PRODUCT MONOGRAPH

GLIZID

(Gliclazide)

40mg/ 80mg tablets

Hypoglycemic sulfonylurea - Oral antidiabetic agent

Manufactured By:

Panacea Biotec Limited.

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PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	**Dosage Form / Strength**	**Approved Indications**
Oral	One tablet contains gliclazide 40 mg/ 80 mg	Non insulin Dependent diabetes (type2) in adults

INDICATIONS AND CLINICAL USE

Non insulin-dependent diabetes (type 2) in adults when dietary measures, physical exercise and weight loss alone are not sufficient to control blood glucose.

CONTRAINDICATIONS

Gliclazide should not be used in:

- Juvenile onset diabetes.
- Diabetes complicated by ketosis and acidosis.
- Pregnancy.
- Diabetics undergoing surgery, after severe trauma or during infections.
- Patients known to have hypersensitivity to other sulphonylureas and related drugs or any of the other tablet ingredients.
- Diabetic pre-coma and coma.
- Severe renal or hepatic insufficiency.

WARNINGS AND PRECAUTIONS

- Hypoglycaemia: all sulphonylurea drugs are capable of producing moderate or severe hypoglycaemia, particularly in the following conditions:

- in patients controlled by diet alone,
- in cases of accidental overdose,
- when calorie or glucose intake is deficient,
- in patients with hepatic and/or renal impairment; however, in long-term clinical trials, patients with renal insufficiency have been treated satisfactorily, using gliclazide at reduced doses.

In order to reduce the risk of hypoglycaemia it is therefore recommended:

- to initiate treatment for non-insulin dependent diabetics by diet alone, if this is possible,
- to take into account the age of the patient: blood sugar levels not strictly controlled by diet alone might be acceptable in the elderly,

- to adjust the dose of gliclazide according to the blood glucose response and to the 24 hour urinary glucose during the first days of treatment.

Dosage adjustments may be necessary:

- on the occurrence of mild symptoms of hypoglycaemia (sweating, pallor, hunger pangs, tachycardia, sensation of malaise). Such findings should be treated with oral glucose and adjustments made in drug dosage and/or meal patterns,

- on the occurrence of severe hypoglycaemic reactions (coma or neurological impairment, see overdose),

- loss of control of blood glucose (hyperglycaemia). When a patient stabilised on any diabetic regimen is exposed to stress such as fever, trauma, infection or surgery, a loss of control may occur. At such times, it may be necessary to increase progressively the dosage of gliclazide and if this is insufficient, to discontinue the treatment with gliclazide and to administer insulin. As with other sulphonylureas, hypoglycaemia will occur if the patients' dietary intake is reduced or if they are receiving a larger dose of gliclazide than required.

- Care should be exercised in patients with hepatic and/or renal impairment and a small starting dose should be used with careful patient monitoring.

ADVERSE REACTIONS

Based on the experience with gliclazide, the following undesirable effects have been reported.

Hypoglycaemia

As for other sulfonylureas, treatment with Gliclazide can cause hypoglycaemia, if mealtimes are irregular and, in particular, if meals are skipped. 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, paresis, sensory disorders, dizziness, feeling of powerlessness, loss of self-control, delirium, convulsions, shallow respiration, bradycardia, drowsiness and loss of consciousness, possibly resulting in coma and lethal outcome.

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 carbohydrates (sugar). However, artificial sweeteners have no effect. Experience with other sulphonylureas shows that hypoglycaemia can recur even when measures prove effective initially.

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 are required.

Gastrointestinal disturbances, including abdominal pain, nausea, vomiting dyspepsia, diarrhoea, and constipation have been reported: if these should occur they can be avoided or minimised if gliclazide is taken with breakfast.

The following undesirable effects have been more rarely reported:

• Skin and subcutaneous tissue disorders: rash, pruritus, urticaria, angioedema, erythema, maculopapular rashes, bullous reactions (such as Stevens-Johnson syndrome and toxic epidermal necrolysis).

• Blood and lymphatic system disorders: Changes in haematology are rare. They may include anaemia, leucopenia, thrombocytopenia, granulocytopenia. These are in general reversible upon discontinuation of medication.

• Hepato-biliary disorders: raised hepatic enzyme levels (AST, ALT, alkaline phosphatase), hepatitis (isolated reports). Discontinue treatment if cholestatic jaundice appears.

These symptoms usually disappear after discontinuation of treatment.

• Eye disorders

Transient visual disturbances may occur especially on initiation of treatment, due to changes in blood glucose levels.

• Class attribution effects:

As for other sulphonylureas, the following adverse events have been observed: cases of erythrocytopenia, agranulocytosis, haemolyticanaemia, pancytopenia, allergic vasculitis, hyponatraemia, elevated liver enzyme levels and even impairment of liver function (e.g. with cholestasis and jaundice) and hepatitis which regressed after withdrawal of the sulfonylurea or led to life-threatening liver failure in isolated cases.

DRUG INTERACTIONS

Care should be taken when giving gliclazide with drugs which are known to alter the diabetic state or potentiate the drug's action.

The hypoglycaemic effect of gliclazide may be potentiated by phenylbutazone, salicylates, sulphonamides, coumarin derivatives, MAOIs, beta adrenergic blocking agents, tetracycline compounds, chloramphenicol, clofibrate, disopyramide, miconazole (oral forms) and cimetidine.

It may be diminished by corticosteroids, oral contraceptives, thiazide diuretics, phenothiazine derivatives, thyroid hormones and abuse of laxatives.

DOSAGE AND ADMINISTRATION

Adults:

The total daily dose may vary from 40 to 320 mg taken orally. The dose should be adjusted according to the individual patient's response, commencing with 40-80 mg daily (1/2 - 1 tablet) and increasing until adequate control is achieved. A single dose should not exceed 160 mg (2 tablets). When higher doses are required, gliclazide should be taken twice daily and according to the main meals of the day.

In obese patients or those not showing adequate response to gliclazide alone, additional therapy may be required.

Elderly:

Plasma clearance of gliclazide is not altered in the elderly and steady state plasma levels can therefore be expected to be similar to those in adults under 65 years. Clinical experience in the elderly to date shows that gliclazide is effective and well tolerated. Care should be exercised, however, when prescribing sulphonylureas in the elderly due to a possible age-related increased risk of hypoglycaemia.

Children:

Gliclazide as with other sulphonylureas, is not indicated for the treatment of juvenile onset diabetes mellitus.

OVERDOSAGE

Taking too much of any medicine can be dangerous. If you take too many GLICLAZIDE tablets at once, call your doctor or your nearest poison control center, or go to the emergency room of your local hospital.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Gliclazide is a hypoglycemic agent of the sulfonylurea group. The hypoglycemic action of Gliclazide is related to an improvement in insulin secretion from the functioning beta cells of the pancreas. It potentiates the insulin release, improves the dynamics of insulin. Increase in postprandial insulin and C-peptide secretion persists after two years of treatment. Gliclazide has extra-pancreatic actions. These metabolic actions are accompanied by hemovascular effects. However, the mechanism of action regarding these effects is still poorly understood. The clinical significance of these effects has not been established.

Effects on insulin release. In type 2 diabetics, 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 response is seen in response to stimulation induced by a meal or glucose.

Extra-pancreatic effects. It has been demonstrated that gliclazide increases peripheral insulin sensitivity:

– In muscle: the action of insulin on glucose uptake, measured during an euglycemic hyperinsulinemic clamp is significantly increased (+35%), due to an improvement in peripheral sensitivity to insulin. This leads to an improvement in diabetes control. Gliclazide acts mainly by potentiating insulin action on muscle glycogen synthetase. Moreover, results of studies on the muscle are consistent with a post-transcriptional action of gliclazide on GLUT4 glucose carriers;

– In the liver: studies on glucose turnover show that gliclazide decreases hepatic glucose production, leading to an improvement in fasting blood glucose levels.

Hemovascular effects. Gliclazide decreases microthrombosis by two mechanisms which may be involved in complications of diabetes:

– A partial inhibition of platelet aggregation and adhesion, with a decrease in the markers of platelet activation (beta thromboglobulin, thromboxane B2):

– A restoration of the vascular endothelium fibrinolytic activity with an increase in t-PA activity.

Antioxidant effects.A controlled clinical study in diabetics has confirmed the antioxidant effects of gliclazide that were already demonstrated in clinical pharmacology: reduction in plasma levels of lipid peroxides, increase in the activity of erythrocyte superoxide dismutase.

Pharmacodynamics

Gliclazide is a hypoglycaemic sulphonylurea differing from other related compounds by the addition of an azabicyclo-octane ring.

In man, apart from having similar hypoglycaemic effect to the other sulphonylureas, gliclazide has been shown to reduce platelet adhesiveness and aggregation and increase fibrinolytic activity. These factors are thought to be implicated in the pathogenesis of long-term complications of diabetes mellitus.

Gliclazide primarily enhances the first phase of insulin secretion, but also to a lesser degree its second phase. Both phases are diminished in non-insulin dependent diabetes mellitus.

Pharmacokinetics

The drug is well absorbed and its half-life in man is approximately 10-12 hours. Gliclazide is metabolised in the liver; less than 5% of the dose is excreted unchanged in the urine.

Preclinical safety data

No data of relevance which is additional to that already included in other sections of the SPC.

STORAGE AND STABILITY

Keep out of reach or sight of children and pets.

GLICLAZIDE should be stored at temperature below 30ºC, protect from light and moisture.

Medicines should not be disposed of down the drain or in household garbage. Ask your pharmacist how to dispose of medicines no longer

SPECIAL HANDLING INSTRUCTIONS

No special requirements.

DOSAGE FORMS, COMPOSITION AND PACKAGING

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

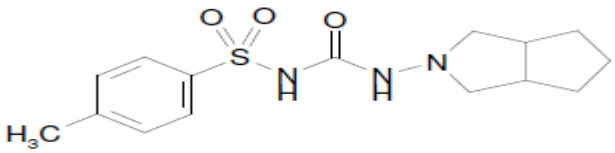
Proper name: Gliclazide

Chemical name: 1-(3-Azabicyclo [3.3.0]-oct-3-yl)-3-(p-tolylsulfonyl) urea

Molecular formula: C15H21N3O3S

Molecular mass: 323.42

Structural formula:



Physicochemical properties: Physical form: white, crystalline powder

Solubility: Practically insoluble in water; freely soluble in dichloromethane; sparingly soluble in acetone.

pKa: 5.8

Partition Coefficient:	pH %	gliclazide in organic phase(water/CHCl3)
	0 to 7	almost 100%
	8.6	80%
	9.0	55%
	10.0	12%

Melting Point: Approximately 168°C

DETAILED PHARMACOLOGY

ANIMAL PHARMACOLOGY

Pharmacokinetics and Metabolism

This has been studied in four animal species (monkey, dog, rabbit and rat) after single or repeated oral administration of gliclazide. The principal characteristics are shown in the table below.

BLOOD KINECTICS OF GLICLAZIDE (PO) IN DIFFERENT SPECIES (SINGLE DOSES)							
Species	Number of subject (doses)	Absorption T_2 (h)	Plasma peak (h)	Volume of distribution (% body weight)		Plasma half- time (h)	
Monkey	4 3 and 50 mg/kg	0.3[1]	1-2[1]	24.4[1]	108[4]	2.9[1]	6.2[4]
Beagle	3 3 and 50 mg/kg	0.7[1]	2-6[1]	21.3[1]	22[4]	10.7[1]	9.9[4]

Rabbit	5 10-25 mg/kg	0.7[2]	3[2]	30.8[2]	50.8[3]	3.9[2]	5.9[3]
Rat	5 10mg/kg	0.5[2]	1[2]	53.8[2]	-	2.5[2]	-

[1] = 3mg/kg PO [2] = 10mg/kg PO

[3] = 25mg/kg PO [4] = 50mg/kg PO

Gliclazide is rapidly absorbed in all species, with a plasma peak observed between 1 and 6 hours. More than 90% of gliclazide is found unchanged in the plasma. Elimination from plasma is monophasic with inter-species variations concerning half-life. Excretion is similar in all species with 60 to 70% of the dose found in urine and 10 to 20% in feces.

The drug is extensively metabolized into at least 5 metabolites and only small amounts of unchanged compound are excreted in the urine.

Hypoglycemic activity

The hypoglycemic action of gliclazide has been observed in the rat, rabbit, guinea pig and dog following intravenous or oral administration. The degree and duration of these effects are dose dependent. Comparison of ED 30 shows that gliclazide is 9 times more active than tolbutamide in the rabbit and 25 times more active in the rat.

The duration of action of gliclazide is also greater than that of tolbutamide. Gliclazide stimulates the insulin secretion and particularly restores the early peak in the isolated perfused pancreas of diabetic rats. This insulinotropic action is related to the transfer of calcium into the pancreatic cell. Gliclazideis not involved in the biosynthesis of insulin induced by glucose but modifies the distribution of calcium in isolated rat pancreas cells.

At the extrapancreatic level, gliclazidepotentialises the action of insulin on the glucose intracellular transfer and influences its oxidation on an isolated adipocyte model when insulin is present in the medium.

Hemovascular activity

Gliclazide delays the development of the mural thrombus formed after electrical lesion of the vascular endothelium in the rat and increases its disaggregation speed.
In dog, gliclazide prevents the formation of capillary ADP-induced platelet aggregates at the retinal level.

These properties can be explained by its action on:

– the platelet behavior: reduction of the platelet adhesiveness in the diabetic rabbit and of platelet aggregation induced by ADP or by collagen in the rabbit;
– the prostaglandin equilibrium: inhibition of the acid arachidonic release and in vitro thromboxan synthesis and increase in the PGI2 production;
– the parietal fibrinolysis: increase in the release of the parietal plasminogen activator (t-PA).

This activator of endothelial origin, acts on plasmin which is the enzyme degrading fibrin.

Gliclazide improves vascular function in diabetic animals by preventing the abnormal contracting effect of acetylcholine after NO synthesis inhibition. Protective properties of gliclazide on capillary permeability have also been demonstrated in the cheek pouch model in streptozotocin-diabetic Syrian hamsters.

Long-term treatment of diabetic sand rats with gliclazide prevents development of arterial lesions.

Other actions

Gliclazide has no action on the central nervous system, autonomic nervous system norrespiratory, gastro-intestinal systems. Treatment of streptozotocin-diabetic rats with gliclazide has shown a significant improvement in heart function.

TOXICOLOGY

ACUTE TOXICITY

The LD50 is greater than 3000 mg/kg in the mouse, rat and dog (i.e. 300 times the therapeutic dose) and more than 2000 mg/kg in the guinea-pig (i.e. 500 times the therapeutic dose).
Symptomatology is essentially linked to the hypoglycemic effect of the drug.

SUB-CHRONIC TOXICITY

– Maximum tolerated dose:

In the dog, this dose is between 150 and 200 mg/kg by daily administration.

– Four-week oral toxicity study in the Beagle dog:

Groups of 4 Beagle dogs (2 males, 2 females), were treated for 30 days with 0, 15, 30, 45 or 90 mg/kg/day. At the dose of 90 mg/kg, 2 animals died as a result of prolonged hypoglycemic coma following 2 weeks of treatment. All others showed normal behaviour, with the exception of an increase in the weight of the liver. No evidence was found of any change in biochemical (apart from the fall in blood glucose), hematological and histopathologicalparameters.

– Two-month oral toxicity study in the guinea-pig:

Groups of 10 guinea-pigs (5 males, 5 females), were treated 6 days out of 7 for 2 months with 0, 25, 50 or 100 mg/kg/day. Only male animals in the 50 mg/kg group showed delayed weight gain. All others had normal biochemical, hematological and histopathological results.

CHRONIC TOXICITY

– Six-month study in the Sprague-Dawley rat:

Groups of 20 rats (10 males, 10 females) weighing 300 g, were treated for 6 days out of 7 for 6 months with 0, 25, 100 or 200 mg/kg/day. Seven deaths occurred as a result of technical problems. All other animals showed normal behaviour andhaematological results. From a biochemical standpoint, blood urea decreased significantly in the male rats as did blood glucose in the males of the 100 mg/kg/day group. Histological examination showed an increase in the weight of the liver and kidneys in male animals, not accompanied by any histological lesion.

A six-month rat study carried out in Japan with higher doses (50, 100, 200, 400 and 800 mg/kg) indicates a possible higher sensibility in the female to the product: slight increases in liver enzymes together with slight decreases in erythrocytes counts, hematocrit values and hemoglobin concentrations at doses of 200 mg/kg and higher.

– Six-month study in the Beagle Dog

Groups of 6 dogs (3 males, 3 females) were treated daily for 6 months with 15 or 30 mg/kg ofgliclazide or 50 mg/kg of tolbutamide.

From a clinical standpoint:

- 3 deaths (one at 15 mg/Kg, two at 30 mg/Kg) in the gliclazide group as a result ofhypoglycemic coma;
- 1 convulsion, 4 cases of severe gastro-intestinal disturbances in the tolbutamide group;
- Weight changes and food consumption were similar with both drugs.
  From a laboratory standpoint:
- 40% fall in blood glucose in animals treated with gliclazide.
- Signs of hepatotoxicity in the tolbutamide group.
  From a histological standpoint:

- Increase in weight of the liver in the 3 deaths of the gliclazide group.
- Increase in the weight of the liver and lesions of toxic hepatitis in 5 animals out of 6 of the tolbutamide group.

– Twelve-month oral toxicity study in the Beagle Dog

Groups of 8 dogs (4 males, 4 females) were treated for 12 months with 0, 12 or 24 mg/kg/day of gliclazide. Four animals in each group were sacrificed after 90 days.

- There were no deaths;
- No evidence of any modification in behaviour and body weight;
- Significant fall in blood glucose;
- Fluctuation in certain parameters (liver enzymes, lipid profile, creatinine);
- At autopsy: swelling of the renal and hepatic parenchyma and at the highest dose a slight increase in the weight of the thyroid and slight decrease in the weight of the pituitary gland.

– Twelve-Month Oral Toxicity Study in the Rhesus Monkey

Groups of 8 rhesus monkeys (4 males, 4 females) were treated daily for 12 months with 0, 20, 60 or 180 mg/kg of gliclazide.

- No evidence was found of any modification in weight gain nor food consumption;
- Significant fall in blood glucose;
- Irregular rise in some liver enzymes in some animals;
- No abnormality by histopathological examination.

Teratogenicity

Teratogenicity studies have been carried out in three species: mouse, rat and rabbit.

– In the CD/SPF mouse (group of 30 females), administration of gliclazide at doses of 0, 50, 200 and 500 mg/kg/day starting from mating and throughout gestation did not modify fertilization and abortion rates and had no apparent teratogenic effect.

– In the CFY-SPF rat (groups of 20 females), administration of gliclazide at doses of 0, 50, 100 and 200 mg/kg/day from the 6th to the 15th day of gestation did not show any embryotoxiceffect.

– In the SD/SPF rat (groups of 60 females), administration of gliclazide at the doses of 0, 15, 30, 60, 120, 240 and 480 mg/kg/day throughout gestation had no effect on fertilization, gestation, mean number of fetuses or incidence of fetal abnormalities. The number of offspring surviving at 48 hours was decreased in the 15, 60, 120 and 480 mg/Kg groups. No other abnormality was seen.

– In the common rabbit (group of 15 females), administration of gliclazide at doses of 0, 10, 25 and 50 mg/kg/day from the 6th to the 18th day of gestation had no effect on the number of fetal resorptions, percentage of abortion nor the mean number of fetuses per litter.

– In the New Zealand rabbit (group of 6 females), administration of gliclazide at doses of 0, 50, 75, 100 and 200 mg/Kg/day for 13 days followed by an observation period of 8 days, was associated with maternotoxicity and embryotoxicity in the form of gastro-intestinal and renal lesions accompanied by anorexia and weight loss. However, there was no evidence of any teratogenic effect.

Fertility and reproduction

– In the SD rat, groups of 40 females and of 20 males were treated for 8 and 70 days respectively, before mating and until weaning in the females, and until 15 days after littering in the males, with gliclazide at doses of 0, 10, 50 and 200 mg/Kg/day. There was no evidence of any change in fertilization nor abortion rates. Fetal resorption, placental hemorrhage and fetal atrophy rates were unaffected. The genital tract of treated parents showed no abnormality imputable to treatment. Noembryotoxic effect was seen on fetuses of females sacrificed before littering. In females in which

gestation was allowed to run to term, a significant decrease in the viability of offspring was seen at 48 hours. No abnormality was seen during the study of fertility and reproduction in first generation offspring born of treated animals.

Mutagenicity of gliclazide

The mutagenic potential of gliclazide has been sought using six mutagenesis tests, i.e.:

– 2 gene mutation tests (Ames test);
– 1 in vitro chromosomal aberration test (human lymphocyte test);
– 2 in vivo chromosomal tests (micronucleus test);
– 1 unscheduled DNA synthesis test.

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PART III: PATIENT INFORMATION

GLIZID

(Gliclazide)

40mg/ 80mg tablets

This leaflet is part III of a three-part "Product Monograph" published when GLIZID was approved for sale in India and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about GLIZID Contact your doctor or pharmacist if you have any questions about the drug.

Generic Name: Gliclazide tablets

- **What the medication is used for**
- **What it does**
- **When it should not be used**
- **What the medicinal ingredient is**
- **What the important nonmedicinal ingredients are**
- **What dosage forms it comes in**
- **BEFORE you use GLIZID talk to your doctor or pharmacist if**
- **Drugs that may interact with GLIZID include**
- **Overdose**
- **Missed Dose**

What the medication is used for:

GLIZID is used to lower blood glucose level in adult patients with type 2 diabetes mellitus in addition to proper diet, exercise and weight reduction.

What it does:

GLIZID belongs to the family of hypoglycemic (antidiabetic) drugs and part of a sub family of medicines called sulfonylureas. It helps improving insulin secretion in the body.

When it should not be used:

GLIZID is contraindicated (must not be taken):

• If you are allergic or hypersensitive to gliclazide, other sulfonylureas, sulfonamides, or to any of the excipients of this product.
• If you have unstable and/or insulin-dependantdiabetes mellitus, juvenile diabetes (type I diabetes), diabetes ketoacidosis, diabetes pre-coma and coma.
• If you are in stressful conditions such as serious infection, trauma or surgery.
• If you have severe liver disease or renal impairment.
• If you receive treatment with miconazole.
• If you are pregnant and/or breast-feeding.

What the medicinal ingredient is:

Gliclazide

What the important nonmedicinal ingredients are:

Colloidal silicon dioxide, hydroxypropyl methylcellulose and stearic acid

What dosage forms it comes in:

GLIZID comes in modified release tablets. Each tablet contains 40mg/ 80mg of gliclazide.

BEFORE you use GLIZID talk to your doctor or pharmacist if:

GLIZID may cause low blood sugar (hypoglycemia).

You should ask your doctor, pharmacist or diabetes educator about symptoms of low blood sugar and what to do if you experience these symptoms. You should also test your blood sugar as instructed by your doctor.

Before you use GLIZID talk to your doctor or pharmacist if:

• you have or have had liver, kidney disease
• you are pregnant or planning to get pregnant
• you are breast-feeding

GLIZID is not recommended for use in children under 18 years of age.

Driving and Operating Machinery:

Alertness and reactions may be impaired due to low blood sugar (hypoglycemia), especially at beginning of the treatment. This may affect your ability to drive or to operate machinery.

Drugs that may interact with GLIZID include:

Other antidiabetic agents (insulin, alpha glucosidase inhibitors, biguanides), long-acting sulfonamides, tuberculostatics, NSAIDs, fibrates, monoamine oxidase inhibitors, salicylates, probenecid, beta-blockers, azole antifungal agents (miconazole and fluconazole via oral and parenteral preparations), H2 receptor antagonists and angiotensin converting enzyme inhibitors, anticoagulants, and barbiturates.

Certain drugs tend to induce hyperglycemia and may lead to loss of blood sugar control. These include diuretics (thiazides, furosemide), corticosteroids, oral contraceptives (estrogen plus progestogen), chlorpromazine, ritodrine, salbutamol, terbutaline, danazol and nicotinic acid in pharmacologic doses.

Do not take any other medicine, unless prescribed or approved by your doctor. If you require medical assistance, inform the medical practitioner that you are taking GLIZID.

Avoid drinking alcoholic beverages and taking medicines containing alcohol while you are taking GLIZID as it can lead to drop in blood sugar (hypoglycemia).

Usual dose:

The recommended starting dose of GLIZID is 1 tablet per day (40mg/ 80mg), even in elderly patients (over 65 years old). The daily dose should not exceed 120 mg.

Take GLIZID once daily at breakfast. Swallow the tablet whole with a glass of water. The tablet must not be chewed or crushed.

You will test your sugar level as directed by your physician to make sure that your blood sugar is being controlled. Your physician should check your progress at regular visits, especially during the first few weeks that you take this medicine.

Overdose:

Taking too much of any medicines can be dangerous. If you take too many GLIZID tablets at once, call your doctor or go to the emergency room of your local hospital or to the nearest Poison Control Centre.

Missed Dose:

If you miss a dose of this medicine, you should not double the dose on the next day.

As with any type of medication, GLIZID is associated with some side effects. It may, however, affect different people in different ways.

The more frequently side effects reported during clinical trials with GLIZID were hypoglycemia (low blood sugar) and indigestion or stomach upsets (diarrhea, constipation, nausea, vomiting, gastritis, flatulence, dyspepsia).

You should know that the usual signs of low blood sugar level (hypoglycemia) are: anxious feeling, drowsiness, chills, cold sweats, confusion, cool pale skin, difficulty in concentration, excessive hunger, fast heartbeat, headache, nausea, nervousness, shakiness, unsteady walk, unusual tiredness or weakness. If you recognize by some of these signs of the drop in blood sugar, immediately eat or drink something containing sugar and notify your doctor without delay. Good sources of sugar are: orange juice, corn syrup, honey, or sugar cubes or table sugar (dissolved in water).

This product monograph, prepared for health professionals can be found at:

(Panacea Biotec Web site)

or by contacting the Panacea Biotec Limited (INDIA)

(Address for correspondence)

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