PRODUCT INFORMATION

Glimel

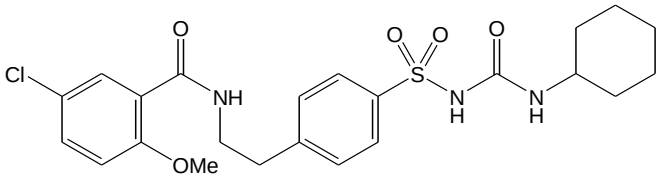
Glibenclamide

NAME OF THE MEDICINE

Active ingredient : Glibenclamide

Chemical name : 1-{4-[2-(5-chloro-2-methoxy-benzamido)ethyl]benzenesulphonyl}-3-cyclohexylurea.

Structural formula :



Molecular formula : $C_{23}H_{28}ClN_3O_5S$

Molecular weight : 494

CAS Registry no. : 10238-21-8

DESCRIPTION

Glibenclamide belongs to the sulphonylurea group of oral antidiabetics. Earlier members of this group are carbutamide, tolbutamide, acetohexamide and chlorpropamide. It is a white odourless, crystalline powder, practically insoluble in water and in ether, slightly soluble in alcohol and sparingly soluble in chloroform.

Each Glimel tablet contains 5 mg of glibenclamide. The tablets also contain the following inactive excipients: microcrystalline cellulose, pregelatinised maize starch, purified talc, colloidal anhydrous silica, magnesium stearate.

PHARMACOLOGY

Oral hypoglycaemia.

Pharmacodynamics

Mechanism of Action

Glibenclamide appears to lower the blood glucose acutely in healthy individuals and patients with type 2 diabetes by stimulating the release of insulin from the pancreas, an effect dependent upon functioning beta cells. It acts in concert with glucose (improved sensitivity of beta cells to physiological glucose stimulus) and leads to an insulin secretion in the rhythm of meals. Other mechanisms of the hypoglycaemic action associated with short-term therapy appear to include reduction of basal hepatic glucose production and enhancement of peripheral insulin action at post-receptor (probably intracellular) sites.

With chronic administration of glibenclamide in patients with type 2 diabetes, the improvement in glucose tolerance persists despite a gradual decline in glucose or meal-stimulated secretion of insulin towards pretreatment levels. Extrapancreatic effects appear to contribute substantially to the hypoglycaemic action of the drug during long term administration. The effects appear to include enhanced peripheral sensitivity to insulin and reduction of basal hepatic glucose production. There is evidence that glibenclamide enhances the peripheral action of insulin at postreceptor (probably intracellular) sites and increases insulin binding and/or the number of insulin receptors.

Glibenclamide also exerts a direct inhibitory effect on glucagon-producing alpha cells of the pancreas and increases the release of somatostatin. However, these two pancreatic extra-beta cell actions may play only a minor clinical role.

In addition to its blood glucose lowering effect, glibenclamide has a mild diuretic action and increases free water clearance.

Pharmacokinetics

Absorption

Glibenclamide is nearly completely absorbed (84 ± 9%) after oral administration and is extensively bound (99%) to serum proteins. The peak serum concentration is reached in two to six hours after taking a 5 mg tablet of glibenclamide and falls within 24 hours to less than 5% of the peak value. The area under the serum concentration time curve (AUC) increases in proportion to increasing doses. Food apparently does not affect the rate or extent of absorption of glibenclamide.

Distribution

Multiple dose studies with glibenclamide in diabetic patients demonstrate drug level concentration-time curves similar to single-dose studies, indicating no build-up of drug in tissue depots. In non-fasting diabetic patients, the hypoglycaemic action of a single morning dose of glibenclamide persists for 24 hours. Serum concentrations of glibenclamide appear to decline in a biphasic manner. The elimination half-life of glibenclamide after intravenous dosage is approximately 2 hours, and 2 to 5 hours after oral administration. Some reports indicate a longer half-life of 8 to 10 hours in patients with diabetes.

Metabolism

Glibenclamide is completely metabolised in the liver. The drug is metabolised at the cyclohexyl ring principally to a 4-trans-hydroxy derivative. A second metabolite, the 3-cis-hydroxy derivative, also occurs. These metabolites contribute some hypoglycaemic action; they are weakly active (0.25% and 2.5%, respectively, as glibenclamide) in rabbits.

Excretion

Glibenclamide is excreted as metabolites in the bile and urine, approximately 50% by each route. In patients with renal insufficiency, depending on the degree of the renal excretion disorder, there is increased elimination of the metabolites via the bile. This dual excretory pathway is qualitatively different from that of other sulphonylureas, which are excreted primarily in the urine.

Glibenclamide appears to be only minimally removed by haemodialysis.

INDICATIONS

Glibenclamide is indicated as an adjunct to diet to lower the blood glucose in patients with non-insulin dependent diabetes mellitus (type 2) whose hyperglycaemia cannot be controlled by diet alone. Because of its broad and predictable action, glibenclamide is often suitable for the management of patients who have failed to respond to other oral antidiabetics.

In initiating treatment for non-insulin-dependent diabetes, diet should be emphasised as the primary form of treatment. Caloric restriction and weight loss are essential in the obese diabetic patient. Proper dietary management alone may be effective in controlling the blood glucose and symptoms of hyperglycaemia. The importance of regular physical activity should also be stressed, and cardiovascular risk factors should be identified and corrective measures taken where possible. If this treatment programme fails to reduce symptoms and/or blood glucose the use of an oral sulfonylurea should be considered. Use of glibenclamide must be viewed by both the physician and patient as a treatment in addition to diet, and not as a substitute for diet or as a convenient mechanism for avoiding dietary restraint.

CONTRAINDICATIONS

1. Known hypersensitivity or allergy to glibenclamide or any of the excipients.
2. Insulin dependent diabetes (type 1 or juvenile onset diabetes) or in those with diabetes complicated by ketosis.
3. Treatment for diabetic ketoacidosis
4. Serious metabolic decompensation with acidosis, in particular precoma and coma.
5. Severe impairment of renal function.
6. Severe hepatic dysfunction.
7. Pregnancy (see **PRECAUTIONS, Use in Pregnancy**).
8. Lactation (see **PRECAUTIONS, Use in Lactation**).
9. Patients treated with bosentan (see **INTERACTIONS WITH OTHER MEDICINES**)

PRECAUTIONS

The treatment of diabetes requires regular checks. Until optimal control is achieved, or when changing from one product to another, or when tablets are not taken regularly, the patient's alertness and capacity to react may be impaired to such an extent that he or she may not be fit to drive or to operate machinery.

When situations of unusual stress arise (e.g. trauma, emergency or elective surgery, febrile infections), blood glucose regulation may deteriorate and a temporary change to insulin may become necessary to maintain good metabolic control.

It should be borne in mind that there is a possibility of cross-sensitivity to sulphonamides and their derivatives. Persons allergic to other sulphonamide derivatives may develop an allergic reaction to glibenclamide as well.

Epidemiological studies suggest that the administration of glibenclamide is associated with an increased risk of cardiovascular mortality, when compared to treatment with metformin or gliclazide. This risk was especially observed in patients with diagnosed coronary diseases.

Hypoglycaemic Reactions

Severe hypoglycaemia, which may be prolonged and is potentially lethal, can be induced by all sulphonylureas.

Debilitated, malnourished or geriatric patients and patients with mild disease or impaired hepatic or renal function should be carefully monitored and dosage of glibenclamide should be carefully adjusted in these patients, since they may be predisposed to developing hypoglycaemia. Renal or hepatic insufficiency may cause increased serum concentrations of glibenclamide and hepatic insufficiency may also diminish gluconeogenic capacity, both of which increase the risk of severe hypoglycaemic reactions.

Alcohol ingestion (see **INTERACTIONS WITH OTHER MEDICINES**) intense or prolonged exercise, deficient caloric intake, use of more than one antidiabetic agent, severe endocrine disorders and adrenal or pituitary insufficiency may also predispose patients to the development of hypoglycaemia.

If risk factors for hypoglycaemia are present, it may be necessary to adjust the dosage of glibenclamide or the entire therapy. This also applies whenever illness occurs during therapy or the patient's lifestyle changes.

Elderly patients are particularly susceptible to hypoglycaemic action of glucose-lowering drugs. Hypoglycaemia may be difficult to recognise in the elderly. The initial and maintenance dosing should be conservative to avoid hypoglycaemic reactions.

Hypoglycaemia can, almost always, be promptly controlled by immediate intake of carbohydrates (glucose or sugar, e.g. in the form of sugar lumps, sugar-sweetened fruit juice or tea).

Despite initially successful countermeasures, hypoglycaemia may recur. Patients must, therefore, remain under close observation.

Severe hypoglycaemia, or a protracted episode, which can only be temporarily controlled by usual amounts of sugar, further requires immediate treatment and follow-up by a physician and, in some circumstances, in-patient hospital care.

Patients receiving glibenclamide should be monitored with regular clinical and laboratory evaluations, including blood and urine glucose determinations, to determine the minimum effective dosage and to detect primary failure (inadequate lowering of blood glucose concentration at the maximum recommended dosage) or secondary failure (loss of control of blood glucose concentration following an initial period of effectiveness) to the drug. Glycosylated haemoglobin measurements may also be useful for monitoring the patient's response to glibenclamide therapy. During the withdrawal period in patients in whom glibenclamide is replacing insulin, patients should be instructed to test their urine for glucose and ketones at least three times daily, and to report the results to their physician; when feasible, patient or laboratory monitoring of blood glucose concentration is preferable. Care should be taken to avoid ketosis, acidosis and coma during the withdrawal period in patients being switched from insulin to glibenclamide. If adequate lowering of blood glucose concentration is no longer achieved during maintenance therapy with glibenclamide, the drug should be discontinued.

As is necessary during treatment with any blood-glucose-lowering drug, the patient and the physician must be aware of the risk of hypoglycaemia. Patients and responsible family members should be made aware of the signs and symptoms of hyperglycaemia and hypoglycaemia and the prompt action required in the event of such occurrences. Symptoms of hyperglycaemia include severe thirst, dry mouth, frequent micturition and dry skin. Possible symptoms of hypoglycaemia include intense hunger, nausea, vomiting, sweating, tremor, pareses, sensory disturbances, restlessness, irritability, aggressiveness, depression, confusion, speech disorders, aphasia, visual disorders, impaired concentration, impaired alertness and reactions, headaches, dizziness, disturbed sleep, helplessness, loss of self-control, delirium, transient neurological disorders such as cerebral convulsions, lassitude, sleepiness, somnolence, loss of consciousness up to and including coma, shallow respiration 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. Patient and responsible family members should know how to respond promptly to such occurrences.

The clinical picture of a severe hypoglycaemic attack may resemble that of a stroke. The symptoms of hypoglycaemia nearly always subside when hypoglycaemia is corrected.

In the presence of a genetic defect in metabolism, the elimination half-life may be prolonged.

Because of its broad and predictable hypoglycaemic effect, Glimel should be taken immediately before breakfast. Patients who eat only a light breakfast should defer the first dose of the day until lunch time.

Some improvement in glucose tolerance may take place after a few weeks' treatment with glibenclamide. The clinical status should be checked within the first four to eight weeks and at regular intervals thereafter so as to ascertain whether it is possible to reduce the dose or cease glibenclamide therapy. Correction of dosage must also be considered whenever the patient’s weight changes, the patient’s lifestyle changes or other factors arise that cause an increased susceptibility to hypoglycaemia or hyperglycaemia.

Haemolytic anaemia

Treatment of patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency with sulphonylurea agents can lead to haemolytic anaemia. Since glibenclamide belongs to the class of sulphonylurea agents, caution should be used in patients with G6PD-deficiency and a non-sulphonylurea alternative should be considered.

Carcinogenicity and mutagenicity

Glibenclamide was not genotoxic in a limited set of assays for gene mutations (Salmonella microsome test (Ames test)) and other genotoxic effects (DNA damage/alkaline elution assay). The clastogenic potential of glibenclamide has not been investigated.

Studies in rats at doses up to 300 mg/kg/day for 18 months showed no carcinogenic effects.

Impairment of fertility

The effects of glibenclamide on fertility have not been investigated.

Use in Pregnancy (Category C)

It is important to achieve strict normoglycaemia during pregnancy. Glibenclamide must not be taken during pregnancy. The patient must change over to insulin during pregnancy. The sulphonylureas may enter the foetal circulation and cause neonatal hypoglycaemia. In animal studies, embryotoxicity and/or birth defects have been demonstrated.

Patients planning a pregnancy must inform their physician. It is recommended that such patients change to insulin.

Category C: Drugs which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful effects on the human foetus or neonate without causing malformations. These effects may be reversible. Relevant texts should be consulted for further details.

Use in Lactation

It is not known whether glibenclamide is excreted in milk or whether it has a harmful effect on the newborn. To prevent possible ingestion with breast milk, glibenclamide must not be taken by breast feeding women. If necessary, the patient must change over to insulin, or must stop breastfeeding.

Paediatric Use

The safety and efficacy of glibenclamide in children have not been established. Glibenclamide is not recommended for use in this patient group.

INTERACTIONS WITH OTHER MEDICINES

An increased incidence of elevated liver enzymes was observed in patients receiving glibenclamide concomitantly with bosentan. Both bosentan and glibenclamide inhibit the bile salt export pump, leading to intracellular accumulation of cytotoxic bile salts. Therefore, this combination should not be used (see **CONTRAINDICATIONS**).

Other drugs given at the same time as sulphonylureas may cause undesirable depression or elevation of the blood sugar level.

Glibenclamide is mainly metabolised by CYP2C9 and to a lesser extent by CYP3A4. This should be taken into account when glibenclamide is co-administered with inducers or inhibitors of CYP2C9.

Drugs which may potentiate the hypoglycaemic action of Glimel include insulin, other oral antidiabetic agents, alcohol, ACE inhibitors, aminosalicylic acid, anabolic steroids and male sex hormones, azapropazone, beta-receptor blockers, bezafibrate, biguanides, chloramphenicol, clarithromycin, clofibrate, clonidine, co-trimoxazole, coumarin derivatives, cyclophosphamide, disopyramide, fenfluramine, fenyramidol, fibrates, fluoxetine, gemfibrozil, guanethidine, heparin, ifosfamide, MAO-inhibitors, miconazole, oxpentifylline (parenteral, in high doses), oxyphenbutazone, para-aminosalicylic acid, phenylbutazone, phenyramidol, phosphamides, probenecid, quinolone antibiotics, ranitidine, reserpine, salicylates, sulphinpyrazone, certain long-acting sulphonamides, tetracycline compounds, tritoqualine and trophosphamide. Highly protein-bound drugs, which may also potentiate the hypoglycaemic action of Glimel due to glibenclamide displacement from plasma proteins, include oral anticoagulants, hydantoins, salicylates and other non-steroidal anti-inflammatory agents.

Drugs which may cause an attenuation of the hypoglycaemic action of Glimel include adrenaline (epinephrine) and other sympathomimetic agents, alcohol, acetazolamide, barbiturates, calcium channel blockers, cimetidine, clonidine, corticosteroids, diazoxide, diuretics, glucagon, isoniazid, large doses of laxatives, nicotinic acid (high dosage), oestrogens, progestogens, phenothiazine derivatives, phenytoin, ranitidine, rifampicin, ritodrine and thyroid hormones.

Concomitant treatment with beta-receptor blockers, clonidine, reserpine, guanethidine or other sympatholytic drugs may mask the warning symptoms of a hypoglycaemic attack. The symptoms of hypoglycaemia may also be milder or absent where hypoglycaemia develops gradually or where there is autonomic neuropathy. In rare

instances, potentiation or attenuation of the blood-sugar lowering effect of glibenclamide have been observed during concomitant treatment with H_2 receptor antagonists, clonidine or reserpine.

In very rare cases, an intolerance to alcohol may occur. Both acute and chronic alcohol intake, or excessive alcohol ingestion by people who drink occasionally, may attenuate the hypoglycaemic effect of glibenclamide or dangerously potentiate it by delaying its metabolic inactivation. Disulfiram-like reactions have occurred very rarely following the concomitant use of alcohol and glibenclamide.

Glibenclamide may either potentiate or weaken the effect of coumarin derivatives.

Glibenclamide may increase cyclosporin plasma concentration and potentially lead to its increased toxicity. Monitoring and dosage adjustment of cyclosporin are therefore recommended when both drugs are co-administered.

Colesevelam binds to glibenclamide and reduces glibenclamide absorption from the gastrointestinal tract. No interaction was observed when glibenclamide was taken at least 4 hours before colesevelam. Therefore glibenclamide should be administered at least 4 hours prior to colesevelam.

Food does not alter the bioavailability or other pharmacokinetic parameters of glibenclamide.

Effects on laboratory tests

It is unknown whether glibenclamide has any effect on laboratory tests.

ADVERSE EFFECTS

Clinical experience in the use of glibenclamide has shown that side effects serious enough to compel discontinuation of therapy are uncommon, even during long-term therapy. However, if adverse effects persist, the drug should be discontinued.

Hypoglycaemia

Hypoglycaemia may not only be severe, but also prolonged and fatal (see **PRECAUTIONS - Hypoglycaemic Reactions** and **OVERDOSAGE**).

Eye Disorders

Especially at the start of treatment, there may be temporary visual impairment due to the change in blood glucose levels. The cause is a temporary alteration in the turgidity and hence the refractive index of the lens, this being dependent on blood glucose level.

Gastrointestinal Reactions

Adverse gastrointestinal effects such as nausea, vomiting, epigastric fullness or sensation of pressure, abdominal pain, anorexia, heartburn, dyspepsia and diarrhoea are the most common adverse reactions to glibenclamide, occurring in about 1 to 2% of patients. Glibenclamide-induced adverse gastrointestinal effects appear to be dose related and may subside following a reduction in dosage. Pancreatitis has been reported rarely.

Dermatological Reactions

Hypersensitivity reactions, allergic or pseudoallergic reactions may occur. Allergic skin reactions e.g. pruritus, erythema, urticaria, erythematous and maculopapular and bullous skin eruptions or psoriasiform drug eruptions occur in 1.5% of treated patients. These may be transient and may disappear despite continued use of glibenclamide; if skin reactions persist, the drug should be discontinued. In isolated cases, mild reactions in the form of urticaria may develop into serious and even life-threatening reactions with dyspnoea and fall in blood pressure, sometimes progressing to shock. In the event of urticaria, a physician must therefore be notified immediately.

A hypersensitivity reaction may be directed against glibenclamide itself, but may alternatively be triggered by excipients. Allergy to sulphonamide derivatives may also be responsible for an allergic reaction to glibenclamide.

In isolated cases, allergic vasculitis may arise and, in some circumstances, may be life-threatening. In isolated cases, hypersensitivity of the skin to light may occur, and sodium concentration in the serum may decrease. Porphyria cutanea tarda and pellagra-like changes have been reported with sulphonylureas.

Haematological Reactions

Anaemia, leukopaenia, thrombocytopaenia, thrombocytopaenic purpura, agranulocytosis, pancytopaenia, eosinophilia, haemolytic anaemia, aplastic anaemia, bone marrow aplasia, eosinophilia and coagulation disorders have been reported with sulphonylureas. Potentially life-threatening changes in the blood picture may occur. They may include, rarely, mild to severe thrombopaenia (e.g. presenting as purpura) and, in isolated cases, haemolytic anaemia, erythrocytopaenia, leucopaenia, granulocytopaenia, agranulocytosis and (for example, due to myelosuppression) pancytopaenia. In principle, these reactions are reversible once glibenclamide has been withdrawn.

Hepatic Reactions

Increased liver enzymes (AST, ALT), abnormal liver function, cholestasis, cholestatic hepatitis, granulomatous hepatitis and bilirubinaemia have been reported with sulfonylureas. In isolated cases there may be hepatitis, elevation of liver enzyme levels and/or cholestasis and jaundice which may progress to life-threatening liver failure but can regress after withdrawal of glibenclamide.

Miscellaneous

Although a causal relationship has not been established, the following adverse effects have been reported in patients receiving glibenclamide: paresthesia, blindness, deafness, diplopia, visual disturbances, tremor, convulsions (other than withdrawal), encephalopathy, confusion, acute psychosis, abnormal renal function, acute renal failure, ocular disturbances (accommodation changes, crystalline lens changes), lactic acidosis, alopecia/hipotrichosis, hyponatraemia, syndrome of inappropriate secretion of antidiuretic hormone (SIADH), arthralgia, arthritis, cerebrovascular disorders, headache, facial oedema, angioedema, weight gain, hypersensitivity vasculitis and increased sweating.

DOSAGE AND ADMINISTRATION

Dosage of glibenclamide must be based on regular blood and urine glucose determinations and must be carefully individualised to obtain optimum therapeutic effect. The dosage of glibenclamide must be the lowest possible dose which is effective. If appropriate glibenclamide dosage regimens are not followed, hypoglycaemia may be precipitated. It is very important not to skip meals after the tablets have been taken.

In newly treated patients with diabetes, stabilisation should be commenced with glibenclamide 2.5 mg daily, taken immediately before breakfast. Patients who eat only a light breakfast should defer the first dose of the day until lunchtime.

After three to five days the blood sugar and urine sugar should be checked. If good control has been achieved, the daily dose of 2.5 mg is continued as maintenance therapy.

If control is unsatisfactory, elevation of the daily dose in steps of 2.5 mg is necessary at intervals of seven days, up to a maximum of 15 mg, or, in exceptional cases, 4 glibenclamide tablets (20 mg) daily.

Daily allotments of up to 10 mg can be taken as a single dose before breakfast; daily dosage in excess of 10 mg should be taken before the evening meal.

As an improvement in control of diabetes is, in itself, associated with higher insulin sensitivity, glibenclamide requirements may fall as treatment proceeds. To avoid hypoglycaemia, timely dose reduction or cessation of glibenclamide therapy must therefore be considered. Mistakes, e.g. forgetting to take a dose, must never be corrected by subsequently taking a larger dose. Measures for dealing with such mistakes (in particular forgetting

a dose or skipping a meal), or in the event a dose cannot be taken at the prescribed time, must be discussed and agreed between physician and patient beforehand.

In the management of type 2 diabetes mellitus, oral hypoglycaemic administration is not a substitute for appropriate dietary control.

When transferring patients from other oral antidiabetic drugs, it is recommended to begin with the usual starting dose (2.5 to 5 mg per day). Depending on the pharmacokinetic and pharmacodynamic characteristics of the previous medication, a drug free transition period may be necessary, in order to avoid overlapping drug effects possibly resulting in hypoglycaemia.

In general, patients who were previously maintained on insulin dosages up to 40 units daily may be transferred directly to glibenclamide and administration of insulin may be abruptly discontinued; the initial glibenclamide dosage is 2.5 to 5 mg daily in patients whose insulin dosage was less than 20 units daily and 5 mg daily in patients whose insulin dosage was 20 to 40 units daily. In patients requiring insulin dosages greater than 40 units daily, an initial glibenclamide dosage of 5 mg daily should be started and insulin dosage reduced by 50%. Subsequently, insulin is withdrawn gradually and dosage of glibenclamide is increased in increments of 1.25 to 2.5 mg daily every two to ten days, according to the patient's tolerance and therapeutic response. During the period of insulin withdrawal, patients should test their urine at least three times daily for glucose and acetone, and should be instructed to report the results to their physician so that appropriate adjustments in therapy may be made if necessary; when feasible, patient or laboratory monitoring of blood glucose concentration is preferable. The presence of persistent ketonuria with glycosuria, ketosis, and/or inadequate lowering or persistent elevation of blood glucose concentration indicates that the patient requires insulin therapy.

If adequate control is no longer possible with diet and glibenclamide (maximum 20 mg daily), good results may be obtained by combined administration of glibenclamide and a biguanide derivative.

OVERDOSAGE

For information on the management of overdose, contact the Poisons Information Centre on 131126.

Pathogenesis

Acute glibenclamide toxicity may result from excessive dosage and numerous conditions may predispose patients to the development of glibenclamide induced hypoglycaemia (see Precautions). Acute overdose as well as long-term treatment with too high a dose of glibenclamide may lead to severe, protracted, life-threatening hypoglycaemia. Fatal hypoglycaemia has occurred with ingestion of as little as 2.5 to 5 mg of the drug.

Manifestations

Acute glibenclamide overdosage is manifested principally as hypoglycaemia, which may be severe and has occasionally been fatal. Severe hypoglycaemia may result in loss of consciousness and seizures, with resultant neurologic sequelae.

Treatment

In case of overdosage with glibenclamide, a doctor has to be called immediately. At the first signs of hypoglycaemia, the patient must immediately take sugar, preferably glucose, unless a doctor has already started care. The patient should be monitored closely until complete recovery is assured.

Mild hypoglycaemic symptoms without loss of consciousness or neurological findings should be treated aggressively with oral glucose and adjustments in glibenclamide dosage and/or meal patterns.

Since hypoglycaemia and its clinical symptoms may recur after apparent clinical recovery (even after several days), close and continued medical supervision and possibly referral to a hospital are indicated. In particular, significant overdosage and severe reactions, e.g. with unconsciousness or other neurological dysfunctions, are emergency cases and require immediate care and hospitalisation.

If hypoglycaemic coma is diagnosed or suspected, administration of glucagon (adults: 0.5 to 1 mg) intravenously, subcutaneously or intramuscularly, or an intravenous infusion of a 20% glucose solution (adults: 40 to 100 mL) is indicated, until the patient recovers consciousness. In infants, glucose must be dosed very carefully, accompanied by close monitoring of blood glucose, taking into account the risk of potentially severe hyperglycaemia. Other symptomatic therapy (e.g. anticonvulsants) should be administered as necessary.

In cases of acute intake of large amounts of glibenclamide, detoxification e.g. by gastric lavage or medicinal charcoal as an absorbent, is indicated.

After acute glucose replacement has been completed, it is usually necessary to give an intravenous glucose infusion in lower concentration to ensure that the hypoglycaemia does not recur. The patient's blood glucose level should be carefully monitored for at least 24 hours. In severe cases with a protracted course, hypoglycaemia, or the danger of slipping back into hypoglycaemia, may persist for several days.

PRESENTATION AND STORAGE CONDITIONS

Glimel (glibenclamide) 5 mg tablet	:	White, flat, bevelled edged tablet, marked GE/5 on one side, α on the reverse. Available in [PVC/PVDC/Al] blister packs* and [HDPE] bottles of 100 tablets. Store below 30°C.

* Not marketed in Australia.

NAME AND ADDRESS OF SPONSOR

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POISONS SCHEDULE OF THE MEDICINE

S4 – Prescription Only Medicine

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (THE ARTG)

20/09/1991

DATE OF MOST RECENT AMENDMENT

18 November 2016

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