital abnormalities linked to uncontrolled diabetes.

Use in Lactation

It is not known whether gliclazide or its metabolites are excreted in breast milk. Given the risk of neonatal hypoglycaemia, GLICLAZIDE MR VIATRIS is contra-indicated in women who are breast feeding. A risk to newborns/infants cannot be excluded.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Gliclazide can have effects on ability to drive and use machines. Patients should be made aware of the symptoms of hypoglycaemia and should be careful if driving or operating machinery, especially at the beginning of treatment.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Good clinical acceptability of gliclazide, has been established in many studies as well as in medical practice.

The safety of a modified release formulation of gliclazide (30 mg - 120 mg) has been evaluated in controlled clinical trials in 955 patients, of which 728 patients were treated in long-term comparative trials, against a gliclazide immediate release formulation (80 mg - 320 mg), for up to ten months. In these comparative trials, the overall incidence and type of adverse events were similar in both groups. Adverse events were generally mild and transient, not requiring discontinuation of therapy.

However, where patients did discontinue due to adverse events, the percentage was lower in the modified release group (2.9%) than in the immediate release group (4.5%).

Hypoglycaemia (see Sections 4.3 CONTRAINDICATIONS and Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE)

The most frequent adverse reaction with gliclazide is hypoglycaemia.

As is the case with all sulfonylurea drugs, hypoglycaemic reactions have been reported following gliclazide administration. However, a number of studies have shown that hypoglycaemia is less common with gliclazide than with glibenclamide.

Possible symptoms of hypoglycaemia are: headache, intense hunger, nausea, vomiting, lassitude, sleep disorders, agitation, aggression, poor concentration, reduced awareness and slowed reactions, depression, confusion, visual

and speech disorders, aphasia, tremor, paraesthesia, flushing or pallor, numbness, chilliness, paresis, sensory disorders, dizziness, feeling of powerlessness, loss of self-control, delirium, convulsions, increased pulse rate, increased blood pressure, shallow respiration, bradycardia, drowsiness and loss of consciousness, apprehensiveness in mild cases possibly resulting in coma and/or death. In addition, signs of adrenergic counter-regulation may be observed: sweating, clammy skin, anxiety, tachycardia, hypertension, palpitations, angina pectoris and cardiac arrhythmia.

Usually, symptoms disappear after intake of carbohydrate such as sugar (artificial sweeteners have no effect). Experience with other sulfonylureas shows that hypoglycaemia can recur even when these measures are initially effective. If a hypoglycaemic episode is severe or prolonged, and even if it is temporarily controlled by intake of sugar, immediate medical treatment or even hospitalisation is required.

In long-term comparative studies, the percentage of patients experiencing hypoglycaemic episodes was similar between patients treated with the modified release formulation of gliclazide (11.6%) and those treated with the immediate release formulation of gliclazide (11.1%). However, the number of hypoglycaemic episodes per 100 patient months was lower in the modified release group (3.5) than in the immediate release group (4.8).

Analysis of elderly patients (over 65 years old) showed less hypoglycaemia than in the general population, with a prevalence of hypoglycaemic episodes lower in the modified release group (2.6 hypoglycaemic episodes for 100 patient months) than in the immediate release group (4.1).

The percentage of patients experiencing hypoglycaemic episodes in the sub-population with renal failure, was similar to that observed in the general population.

Adverse events reported during controlled clinical trials with the modified release formulation of gliclazide were those expected in an ageing population with diabetes.

Adverse events that were reported in at least 2.0% of patients, in long-term controlled clinical studies, are presented in the following table. The most frequent adverse events were not specifically related to the disease (such as respiratory infections or back pain).

Treatment emergent adverse events* (listed by body system) occurring in ≥ 2.0% of patients in long-term controlled clinical trials

	Gliclazide modified release tablets (30 mg - 120 mg) (n=728) %	**Gliclazide immediate release tablets (80 mg - 320 mg) (n=734) %**
Resistance mechanism		
Infection, viral	7.7	5.6
Respiratory		
Rhinitis	4.4	4.6
Bronchitis	4.4	4.6
Pharyngitis	4.3	3.5
Upper respiratory infection	3.3	3.7
Coughing	2.1	2.0
Musculo-skeletal		
Back pain	5.2	4.1
Arthralgia	3.0	3.5
Arthrosis	2.2	2.2
Secondary term		
Inflicted injury	4.3	4.5

Body as a whole		
Headache	3.8	4.6
Asthenia	2.2	2.6
Cardiovascular		
Hypertension	3.2	3.7
Angina pectoris	2.1	2.2
Urinary		
Urinary tract infections	2.6	3.0
Gastrointestinal		
Diarrhoea	2.5	2.0
Central, periph., nervous system	2.2	2.3
Dizziness		
Metabolism and nutrition		
Hyperglycaemia	1.9	2.2

*whatever the relationship to treatment

Analysis of adverse events in sub-populations showed a similar pattern to that seen in the general population. Gender, age and renal impairment had no significant influence on the safety profile of the modified release formulation of gliclazide.

Other adverse effects

Gastrointestinal disturbances (reported with gliclazide), including nausea, dyspepsia, diarrhoea, abdominal pain, vomiting and constipation may be avoided or minimised if gliclazide is taken with breakfast.

The following adverse effects have been rarely reported:

Skin and subcutaneous tissue disorders:

Pruritus, urticaria, maculopapular rashes, rash, angioedema, erythema and bullous reactions (such as Stevens-Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN) (as with other sulfur-containing medications) and autoimmune bullous disorders and exceptionally, drug rash with eosinophilia and systemic symptoms (DRESS).

Blood and lymphatic system disorders (as with other sulfonylurea medications):

Anaemia, leucopenia, thrombocytopenia and agranulocytosis. These are in general reversible upon discontinuation of medication.

Hepatobiliary disorders:

Elevations of serum bilirubin and hepatic enzymes (AST, ALT, alkaline phosphatase) levels, pancreatitis acute and exceptionally, hepatitis (isolated reports). Treatment should be discontinued if cholestatic jaundice appears. These symptoms usually disappear after discontinuation of treatment.

Investigations:

Occasional elevations of serum creatinine, blood urea nitrogen.

Eye disorders:

Transient visual disturbances may occur due to changes in blood glucose levels, particularly on initiation of treatment. As with any glucose-lowering medication, transient visual disturbances may occur on initiation of treatment due to changes in blood glucose levels.

Class effects

The following adverse events have been observed with sulfonylureas: cases of erythrocytopenia, agranulocytosis, haemolytic anaemia, pancytopenia and allergic vasculitis, hyponatremia, elevated liver enzyme levels and even impairment of liver function (e.g. with cholestasis and jaundice) and hepatitis which regressed after withdrawal of the sulphonylurea or led to life-threatening liver failure in isolated cases.

Reporting Suspected Adverse Effects

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Overdose of sulfonylureas may cause hypoglycaemia. It should be noted that the dosage which causes such hypoglycaemia varies widely and may be within the accepted therapeutic range in sensitive individuals.

Moderate symptoms of hypoglycaemia (without loss of consciousness or neurological signs), should be corrected by carbohydrate intake, dose adjustment and/or modification of diet. Strict monitoring should be continued until the doctor is sure that the patient is out of danger.

Severe hypoglycaemic reactions are possible (with coma, convulsions or other neurological disorders) and must be treated as a medical emergency, requiring immediate hospitalisation.

If hypoglycaemic coma is diagnosed or suspected, the patient should be given a rapid I.V. injection of 50 mL of concentrated glucose solution (20 to 30%). This should be followed by continuous infusion of a more dilute glucose solution (10%) at a rate necessary to maintain blood glucose levels above 5 mmol/L. It is recommended that patients should be monitored closely for a 48 hour period at least. Some sulfonylurea-induced hypoglycaemias may be refractory to treatment and susceptible to relapse especially in elderly or malnourished patients.

Plasma clearance of gliclazide may be prolonged in patients with hepatic disease. However, due to the strong binding of gliclazide to proteins, dialysis is not effective in these patients.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of Action

Gliclazide reduces blood glucose levels by stimulating insulin secretion from the β -cells of the islets of Langerhans. Gliclazide shows high affinity, strong selectivity and reversible binding to the β -cell K_{ATP} channels with a low affinity for cardiac and vascular K_{ATP} channels. Increased postprandial insulin and C-peptide secretion persists after two years of treatment.

In type II diabetes, gliclazide restores the first peak of insulin secretion in response to glucose and increases the second phase of insulin secretion. A significant increase in insulin release is seen in response to stimulation induced by a meal or glucose.

Gliclazide also has extra-pancreatic effects and haemovascular properties. It has been shown to increase peripheral insulin sensitivity:

- In muscle, euglycaemic hyperinsulinaemic clamp studies with gliclazide have demonstrated significantly increased (35%) insulin mediated glucose uptake which may improve diabetes control. Gliclazide potentiates insulin action on muscle glycogen synthase. These effects are consistent with a post-transcriptional action of gliclazide on GLUT4 glucose transporters.

- Studies on glucose turnover have further shown that gliclazide decreases hepatic glucose production, leading to an improvement in fasting blood glucose levels.

Gliclazide has been shown in some studies to have actions independent of that on glucose levels. These haemovascular effects of gliclazide include:

- Partial inhibition of platelet aggregation and adhesion with a decrease in markers of platelet activation (beta thromboglobulin, thromboxane B2).
- Increased vascular endothelial fibrinolytic activity (increased tPA activity).
- Anti-oxidant properties, notably a reduction in plasma lipid peroxides and increased erythrocyte superoxide dismutase activity.
- Inhibition of the increased adhesiveness of type II diabetic patient's monocytes to endothelial cells in vitro.

The anti-oxidant, platelet inhibiting and fibrinolytic actions of gliclazide involve processes which have been implicated in the pathogenesis of vascular complications of type II diabetes. There is no clinical evidence that the haemovascular effects of gliclazide are of therapeutic benefit in type II diabetes patients.

Clinical Trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Hydration of the tablets induces formation of a gel to activate drug release. Plasma levels increase progressively, resulting in a plateau-shaped curve from the sixth to the twelfth hour after administration. Intra-individual variability is low. Gliclazide is completely absorbed and food intake does not affect the rate or degree of absorption.

Distribution

Plasma protein binding is approximately 95%. The relationship between the dose administered and the area under the concentration curve as a function of time is linear for doses of gliclazide up to 90 mg/day. At the highest evaluated dose (135 mg/day), the AUC increases slightly more than proportionally to the dose.

Metabolism

Gliclazide is mainly metabolised in the liver, the products of which are extensively excreted in the urine.

Excretion

Less than 1% of unchanged drug is recovered in the urine. No active metabolites have been detected in plasma. The clearance of gliclazide has been found to be slightly reduced as a function of age. This reduction, however, is not considered to be clinically significant. The elimination half- life of gliclazide is approximately 16 hours.

No clinically significant modifications in the pharmacokinetic parameters have been observed in elderly patients.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

GLICLAZIDE MR VIATRIS includes the following excipients:

- hypromellose
- microcrystalline cellulose
- magnesium stearate

6.2 INCOMPATIBILITIES

See **Section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS**.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C. Store in original container. Protect from moisture.

6.5 NATURE AND CONTENTS OF CONTAINER

GLICLAZIDE MR VIATRIS 30 mg: HDPE bottle with CR cap or PVC/Al or PVC/PVDC/Al blister pack in packs of 100 tablets

Some strengths, pack sizes and/or pack types may not be marketed.

Australian Register of Therapeutic Goods (ARTG)

AUST R 295541 – GLICLAZIDE MR VIATRIS gliclazide 30 mg modified release tablet blister pack

AUST R 295540 - GLICLAZIDE MR VIATRIS gliclazide 30 mg modified release tablet bottle

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

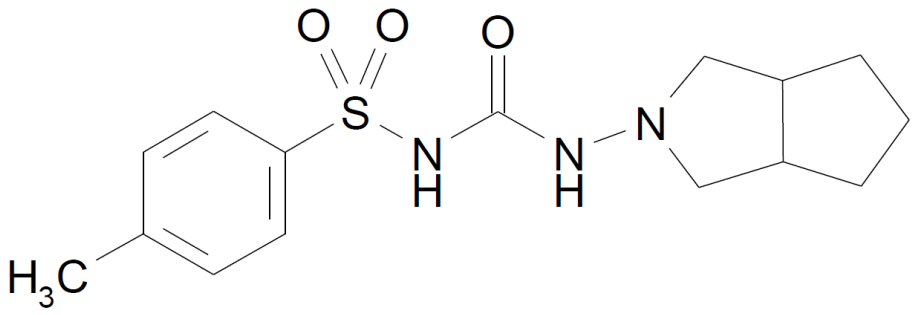
In Australia, any unused medicine or waste material should be disposed of by taking it to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Gliclazide is an oral hypoglycaemic sulfonylurea which differs from other related compounds by an N-containing heterocyclic ring with an endocyclic bond.

It is a white or almost white powder, practically insoluble in water, freely soluble in dichloromethane, sparingly soluble in acetone and slightly soluble in ethanol 96%. The melting point of gliclazide is approximately 168°C.

Chemical Structure



Chemical name	:	1-(3-azabicyclo[3.3.0] oct-3-yl)-3-p-tolylsulfonylurea
Molecular formula	:	$C_{15}H_{21}N_3O_3S$
Molecular weight	:	323.4

CAS Number

21187-98-4

7 MEDICINE SCHEDULE (POISONS STANDARD)

S4 (Prescription Only Medicine)

8 SPONSOR

Alphapharm Pty Ltd trading as Viatris

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Millers Point NSW 2000

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Phone: 1800 274 276

9 DATE OF FIRST APPROVAL

31/03/2023

10 DATE OF REVISION

09/07/2024

Summary Table of Changes

Section Changed	Summary of New Information
4.4	Addition of “debilitated patients” to factors that may increase risk of hypoglycaemia. Effects of oral hypoglycaemic agents Poor Blood Glucose Control Use in renal and hepatic impairment Patients with Porphyria

4.5	Additional interactions Additional characteristics of disulfiram-like reaction Additional information for Danazol
4.7	Additional information on impact on driving and using machinery
4.8	Addition of "pancreatitis acute" Additional symptoms of hypoglycaemia
4.9	Information on relapse for elderly or malnourished patients

GLICLAZIDE MR VIATRIS_pi\Jul24/00 (CCDS 27-Nov-2023)