

Oral Hypoglycemic Agent GLIMITAB (Glimepiride)

COMPOSITION

Each tablet contains Glimepiride – 1 mg.

Each tablet contains Glimepiride – 2 mg.

DESCRIPTION

Glimepiride is an Oral Hypoglycemic Agent belonging to the sulfonylurea group. Both in healthy persons and in patients with type II diabetes mellitus, glimepiride decreases blood sugar concentrations, 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. In addition, glimepiride has extrapancreatic (insulin-sensitizing and insulinmimetic) effects.

INDICATIONS

Non-insulin-dependent (type II) diabetes, whenever blood sugar levels cannot be controlled adequately by diet, physical exercise and weight reduction alone.

GLIMITAB may also be used in combination with insulin.

DOSAGE

In principle, the desired blood sugar level governs the dosage of GLIMITAB. The dosage of glimepiride must be the lowest which is sufficient to achieve the desired metabolic control.

Treatment with GLIMITAB must be initiated and monitored by a doctor. The patient must take GLIMITAB at the times and in the doses prescribed by the doctor. 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 situations where a dose cannot be taken at the prescribed time must be discussed and agreed between doctor and patient beforehand. If it is discovered that too high a dose or an extra dose of GLIMITAB has been taken, a doctor must be notified immediately.

The initial and the maintenance doses are set based on the results of regular checks of glucose in blood and urine. Monitoring of glucose levels in blood and urine also serves to detect either primary or secondary failure of therapy.

Initial dose and dose titration:

The usual initial dose is 1 mg GLIMITAB once daily. If necessary, the daily dose can be raised. It is recommended that the increase be guided by regular blood sugar monitoring, and that the dose be increased gradually, i.e. at intervals of one to two weeks and according to the following dose steps: 1 mg – 2 mg – 3 mg – 4 mg – 6 mg (and – in exceptional cases – 8 mg).

Dose range in patients with well-controlled diabetes: The usual dose range in patients with well controlled diabetes is 1 to 4 mg GLIMITAB daily. Only some patients benefit from daily doses of more than 6 mg.

Distribution of doses:

Timing and distribution of doses are to be decided by the doctor, taking into consideration the patient's current life-style. Normally a single daily dose of GLIMITAB is sufficient. It is recommended that this dose be taken immediately before a substantial breakfast or – if none is taken – immediately before first main meal. It is very important not to skip meals after the tablets have been taken.

Secondary dosage adjustment:

As the control of diabetes improves, sensitivity to insulin increases; therefore, glimepiride requirements may fall as treatment proceeds. To avoid an excessive reduction in blood sugar (hypoglycaemia), timely dose reduction or cessation of GLIMITAB therapy must be considered.

A dose adjustment must also be considered whenever the patient's weight or life-style changes, or other factors causing an increased susceptibility to hypoglycaemia or to an excessive increase in blood sugar levels (hyperglycaemia) arise (see under Special Warnings and Precautions).

Duration of treatment:

Treatment with GLIMITAB is normally a long-term therapy.

Changeover from other Oral Antidiabetics to GLIMITAB:

There is no exact dosage relationship between GLIMITAB and other blood-sugar-lowering agents. When substituting GLIMITAB for other such agents, the initial daily dose is

1 mg; this applies even in changeovers from the maximum dose of another oral bloodsugar-lowering agent. Any GLIMITAB dose increase should be in accordance with guidelines given above in "Initial dose and dose titration". Consideration must be given to the potency and duration of action of the previous blood-sugar-lowering agent. It may be necessary to interrupt treatment to avoid additive effects which would increase the risk of hypoglycaemia.

Use in Combination with Insulin:

Whenever blood sugar levels cannot be controlled adequately with the maximum daily dose of GLIMITAB, insulin may be given concomitantly. In this case, the current dose of GLIMITAB remains unchanged. Insulin treatment is started at a low dose, which is subsequently increased stepwise according to the desired blood sugar level. Combined treatment should be initiated under close medical supervision.

Administration

GLIMITAB tablets must be swallowed whole without chewing and with sufficient amounts of liquid (approx. 1/2 glass of water).

Contraindications

GLIMITAB is not suitable for the treatment of insulin-dependent (type I) diabetes mellitus (e.g., for the treatment of diabetics with a history of ketoacidosis), of diabetic ketoacidosis, or of diabetic precoma or coma.

GLIMITAB must not be used in patients hypersensitive to glimepiride, other sulfonylureas, other sulfonamides, or to any of the excipients (risk of hypersensitivity reactions).

No experience has been gained concerning the use of GLIMITAB in patients with severe impairment of liver function and in dialysis patients. In patients with severe impairment of renal or hepatic function, change-over to insulin is indicated, not least to achieve optimal metabolic control.

Pregnancy and Lactation

To avoid risk of harm to the child, GLIMITAB must not be taken during pregnancy; a changeover to insulin is necessary. Patients planning a pregnancy must inform their doctor, and should change over to insulin. Ingestion of glimepiride with the breast milk may harm the child. Therefore, GLIMITAB must not be taken by breast-feeding women, and a changeover to insulin or discontinuation of breast-feeding is necessary.

Special Warnings and Precautions

To achieve the goal of treatment with GLIMITAB – optimal control of blood sugar – adherence to correct diet, regular and sufficient physical exercise and, if necessary, reduction of body weight are just as necessary as regular intake of GLIMITAB.

Clinical signs of hyperglycaemia are, e.g., increased urinary frequency, intense thirst, dryness of the mouth, and dry skin. When starting treatment, the patient must be informed about the effects and risks of GLIMITAB and about its role in conjunction with dietary measures and physical exercise; the importance of adequate cooperation must also be stressed. In the initial weeks of treatment, the risk of hypoglycaemia may be increased and necessitates especially careful monitoring.

Factors favouring hypoglycaemia include:

- unwillingness or (more commonly in older patients) incapacity of the patient to cooperate,
- undernutrition, irregular mealtimes, or skipped meals,
- imbalance between physical exertion and carbohydrate intake,

- alterations of diet,
- consumption of alcohol, especially in combination with skipped meals,
- impaired renal function,
- severe impairment of liver function,
- overdosage with GLIMITAB,
- 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 adrenocortical insufficiency).
- concurrent administration of certain other medicines (see “Interaction”).

The patient must inform the doctor about such factors and about hypoglycaemic episodes, since this require particularly careful monitoring.

If such risk factors for hypoglycaemia are present, it may be necessary to adjust the dosage of GLIMITAB 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(see under “Adverse reactions”) may be milder or absent where hypoglycaemia develops gradually, in the elderly, and in patients with a certain type of nervous disease (autonomic neuropathy) or those receiving concurrent treatment with beta-blockers, clonidine, reserpine, guanethidine, or other sympatholytic drugs.

Hypoglycaemia can almost always be promptly controlled by immediate intake of sugar, e.g., in the form of glucose, sugarcubes, sugar-sweetened beverages. Patients should always carry at least 20 grams of glucose with them for this purpose (food or beverages containing artificial sweeteners – such as diet foods or drinks – are ineffective in controlling hypoglycaemia). They may require the assistance of other persons to avoid complications.

It is known from other sulfonylureas that, despite initially successful countermeasures, hypoglycaemia may recur. Therefore, continued close observation is necessary. Severe hypoglycaemia requires, in addition, immediate treatment and follow-up by a doctor and, in some, circumstances, hospitalization.

If treated by different doctors (upon, e.g., admission to hospital after an accident, illness while on holiday), the patients must inform them about their diabetes and previous treatment.

In exceptional stress situations (e.g. trauma, surgery, febrile infections) blood sugar control may deteriorate, and a temporary change to insulin may be necessary.

During treatment with GLIMITAB, glucose levels in blood and urine must be

check regularly, as should, additionally, the proportion of glycated hemoglobin.

Alertness and reactions may be impaired due to hypo- or hyperglycaemia, especially when beginning or after altering treatment, or when GLIMITAB is not taken regularly. Such impairment may, for example, affect the ability to operate a vehicle or machinery.

Drug Interactions

Patients who take or discontinue taking certain other medicines while undergoing treatment with GLIMITAB may experience changes in blood sugar control.

Based on experience with GLIMITAB and on what is known of other sulfonylureas, the following interactions must be considered: Potentiation of the blood-sugar-lowering effect and, thus, in some instances hypoglycaemia may occur when one of the following drugs is taken, for example: insulin and other oral antidiabetics, ACE inhibitors, allopurinol, anabolic steroids and male sex hormones, chloramphenicol, coumarin derivatives, cyclophosphamide, disopyramide, fenfluramine, fenyramidol, fibrates, fluoxetine, guanethidine, ifosfamide, MAO inhibitors, miconazole, para-aminosalicylic acid, pentoxifylline (high dose parenteral), phenylbutazone, azapropazone, oxyphenbutazone, probenecid, quinolones, salicylates, sulfinpyrazone, sulfonamides, tetracyclines, tritoqualine, trofosfamide.

Weakening of blood-sugar-lowering effect and thus, raised blood sugar levels may occur when one of the following drugs is taken, for example: acetazolamide, barbiturates, corticosteroids, diazoxide, diuretics, epinephrine (adrenaline) and other sympathomimetic agents, glucagon, laxatives (after protracted use), nicotinic acid (in high doses), estrogens and progestogens, phenothiazines, phenytoin, rifampicin, thyroid hormones.

H₂ receptor antagonists, beta-blockers, clonidine and reserpine may lead to either potentiation or weakening of the blood-sugar-lowering effect.

Beta-blockers decrease glucose tolerance. In patients with diabetes mellitus, this may lead to deterioration of metabolic control. In addition, beta-blockers may increase the tendency to hypoglycaemia (due to impaired counter-regulation).

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 weaken the blood-sugar lowering action of GLIMITAB unpredictably. The effect of coumarin derivatives may be potentiated or weakened.

Adverse Reactions

Based on experience with GLIMITAB and on what is known of other

sulfonylureas, the following adverse effects must be considered:

Hypoglycaemia: As a result of the bloodsugar-lowering action of GLIMITAB, hypoglycaemia may occur, and may also be prolonged.

Possible symptoms of hypoglycaemia include headache, ravenous hunger, nausea, vomiting, lassitude, sleepiness, disordered sleep, restlessness, aggressiveness, impaired concentration, alertness and reactions, depressions, confusions, difficulty in speaking and even speech loss, visual disorders, tremor, pareses, sensory disturbances, dizziness, helplessness, loss of self-control, delirium, cerebral convulsions, somnolence and loss of consciousness up to and including coma, shallow respiration and slow heart rate (bradycardia). In addition, signs of adrenergic counter-regulation may be present such as sweating, clammy skin, anxiety, rapid heart rate (tachycardia), hypertension, palpitations, angina pectoris, and cardiac arrhythmias. The clinical picture of a severe hypoglycaemia nearly always subsides when hypoglycaemia is corrected. The symptoms of hypoglycaemia nearly always subside when hypoglycaemia is corrected.

Eyes: Especially at the start of treatment, temporary visual impairment may occur due to the change in blood sugar levels.

Digestive tract: Occasionally, gastrointestinal symptoms such as the following may occur: nausea, vomiting, sensations of pressure or fullness in the epigastrium, abdominal pain and diarrhea.

In rare cases, liver enzyme levels may increase. In isolated cases, impairment of liver function (e.g. with cholestasis and jaundice) and hepatitis may develop, possibly leading to liver failure.

Blood: Severe changes in the blood picture may occur: Rarely thrombopenia and, in isolated cases, leucopenia, haemolytic anaemia or e.g. erythrocytopenia, granulocytopenia, agranulocytosis, and pancytopenia (e.g. due to myelosuppression) may develop.

Other adverse reactions: Occasionally, allergic or pseudo allergic reactions may occur, e.g. in the form of itching, urticaria or rashes. Such reactions may be mild, but also may become more serious and may become dyspnoea and a fall in blood pressure, sometimes progressing to shock. If urticaria occurs, a doctor must be notified immediately. In isolated cases, a decrease in serum sodium inflammation of blood vessels (allergic vasculitis) and hypersensitivity of the skin to light may occur.

Please speak with your doctor if you notice any of the adverse effects listed in this package insert or any other undesired effects or unexpected changes.

Since some adverse effects (e.g., severe hypoglycaemia, certain changes in the blood picture, severe allergic or pseudoallergic reactions, or liver failure) may

under certain circumstances become life-threatening, it is essential that, if sudden or severe reactions do occur, you inform a doctor at once, and on no account continue taking the drug without a doctor's express guidance.

Overdose

GLIMITAB overdose may lead to severe and sometimes life-threatening hypoglycaemia and may require hospitalization even as a precautionary measure. Significant overdose with severe reactions is a medical emergency and will necessitate immediate treatment and hospitalization.

Mild episodes of hypoglycaemia can usually be treated with oral carbohydrates. Adjustments in dosage, meal patterns or physical activity may be necessary. More severe episodes with coma, seizure or neurologic impairment may be treated with glucagon (intramuscular or subcutaneous) or concentrated glucose solution (intravenous). If life-threatening amounts have been ingested, detoxification (by, e.g., gastric lavage, activated charcoal) will be necessary.

Sustained administration of carbohydrates and observation may be necessary because hypoglycaemia may recur after apparent clinical recovery.

Storage

Store at a temperature not exceeding 30°C.

Shelf Life

36 months. Do not use later than the date of expiry.

Keep medicines out of the reach of children.

Presentation

Glimitab 1 mg tablet: Blister pack of 10 Strips

Glimitab 2 mg tablet: Blister pack of 10 Strips