GLICLADA MR TABLETS *Consumer Medication Information Leaflet (RiMUP)*

Gliclazide 30 mg

What is in this leaflet

What Gliclada is used for

Gliclada is a medicine which reduces blood sugar levels. It is used for the treatment of a certain type of diabetes (type 2 diabetes mellitus) in adults when dietary measures, physical exercise and weight loss alone are not sufficient to control blood glucose.

How Gliclada works

Gliclada reduces blood glucose levels by stimulating the secretion of a hormone, called insulin, from the pancreatic gland.

Before you use Gliclada

When you must not use it

- if you are allergic (hypersensitive) to gliclazide, any of the excipients or other sulphonylureas and sulphonamides.
- if you have insulin-dependent diabetes (type 1).
- if you have a severe condition due to diabetes, called diabetic pre-coma and coma.
- if you have ketone bodies and sugar in your urine (diabetic ketoacidosis). if you have a severe liver or kidney disorder (in these cases, the use of insulin is recommended).
- if you are concomitantly treated with a drug called miconazole.
- if you are breast-feeding.

Before you start to use it

Please tell your doctor if you have:

Kidney and liver impairment
If you have kidney or liver impairment, the pharmacokinetics and/or pharmacodynamics of gliclazide may be altered and its action increased. In this case, a hypoglycaemic episode may be prolonged, so appropriate management should be initiated.

Pregnancy
There is no experience with the use of gliclazide during pregnancy in humans, even though there are few data on other sulphonylureas.
In animal studies, gliclazide is not teratogenic (does not cause inborn malformations).

Control of diabetes should be obtained before the time of conception to reduce the risk of inborn abnormalities linked to uncontrolled diabetes.

Oral antidiabetic agents are not suitable; insulin is the agent of first choice for treatment of diabetes during pregnancy. It is recommended that oral antidiabetic therapy is changed to insulin before a pregnancy is attempted, or as soon as pregnancy is discovered.

Lactation
It is not known whether gliclazide or its metabolites (substances derived from gliclazide in the body) are excreted in breast milk. Given the risk of hypoglycaemia in newborn babies, the medicinal product must not be used in breast-feeding mothers.

Special information about some of the ingredients
Gliclada contains lactose. If you have rare inherited problems of how your body deals with sugar called galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption you should not take this medicinal product.

Taking other medicines

The products that are likely to increase the risk of hypoglycaemia

Contraindicated combination (must not be taken)

Miconazole (systemic route, oromucosal gel): increases the hypoglycaemic effect with possible onset of hypoglycaemic symptoms, or even coma (state of deep unconsciousness).

Combinations which are not recommended

- Phenylbutazone (systemic route): increases the hypoglycaemic effect of Gliclada and other similar drugs (sulphonylureas). It is preferable to use a different agent with similar action (anti-inflammatory), or else you should carefully self-monitor your glucose levels. Where necessary, your doctor will adjust the dose during and after treatment with the anti-inflammatory agent.
- Alcohol: increases the hypoglycaemic reaction (by blocking the body response to low blood sugar), which can lead to the onset of hypoglycaemic coma (deep unconsciousness). Alcohol and medicinal products containing alcohol should be avoided.

Combinations requiring precautions for use
Potentiation of the blood glucose lowering effect and thus, in some instances, hypoglycaemia may occur when one of the following medicinal products is taken, for example: other antidiabetic agents (insulins, acarbose, biguanides), beta-blockers, fluconazole, angiotensin converting enzyme inhibitors (captopril, enalapril), H2-receptor antagonists, MAOIs, sulphonamides, and nonsteroidal anti-inflammatory agents.

The products that may cause an increase in blood glucose levels

Combination which is not recommended

Danazol: diabetogenic (blood sugar increasing) effect of danazol. If the use of this active substance cannot be avoided, you should take care and monitor regularly your urine and blood glucose levels. It may be necessary for your doctor to adjust the dose of the antidiabetic agent during and after treatment with danazol.

Combinations requiring precautions during use

- Chlorpromazine - neuroleptic agent (agent for the treatment of psychiatric diseases): high doses (>100 mg per day) increase blood glucose levels (reduced insulin release). You should take care and monitor regularly your

blood glucose levels. It may be necessary for your doctor to adjust the dose of the antidiabetic active substance during and after treatment with the neuroleptic agent.
- Glucocorticoids (applied through the mouth, or by an injection (systemic) and local route: injection in the joint, skin application, application through the anus) and tetracosactrin: increase in blood glucose levels with possible ketosis (reduced tolerance to carbohydrates due to glucocorticoids). It is important that you monitor regularly your blood glucose levels particularly at the start of treatment. It may be necessary for your doctor to adjust the dose of the antidiabetic active substance during and after treatment with glucocorticoids.
- Ritodrine, salbutamol, terbutaline (through an injection route): increased blood glucose levels due to special drug effects. It is important that you monitor regularly your blood glucose levels. If necessary, your doctor is going to switch your therapy to insulin.

Combination which must be taken into account

Anticoagulant therapy, i.e. against blood clotting (e.g. warfarin): Gliclada and other sulphonylureas may lead to potentiation of anticoagulation (blockage of blood clotting) during concurrent treatment. Adjustment of the anticoagulant dose may be necessary.

How to use Gliclada

How much to use

Oral use.

For adult use only.

The daily dose may vary from 1 to 4 tablets per day, i.e. from 30 to 120 mg taken once daily.

It is recommended that the tablets be taken with breakfast.

As with any antidiabetic agent, the dose of Gliclada should be adjusted according to how you respond to the treatment.

Initial dose

The recommended starting dose is 30 mg daily.

If blood glucose is effectively controlled, this dose may be used for maintenance treatment. If blood glucose is not adequately controlled, the dose may be increased to 60, 90 or 120 mg daily, in successive steps. The interval between each dose increment should be at least 1 month, except in patients whose blood glucose has not reduced after two weeks of treatment. In such cases, the dose may be increased at the end of the second week of treatment.

The maximum recommended daily dose is 120 mg.

Switching from another oral antidiabetic agent to Gliclada

Gliclada can be used to replace other antidiabetic agents. Your doctor will take into account how your previous drug worked and adjust the dose and the schedule of Gliclada appropriately. A transitional period is generally not necessary. A starting dose of 30 mg should be used and this should be adjusted according to laboratory test results, as described above.

Combination treatment with other antidiabetic agents

Gliclada can be given in combination with other agents for blood sugar control. In case of such need, your doctor will closely control your treatment. If you are not adequately controlled on Gliclada, concomitant therapy with insulin can be initiated by your doctor.

Elderly

In elderly patients (over 65 years of age), Gliclada should be prescribed using the same dosing regimen as the one recommended for patients under 65 years of age.

Patients with mild to moderate kidney impairment

The same dosing regimen can be used as in patients with normal kidneys, but with careful patient control. These data have been confirmed in clinical trials.

If you are at risk of hypoglycaemia

It is recommended that the minimum daily starting dose of 30 mg is used.

Children

There is no experience in children.

When to use it

It is recommended that the tablets be taken with breakfast.

How long to use it

You should take Gliclada for as long as your doctor told you.

If you forget to use it

If you forget your tablet(s) on one day, continue taking your tablet(s) as usual on the following day. You must not increase the next dose you take.

Do not take a double dose to make up for a forgotten tablet.

If you use too much (overdose)

An overdose of sulphonylureas may cause hypoglycaemia. Moderate symptoms of hypoglycaemia, without any loss of consciousness or neurological signs, can be corrected by carbohydrate intake, dose adjustment and/or change of diet. In the case of overdose, you will be monitored and, depending on your condition the doctor will decide if further monitoring is necessary. Dialysis is of no benefit in this situation.

While you are using it

You should observe the treatment plan prescribed by your doctor to achieve the recommended blood sugar levels. This means regular tablet intake in addition to a dietary regimen and physical exercise. During gliclazide treatment regular monitoring of your blood sugar level is necessary.

Poor blood glucose control

Blood glucose control in a patient receiving antidiabetic treatment may be affected by any of the following: fever, injury, infection or surgical intervention. In some cases, it may be necessary to administer insulin.

The efficacy of any antidiabetic agent, including Gliclada, is attenuated over time in many patients.

This may be due to progression in the severity of the diabetes, or to a reduced response to treatment.

This phenomenon is known as secondary failure which is distinct from primary failure, when an active substance is ineffective as first-line treatment. Adequate dose adjustment and dietary compliance should be considered before

classifying the patient as secondary failure.

Laboratory tests
Measurement of fasting blood glucose levels or $_{HbA1C}$ (a substance that indicates how well your blood sugar is controlled) levels is recommended in assessing blood glucose control. Blood glucose self-monitoring may also be useful.

Things you must do

If you have hypoglycemia, you should have regular meals, including breakfast. It is important to have a regular carbohydrate intake due to the increased risk of hypoglycaemia. Some cases of hypoglycemia may be severe and prolonged. Hospitalization may be necessary and glucose administration may need to be continued for several days.

Factors which increase the risk of hypoglycaemia:
- lack of following doctor's orders, insufficient intake of food, irregular mealtimes, skipping meals, periods of fasting or dietary changes,
- imbalance between physical exercise and carbohydrate intake,
- kidney or liver problems,
- taking too many tablets of Gliclada, problems with some glands that produce different hormones (functional disorders of the thyroid gland, of the pituitary gland or the adrenal cortex), prolonged or high-dose therapy with drugs called corticosteroids,
- severe diseases of blood vessels (severe disease of blood vessels that supply the heart, severe disease of principal blood vessels supplying the head region, blood vessel generalized disease),
- concomitant administration of certain other medicinal products (see section Interaction with other medicinal products and other forms of interaction).

In order to prevent hypoglycaemia to occur, you have to follow the dietary advice. Furthermore, you are recommended to take regular exercise and monitor your blood sugar levels regularly in order to diminish the risk of hypoglycaemia.

In most cases the symptoms of hypoglycemia vanish very quickly when you consume some form of sugar, e.g. sugar cubes, sweet juice, sweetened tea. You should therefore always take some form of sugar with you (sugar cubes). Remember that sweeteners are not effective. Please contact your doctor or the nearest hospital if taking sugar does not help or if the symptoms recur.

Things you must not do
You must not skip the meal while taking Gliclada, since you can experience hypoglycaemia, particularly if you have an underlying increased risk of hypoglycaemia (see section Things you must do).

Things to be careful of
Gliclada has mild or moderate influence on the ability to drive and use machines.

You should be aware of the symptoms of hypoglycaemia (see section Side effects) and should be careful if driving or operating machines, especially at the beginning of treatment.

Side effects

Hypoglycaemia
As with other sulphonylureas, treatment with Gliclada can cause hypoglycaemia if mealtimes are irregular and, in particular, if meals are skipped. Possible symptoms of hypoglycaemia are: headache, intense hunger, feeling sick, vomiting, feeling tired, drowsiness, sleep disorders, agitation, aggression, poor concentration, reduced awareness and slowed reactions, depressed mood, confusion, sight or speech disorders, involuntary trembling of hands, decreased ability to move your limbs, disorders of your senses (e.g. touch), dizziness, feeling of powerlessness, loss of self-control, delirium, severe cramps, shallow breathing, slow heart rate, drowsiness and loss of consciousness, possibly resulting in coma (deep loss of consciousness) and death.. In addition, signs of nervous system response may be observed: sweating, clammy skin, anxiety, accelerated heart rate, high blood pressure, unpleasant feeling of a heartbeat, chest pain and irregular heartbeat. 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 is required.

Frequency of undesirable effects listed by individual organ systems:

Blood and lymphatic system disorders
Rare: blood cells disorders. These are in general reversible upon discontinuation of gliclazide.

Rare cases of blood cells disorders have been described with other sulphonylureas.

Eye disorders
Transient sight disturbances may occur especially on the beginning of treatment, due to changes in blood sugar levels.

Gastrointestinal disorders
Uncommon: gastrointestinal disturbances, including stomach pain, feeling sick, vomiting, uncomfortable feeling in the stomach, diarrhea and constipation. If these should occur, they can be avoided or minimized by taking gliclazide with breakfast.

Hepatobiliary disorders
Rare: raised liver enzyme blood levels (AST, ALT, alkaline phosphatase);
Very rare: liver inflammation (isolated reports); if jaundice appears, treatment should be discontinued.
With other sulphonylureas, the following cases were rarely observed: elevated liver enzyme levels and even impairment of liver function (e.g. with cholestasis and jaundice) and liver inflammation, which improved after withdrawal of the sulphonylurea or led to life-threatening liver failure in isolated cases. These

symptoms usually disappear after discontinuation of treatment.

Skin and subcutaneous tissue disorders
Rare: urticaria, different rashes (red skin, hives, blisters, skin peeling), itching. With other sulphonylureas, allergic blood vessel inflammation was observed very rarely.
If severe undesirable effects occur, treatment should be discontinued.

You may report any side effects or adverse drug reactions directly to the National Centre for Adverse Drug Reaction Monitoring by calling Tel: 03-78835550, or visiting the website portal.bpfk.gov.my (Consumers →Reporting).

Storage and Disposal of Gliclada

Storage
Keep out of the reach and sight of children.
Do not store above 25°C. Store in the original package.
Do not use your medicine after the expiry date which is stated on the pack after 'EXP'. The expiry date refers to the last day of that month.

Disposal
No special requirements.
Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

Product Description

What it looks like
The tablets are white, oval, biconvex.

Ingredients

Active ingredient
- Gliclazide

Inactive ingredients
- Lactose monohydrate
- Hypromellose
- Calcium carbonate
- Colloidal anhydrous silica
- Magnesium stearate

MAL number:
MAL10110008A

Manufacturer
KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia

Product Registration Holder
PAHANG PHARMACY SDN. BHD., Lot 5979, Jalan Teratai, 5 $^{1}/_{2}$ Miles, Off Jalan Meru, 41050 Klang, Selangor, Malaysia.

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