

DATA SHEET

NAME OF THE MEDICINE

Glizon

gliclazide 80mg tablet

DESCRIPTION

Active Ingredient:

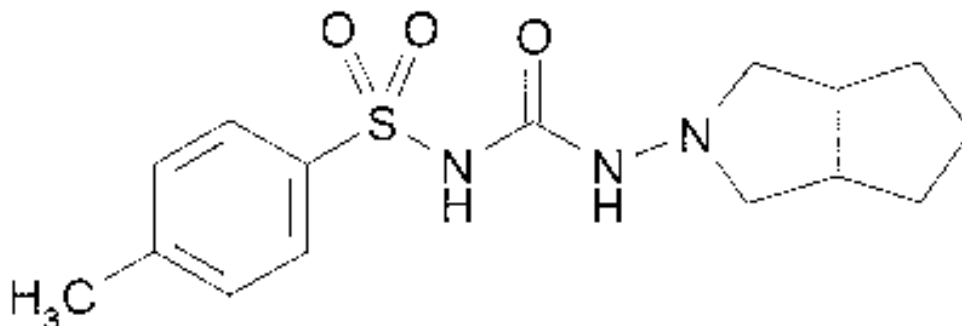
Gliclazide is a white or almost white powder, practically insoluble in water, freely soluble in dichloromethane, sparingly soluble in acetone and slightly soluble in ethanol 96%. The melting point of gliclazide is approximately 168°C.

Chemical Name: 1-(3-azabicyclo[3.3.0]oct-3-yl)-3-p-tolylsulphonylurea

CAS Registry Number: 21187-98-4

Molecular Formula: C₁₅H₂₁N₃O₃S

Chemical Structure:



Excipients:

Lactose monohydrate, hydrated silica, purified talc, magnesium stearate and pregelatinised maize starch.

PHARMACOLOGY

Mode of action

Gliclazide stimulates insulin secretion from functional pancreatic β -cells and increases the sensitivity of the β -cells to a glucose stimulus (some residual β -cell function is therefore necessary). Gliclazide restores the diminished first-phase of insulin secretion noted in non-insulin dependant diabetes mellitus.

Any long-term hypoglycaemic activity of gliclazide can be attributed to an ability to maintain its effect on insulin secretion. Extrapancreatic effects may also be involved in

the long-term efficacy of gliclazide. Extrapancreatic effects demonstrated for gliclazide include improvement in insulin mediated glucose utilisation and potentiation of postreceptor insulin sensitive pathways.

At normal therapeutic doses in man, gliclazide reduces platelet adhesiveness and aggregation.

PHARMACOKINETICS

Absorption

Gliclazide is absorbed in the gastrointestinal tract reaching peak serum concentrations within 4 to 6 hours.

Single dose studies have demonstrated that maximal falls in blood glucose levels (23% of an 80 mg dose; 30% of a 160 mg dose) occur approximately five hours after drug administration; nine hours after a dose of 160 mg, a reduction of 20% was still in evidence.

The half-life of gliclazide is approximately 12 hours.

Distribution

Gliclazide is distributed to the extracellular fluid. In animals, high concentrations of the drug were found in the liver, kidneys, skin, lungs, skeletal muscle, intestinal and cardiac tissue. Penetration of gliclazide into the central nervous system was negligible. Gliclazide crosses the placental barrier and penetrates the foetus. The apparent volume of distribution of gliclazide (20 to 40% expressed as a percentage bodyweight) is low and probably reflects the high degree of protein binding (94.2% at a plasma concentration of approximately 8 µg/mL).

Metabolism and excretion

Little information is available in the metabolism of gliclazide. At least eight metabolites (three major) have been identified by thin layer and gas-liquid chromatography. Some of these are glucuronic acid conjugates; only one of the metabolites has been identified (p-toluene sulfonamide). The liver is the probable site of metabolism.

Approximately 70% of the administered dose appears to be excreted in the urine and 11% in the faeces. The urinary excretion of the drug is slow and the maximum rates do not occur until 7 to 10 hours after initial administration. The metabolic products are detectable in the urine 120 hours after oral administration. Faecal elimination is usually complete within 144 hours of oral administration.

INDICATIONS

Adult onset diabetes mellitus (type 2) that cannot be controlled by diet alone.

CONTRAINDICATIONS

This medication is contra-indicated in the following cases:

- Hypersensitivity to gliclazide, other sulfonylureas, sulfonamides, or to any of the excipients,
- Type I diabetes, diabetic keto-acidosis, diabetic pre-coma,
- Severe renal or hepatic insufficiency,
- Treatment with miconazole (refer to Interactions),
- Pregnancy and lactation (refer to Use in pregnancy and Use in lactation).

PRECAUTIONS

Monitoring of diabetic state

As with other antidiabetic therapies, patients must be under close medical supervision. Particular care must be taken during the initial period of stabilisation. Patients treated with gliclazide should be monitored regularly to ensure optimal control of the diabetic state, and where necessary, for adjustment of dosage.

Transferring to gliclazide

Patients who have been previously treated with sulfonylureas or biguanides alone or in combination may be transferred to gliclazide. When gliclazide is administered as sole therapy to patients who have previously required combination therapy (e.g. biguanides and sulfonylureas), careful observation is essential during the transitional phase. It is not generally recommended that insulin treated patients be transferred to gliclazide.

Patient awareness

Comprehensive instructions must be given to the patient about the nature of the disease and what must be done to detect and prevent complications.

Acute complications such as severe trauma, fever, infection or surgery

These acute complications provoke additional metabolic stress which accentuate the predisposition to hyperglycaemia and ketosis. Patients presenting with such conditions may require insulin to maintain control. It is not appropriate to increase the dosage of gliclazide.

Hypoglycaemia

Close observation and careful initiation and adjustment of dosage is mandatory in patients who are elderly and debilitated, malnourished, semistarved or simply neglecting dietary restrictions. In such patients severe hypoglycaemia may occur with all sulfonylureas and may require corrective therapy over a period of several days. Certain conditions such as alcoholism, insulinoma, adrenal thyroid and pituitary insufficiency increase the sensitivity to sulfonylureas and may dispose to hypoglycaemia.

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 pregnancy (Category C)

It is important to achieve strict normoglycaemia during pregnancy. Oral hypoglycaemic agents should be replaced by insulin. The sulfonylureas may enter the fetal circulation and cause neonatal hypoglycaemia. In animal studies embryo-toxicity and/or birth defects have been demonstrated with some sulfonylureas.

Gliclazide should not be used in pregnant women although animal studies of gliclazide have not shown any teratogenic effect. From a clinical point of view, there are no adequate data to allow evaluation of the possible malformative or foetotoxic effects of gliclazide, when administered during pregnancy.

Use in lactation

In the absence of data on the transfer of gliclazide into breast milk, and given the risk of neonatal hypoglycaemia, breast-feeding is contra-indicated during treatment with this product.

Interactions with other medicines

Disturbances of blood sugar control.

As with all hypoglycaemics, caution should be observed in administering thiazide diuretics to patients on gliclazide therapy, since thiazides have been reported to aggravate the diabetic state. Other drugs which may adversely affect blood sugar control with hypoglycaemic agents in some patients, include barbiturates, chlorpromazine, danazol, glucocorticoids, oestrogens and progestogens, salbutamol, terbutaline.

Potentiation of hypoglycaemic effect

Certain drugs may potentiate the effect of gliclazide and thereby increase the risk of hypoglycaemia.

These include insulin, biguanides, sulfonamides, clofibrate, salicylates, coumarin derivatives, chloramphenicol, MAOI's, β -blockers, cimetidine, ACE inhibitors, fluconazole, miconazole (Note: miconazole is contra-indicated with gliclazide) and nonsteroidal anti-inflammatory agents.

Alcohol

Acute alcohol intoxication potentiates the hypoglycaemic action of all sulfonylurea agents. Furthermore, ingestion of alcohol may cause a disulfiram-like reaction with characteristic flushing of the face, throbbing headache, giddiness, tachypnoea, tachycardia or angina pectoris.

Chronic alcohol abuse may, as a result of liver enzyme induction stimulate the metabolism of sulfonylurea drugs and shorten plasma half life and duration of action.

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.

ADVERSE REACTIONS

Adverse reactions have occurred in some 12% of cases in clinical studies. However, approximately 2% of patients were withdrawn from therapy because of adverse reactions, notably hypoglycaemia, gastrointestinal disturbances (constipation, nausea, epigastric discomfort and heartburn), dermatological reactions (rash and transient itching), and biochemical abnormalities (elevated serum creatinine, increased serum alkaline phosphatase, raised serum AST, elevated BUN and raised serum bilirubin). Headache, slight disulfiram like reactions and lassitude have also been reported.

Serious reactions which have been reported with other sulfonylureas are leucopenia, thrombocytopenia, agranulocytosis, pancytopenia, haemolytic anaemia, cholestatic jaundice and gastrointestinal haemorrhage. These reactions have not been reported with gliclazide.

As is the case with all forms of antidiabetic therapy, hypoglycaemic reactions have occasionally been reported following DIAMICRON administration. Severe hypoglycaemia, though very rarely reported, may occur in patients receiving gliclazide.

DOSAGE AND ADMINISTRATION

The dosage of gliclazide should be carefully titrated to maintain optimal control at the various possible dose levels. Dosage should be initiated at 40mg (1/2 tablet) daily and may be increased if necessary up to 320mg (4 tablets) daily. Doses up to 160mg daily may be taken in a single dose but preferably at the same time each morning. Doses in excess of 160mg should be taken in divided doses in the morning and evening. In general, the dosage will depend on the severity of the glycaemia with ongoing adjustments made in order to obtain the optimal response at the lowest dosage. Treatment with gliclazide does not obviate the necessity of maintaining standard dietary regulations.

OVERDOSAGE SYMPTOMS

Overdose of sulfonylureas may cause hypoglycaemia.

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 should 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 50mL 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 5mmol/L. It is recommended that patients should be monitored closely for a 48 hour period at least.

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.

PRESENTATION AND STORAGE CONDITIONS

Tablets, 80 mg available in 100's blister pack.

The tablets are round and white, with a score on one surface.

Store below 25°C

Glizon has a shelf-life of 36 months

MEDICINE CLASSIFICATION

Prescription medicine

NAME AND ADDRESS OF THE SPONSOR

Douglas Pharmaceuticals Ltd
Central Park Drive
Lincoln Auckland

P O Box 45 027
Auckland 0651

Telephone (09) 835 0660

DATE OF PREPARATION

November 2011