DESCRIPTION

Gliclazide (Glizid) is a second generation sulphonylurea oral hypoglycaemic agent used in the
treatment of non-insulin dependent diabetes mellitus (NIDDM). It has been recommended for use
on the basis of both its metabolic and non metabolic effects. Glizid Tablet BP 40 mg is white to
off-white, round, flat, uncoated, bevel edged tablet, scored on one side and "GLIZID" imprinted on
the other.

COMPOSITION

Each uncoated tablet contains:
Gliclazide BP 40 mg

PHARMACOLOGY

Gliclazide reduces blood glucose levels by correcting both defective insulin secretion and
peripheral insulin resistance. This occurs by closure of $K^+$ channels in the $\beta$-cells of pancreas,
subsequently calcium channels open, leading to increase in intracellular calcium and induction of
insulin release. Gliclazide also increases the sensitivity of $\beta$-cells to glucose. Gliclazide also
restores peripheral insulin sensitivity, such as decreasing hepatic glucose production, and
increasing glucose clearance. Gliclazide also has anti-platelet adhesive activity and reduces
levels of free radicals, thereby preventing vascular complications. Gliclazide also has been
reported to reduce plasma cholesterol and triglyceride levels after repeated administration.

PHARMACOKINETICS

Single oral dose of gliclazide, 80 to 120 mg results in a $C_{\text{max}}$ of 2.2 to 8 mg/l within 2 to 8 hours.
Steady state concentrations are achieved after 2 days of administration of 40-120 mg of
gliclazide. Administration of gliclazide with food reduces $C_{\text{max}}$ and delays $T_{\text{max}}$. The volume of
distribution is low due to extensive protein binding (85-97%). The half life of gliclazide varies from
8.1 - 20.5 hours after single dose administration. Gliclazide is extensively metabolised to 7
metabolites predominantly excreted in the urine, the most abundant being the carboxylic acid
derivative; 60-70% of the dose is excreted in the urine and 10-20% in the faeces.

INDICATIONS
Non-insulin dependent diabetes mellitus; diabetes with or without obesity in adults, diabetes in the elderly, diabetes with vascular complications.

**CONTRAINDICATIONS**

Insulin-dependent diabetes mellitus, diabetic coma, precoma and extreme imbalance with tendency to acidosis, hepatic or renal failure, surgical stress or acute infection.

**WARNINGS**

Hypoglycaemia may occur if the patient's dietary intake is reduced or after accidental or deliberate overdose or after severe exercise, trauma and stress. Hypoglycaemic symptoms can be reduced by prescribing a diabetic meal plan. Immediate intervention should be done if signs and symptoms of hypoglycaemia occur.

**PRECAUTIONS**

Adjust dose of gliclazide according to blood and urinary glucose levels during the first few months. Begin treatment with low doses in patients with renal and/or hepatic impairment.

**Usage in pregnancy**

Contraindicated.

**DRUG INTERACTIONS**

Diuretics, barbiturates, phenytoin, rifampicin, corticosteroids, estrogens, estroprogestogens and pure progestogens may reduce the glycaemic control. Its hypoglycaemic action may be potentiated by salicylates, phenylbutazone, sulphonamides, beta-blockers, clofibric acid, vitamin k antagonist, allopurinol, theophylline, caffeine and monoamine oxidase inhibitors. Concomitant administration of miconazole, perhexilene or cimetidine with gliclazide may result in hypoglycaemia. Concomitant administration of gliclazide with agents that increase blood glucose levels should not be considered without careful monitoring of blood glucose levels to avoid hyperglycaemia.

**ADVERSE REACTIONS**
Gastrointestinal disturbances - Nausea, diarrhoea, gastric pain, constipation and vomiting.
Dermatological effects - Rash, pruritus, urticaria, erythema and flushing.
Miscellaneous - Headache and dizziness.
Gliclazide appears to be associated with a low incidence of hypoglycaemia. Gliclazide may have the potential to produce adverse cardiovascular effects, however gliclazide has been an established agent for the treatment of NIDDM for a number of years without adverse cardiovascular effects.

OVERDOSAGE AND TREATMENT

Hypoglycaemia may occur in case of an overdosage. In the event of an overdosage, gastric lavage should be performed and correction of hypoglycaemia attempted by intravenous adminsitration of hypertonic glucose (10 or 30%) with continued monitoring of the patient's blood glucose levels.

DOSAGE AND ADMINISTRATION

Glisid therapy should be commenced with a total daily dose of 40-80 mg; may be increased to a maximum of 320 mg/day depending on the blood glucose response. Control is obtained in the majority of cases by 160 mg daily. It should be administered with morning and evening meals (i.e. twice daily), if dosage is higher than 160 mg.

STORAGE INSTRUCTIONS

Store in a cool, dry and dark place.

REFERENCES

1. Palmer K J and Brogden RN
   Gliclazide - An update of its pharmacological properties and therapeutic efficacy in Non-Insulin-Dependent diabetes mellitus.
   Drugs, 1993; 46(1): 92-125