GLIMIN TABLETS 2mg
Glimepiride 2mg

Description
Green colour, oblong shaped with flat surface tablet.

Composition
Each tablet contains Glimepiride 2mg

Mode of action
Glimepiride is a sulfonylurea. Glimepiride decreases blood glucose concentration mainly by stimulating insulin release from pancreatic beta cells. This effect is based predominantly on an improved responsiveness of the pancreatic beta cells to the physiological glucose stimulus.

Glimepiride also has extra pancreatic (insulin-sensitizing and insulin-mimetic) effects.
The effect of Glimepiride is dose-depended over the dose range of 1 to 6mg. The physiological response to acute physical exercise, i.e. reduction of insulin secretion, is still present with Glimepiride.

Summary of pharmacodynamics and pharmacokinetics
There was no significant difference in effect regardless of whether the drug was given 30 minutes or immediately before a meal. In diabetic patients, metabolic control over 24 hours can be achieved with a single dose.

The absolute bioavailability of Glimepiride is complete. Food intake has no relevant influence on absorption. Maximum serum concentrations are reached approximately 2.5 hours after oral intake and there is a linear relationship between dose and both maximum concentration and area under the time/concentration curve.

Glimepiride has a high protein binding (>99%). Mean dominant serum half-life, which is of relevance for the serum concentration under multiple-dose conditions, is about 5 to 8 hours. After single dose radio labelled Glimepiride, 58% of the radioactivity was recovered in the urine, and 35% in the faeces. No unchanged substance was detected in the urine.

Pharmacokinetic was similar in males and females, as well as in young and elderly patients.

Indications
Glimepiride is indicated as an adjunct to diet and exercise in Non-insulin-dependent (type II) diabetes, whenever blood sugar levels cannot be controlled adequately by diet, physical exercise and weight reduction alone. Glimin may also be used in combination with an oral antidiabetic containing metformin or with insulin.

Adverse reactions/side effects
Hypoglycaemia
Hypoglycaemia (sometimes life-threatening) may occur as a result of the blood-glucose-lowering action of Glimepiride. This happens when there is an imbalance between Glimepiride dosage, carbohydrate intake (Diet), physical exercise and other factors influencing metabolism.
Possible symptoms of hypoglycaemia include headache, ravenous hunger, nausea, vomiting, lassitude, sleepiness, sleep disorders, restlessness, aggressiveness, impaired concentration, impaired alertness and reactions, depression, confusion, speed disorders, aphasia, visual disorders, tremor, paresis, sensory disturbances, dizziness, helplessness, loss of self-control, delirium, cerebral convulsions, somnolence and 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 sin, anxiety, tachycardia, hypertension, palpitations, angina pectoris and cardiac arrhythmias. The clinical picture of a severe hypoglycaemic attack may resemble that of a stroke. The symptoms of hypoglycaemia may persist if hypoglycaemia is corrected.

Eyes
Especially at the start of treatment there may be temporary visual impairment due to the changes 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.

Digestive tract
Occasionally, gastrointestinal symptoms such as nausea, vomiting, sensations of pressure or fullness in the epigastrium, abdominal pain and diarrhea may occur. In isolated cases, there may be elevation of liver enzyme levels, impairment of liver function (e.g. with cholestasis and jaundice) and hepatitis which may also lead to life-threatening liver failure.

Blood
Potentially life-threatening changes in the blood picture may occur, such as thrombocytopenia and in isolated cases, leucopenia. Glimepiride in addition to the above, may cause haemolytic anaemia or erythrocytopenia, granulocytopenia, agranulocytosis and (e.g. due to myelosuppression) pancytopenia.
Allergic or pseudoallergic reactions may occur such as itching, urticaria or rashes. These mild reactions may develop into serious and even life-threatening reactions with dyspnoea and a fall in blood pressure, sometimes progressing to shock. In the event of urticaria a physician must therefore be notified immediately.

In isolated cases, a decrease in serum sodium concentration has been seen and allergic vasculitis or hypersensitivity of skin to light may occur.

If any of these reactions occur a doctor should be consulted.

Alertness and reactions may be impaired due to hypo – or hyperglycaemia, especially when beginning or after altering treatment or when Glimepiride is not taken regularly. This may for example, affect the ability to drive or to operate machinery.

Precautions/warnings
SPECIAL WARNING ON INCREASED RISK OF CARDIOVASCULAR MORTALITY. The administration of oral hypoglycaemic drugs has been reported to be associated with increased cardiovascular mortality as compared to treatment with diet alone or diet plus insulin. This warning is based on the study conducted by the University Group Diabetes Program (UGDP), a long-term, prospective clinical trial designed to evaluate the designed the evaluate the effectiveness of glucose-lowering drugs in preventing or delaying vascular complications in patients with non-insulin-dependent diabetes. The study involved 823 patients who were randomly assigned to one of four treatment group. UGDP reported that patients treated for 5 to 8 years with diet plus a fixed dose of tolbutamide (1.5 grams per day) had a rate of cardiovascular mortality approximately 2-1/2 times that of patients treated with diet alone. A significant increase in total mortality was not observed but the use of tolbutamide was discontinued based on the increase in cardiovascular mortality, thus limiting the opportunity for the study to shown an increase in overall mortality.
Despite controversy regarding the interpretation of these results, the findings of the UGDP study provide an adequate basis for this morning. The patient should be informed of the potential risks and advantages of Glimepiride (Glimepiride tablets) and of alternative modes of therapy. Although only one drug in the sulfonylurea class (tolbutamide) was included on this study, it is prudent from a safety standpoint to consider that this warning may also apply to other oral hypoglycaemic drugs in this class. In view of their close similarities in mode of action and chemical structure.

Glimepiride can encourage weight gain and should be prescribed only if poor control and symptoms persist despite adequate attempts at dieting.

Special precautions
Treatment with Glimepiride must be initiated and monitored by a physician. The patient must take Glimepiride at the times and in the doses prescribed by the doctor, normally at the same time every day. To achieve the goal of treatment of Glimepiride – optimal control of blood glucose - adherence to correct diet, regular and sufficient physical exercise and if necessary, reduction of body weight are just as necessary as regular ingestion of Glimepiride.

Clinical signs of still insufficiently lowered blood glucose (hyperglycaemia) are e.g. increased urinary frequency (polyuria), intense thirst, dryness of the mouth and dry skin.
In the initial weeks of treatment the risk of hypoglycaemia may be increased and necessitates especially careful monitoring.

Factors favouring hypoglycaemias include:
- Unwillingness or (more commonly in older patients) incapacity of the patient to co-operate.
- Undernourishment, irregular meal times or skipped meals.
- Imbalance between physical exertion and carbohydrate intake.
- Alteration of diet.
- Consumption of alcohol, especially in combination with skipped meals.
- Impaired renal function.
- Severe impairment of liver function.
- Overdosage with Glimepiride.
- Certain uncompensated disorders of the endocrine system affecting carbohydrate metabolism or counter-regulation of hypoglycaemia (as for example in certain disorders of thyroid function and in anterior pituitary or corticoadrenal insufficiency).
- Concurrent administration of certain other medicines.
- Treatment with Glimepiride in the absence of any indication.
- The patient must inform the physician about such factors and about hypoglycaemic episodes since they may indicate the need for particularly careful monitoring. If such risk factors for hypoglycaemia are present, it may be necessary to adjust the dosage of Glimepiride or the entire therapy. This also applies whenever illness occurs during therapy or the patient's life-style changes.
  Those symptoms of hypoglycaemia which reflect the body's adrenergic counter-regulation (refer to "Adverse effects") may be milder or absent where hypoglycaemia develops gradually, in the elderly and where there is autonomic neuropathy or where the patient is receiving concurrent treatment with beta-blockers, clonidine, reserpine, guanethidine or other sympatholytic drugs.
  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 sugar sweetened tea). For this purpose patients must carry a minimum of 20 grams of glucose with them at all times. They may require the assistance of other persons to avoid complications. Artificial sweeteners are ineffective in controlling hypoglycaemia.
  It is known from other sulfonylureas that, despite initially successful countermeasures, hypoglycaemia may recur. Patients must therefore remain close observation. Severe hypoglycaemia further requires immediate treatment and follow-up by a physician and in some circumstances, in patient hospital care.

In exceptional stress situations (e.g. trauma, surgery, febrile infections) blood glucose regulation may deteriorate and a temporary changes to insulin may be necessary to maintain good metabolic control.
Insulin is the treatment of choice for non-insulin dependent diabetes mellitus (NIDDM) with renal and hepatic dysfunction. No experience has been gained concerning the use of Glimepiride in patients with impairment of liver function. In patient with severe impairment of renal function, changes over to insulin is indicates, to achieve optimal metabolic control. (See contra-indications).

Contraindications
Glimepiride must not be used in patient hypersensitive to Glimepiride, other sulphonylureas, and other sulfonamides. Glimepiride should not be use while breastfeeding and insulin therapy should be substituted during pregnancy. Glimepiride should be avoided where possible in severe hepatic and renal impairment and in porphyria.

Dosage and directions for use
Glimin Tablets 2mg are take orally.

In principle, the dosage of Glimepiride is determined by the desired blood glucose level. The dosage of Glimepiride must be the lowest which is sufficient to achieve the desired metabolic control.
Treatment with Glimepiride must be initiated and monitored by a doctor. Glimepiride must be taken at the times and in the doses prescribed. During treatment with Glimepiride glucose levels in blood and urine must be measured regularly. In addition, it is recommended that regular determinations of the proportion of glycated haemoglobin be carried out.

If a patient forgets to take a dose, this must never be corrected by subsequently taking a larger dose. Measures for dealing with such situations (in particular forgetting a dose or skipping a meal) where a dose cannot be taken at the prescribed time must be discussed and agreed between physician and patient beforehand.

If it is discovered that too high a dose or an extra dose of Glimepiride has been taken, a physician must be notified immediately.
Initial dose and titration
The usual initial dose is 1mg Glimepiride once daily.
If necessary the daily dose can be increased. It is recommended that the increase be guided by regular blood glucose monitoring and that the dose be increased gradually i.e. at intervals of one to two weeks and according the following dose steps: 1mg-2mg-3mg-4mg-6mg. Daily doses of more than 6mg are more effective only in minority of patients. A maximum of 8mg day may not be exceeded.

Dose range in patient with well controlled diabetes:
Usual daily doses in patient with well controlled diabetes are 1 to 4 mg Glimepiride.
Distribution of doses:
Timing and distribution of doses are to be decided by the physician, taking into consideration the patient's current life-style.
Normally a single daily dose of Glimepiride is sufficient.
It is recommended that this dose be taken immediately before a substantial breakfast or-if none is taken- immediately before the first main real.
It is very important not to skip meals after the tablet(s) have been taken.

Secondary dosage adjustment:
An improvement in the control of diabetes is associated with higher insulin sensitivity therefore Glimepiride requirement may fall as treatment proceeds. To avoid hypoglycaemia, dose reduction or cessation of Glimepiride therapy must therefore be considered in time. Correction of dosage must also be considered whenever the patient's weight changes, the patients lifestyle changes or other factors arise which cause an increased susceptibility to hypoglycaemia or hyperglycaemia (refer to "Special Precautions").

Duration of treatment:
Treatment with Glimepiride is normally long-term therapy.

Changes-over from other oral antidiabetics to Glimepiride:
There is no exact dosage relationship between Glimepiride and other oral antidiabetics. When substituting Glimepiride for other oral antidiabetics, it is recommended that the procedure be the same as for initial dosage, starting with daily doses of 1mg. This applies even in case where the patient is being switched from the maximum dose of another oral antidiabetic.

Use in pregnancy and lactation
Pregnancy
Glimin is contra-indicated during pregnancy. The use of insulin is required under such circumstances. Patients who consider pregnancy should inform their physician.

Lactation
Because sulphonylurea-derivatives like glimepiride pass into the breast milk, Glimin must not be taken by breast-feeding women.

Effects on ability to drive & use machine
No studies on the effects on the ability to drive and use machines have been performed.

The patient's ability to concentrate and react may be impaired as a result of hypoglycaemia or hyperglycaemia or, for example, as a result of visual impairment. This may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or operating machinery).

Patients should be advised to take precautions to avoid hypoglycaemia whilst driving. This is particularly important in those who have reduced or absent awareness of the warning symptoms of hypoglycaemia or have frequent episodes of hypoglycaemia.
It should be considered whether it is advisable to drive or operate machinery in these circumstances.

Drug interactions
Patients who taken or discontinue taking certain other medicines while undergoing treatment with Glimepiride may experience changes in blood glucose control.

The following interactions must be considered;
Potentiation of the blood-glucose-lowering effect and, thus, in some instances hypoglycaemia may occur when one of the following drugs is taken, for examples: insulin and other oral antidiabetics, MAO inhibitors, ACE inhibitors, miconazole, anabolic steroids and male sex hormones, para-aminosalicyclic acid, chloramphenicol, pentoxifylline (high dose parenteral), coumarin derivatives, phenylbutazone, azapropazone, oxyphenbutazone, cyclophosphamide, probenecid, disopyramide, quinolones, fenfluramine, salicylates, fenyramidol, sulphinpyrazone, fibrates, sulfonamide antibiotics, fluoxetine, tetracyclines, guanethidine, tritoqualine, ifosfamide, trofosfamide.
Weakening of the blood-glucose-lowering effect and thus raised glucose levels may occur when one of the following drug is taken for example: acetazolamide, laxatives (after protracted use), barbiturates, nicotinic acid (in high doses), corticosteroids, oestrogens and progestogens, diazoxide, phenothiazines, diuretics, phenytoin, epinephrine (adrenaline) and other sympathomimetic agents, rifampicin, glucagons, thyroid hormones.

H2 receptor antagonists, beta-blockers, clonidine and reserpine may lead to either potentiation or weakening of the blood-glucose-lowering effects. Under the influence of sympatholytic drugs such as beta-blockers, clonidine, guanethidine and reserpine, the signs of adrenergic counter-regulation to hypoglycaemia may be reduced or absent. Both acute and chronic alcohol intake may potentiate or weaker the blood-glucose-lowering action of Glimepiride in an unpredictable fashion.
The effect of coumarin derivatives may be potentiated or weakened.

Overdosage, symptoms and treatment
Overdosage of sulfonylureas, including Glimepiride can produce hypoglycemia. Mild hypoglycemic symptoms without loss of consciousness or neurologic findings should be treated aggressively with oral glucose and adjustments in drug dosage and/ or meal patterns. Close monitoring should continue until the physician is assured that the patient is out of danger.

Severe hypoglycemic reactions with coma, seizure or other neurological impairment occur infrequently but constitute medical emergencies requiring immediate hospitalization. If hypoglycemic coma is diagnosed or suspected the patient should be given a rapid intravenous injection of concentrated (50%) glucose solution. This should be followed by a continuous infusion of a more dilute (10%) glucose at a rate will maintain the blood glucose at a level above 100mg/dl. Patients should be closely monitored for a minimum of 24 to 48 hours, because hypoglycemia may recur after apparent clinical recovery.

Storage conditions
Store at or below 30°C. Protect from light. Keep out of reach of children.

Shelf-life
36 months from the date of manufacture if kept as recommended.

Package
Blister Pack : 30 tablets, 50 tablets , 100 tablets and 600 tablets.

Registration number
Glimin Tablets 2mg - MAL07082872AZ

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