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For the use of a Medical Practitioner or a Hospital or a Laboratory only	
DIABEND	
Gliclazide Tablets BP 80mg	
Name and Strength of Active Ingredient(s) Gliclazide Ph. Eur....80 mg	
Dosage Form Oral- Uncoated Tablets	
Product Description DIABEND - Gliclazide Tablets BP 80mg, is White, flat circular bevelled edge uncoated tablets with cross scoring on one side and plain on other side Each uncoated tablet contains: Gliclazide Ph. Eur.....80 mg	
Pharmacodynamics Pharmacotherapeutic group: Sulfonylurea- Oral Antidiabetic (Alimentary tract and metabolism), ATC code: A10BB09. Mechanism of action Gliclazide reduces blood glucose levels by stimulating the insulin secretion βcells in the islets of Langerhans.	
Pharmacodynamic effects 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.	
Haemovascular properties: Gliclazide decreases microthrombosis by two mechanisms which may be involved in the complications of diabetes: - a partial inhibition of platelet aggregation and adhesion with a decrease in the markers of platelet activation (beta-thromboglobulin, thromboxane B2), - an action on the vascular endothelium fibrinolytic activity with an increase in tPA activity).	
Pharmacokinetics Absorption Gliclazide is rapidly absorbed from the gastrointestinal tract and maximum blood concentrations are attained between the 11th and the 14th hour after administration. Distribution In humans, binding to proteins is 94.2%. Elimination As the apparent terminal elimination half-life for gliclazide is 20 hours in humans, the drug can be administered in two daily doses. Elimination is mainly in the urine: less than 1% of the dose ingested is found unchanged in the urine.	
Indication Non-insulin dependent diabetes, in association with an adapted diet, in cases where dietary measures alone provide inadequate control blood glucose levels.	
Recommended Dose Posology RESTRICTED TO ADULTS. As with any hypoglycaemic agent, the dosages should be adjusted to the particular circumstances. In the event of a transitory loss of blood glucose control in a patient where good control is usually achieved by diet, it may be sufficient to administer this product for a short period.	
<i>Patient under the age of 65</i>	
Initial dose: The recommended initial dose is one tablet per day.	
Dosage steps: Adjustments in posology are usually made in steps of one tablet at a time, depending on the response in blood glucose. At least 14 days should separate successive steps in the dose.	
Maintenance treatment: The posology can vary from 1 to 3, or rarely 4, tablets per day. The standard dosage is 2 tablets a day, as 2 daily doses.	
<i><u>Patients at particular risk:</u></i>	
Patients over the age of 65: Begin the treatment with a half-tablet once a day. The dose can be progressively increased until the patient's blood glucose is satisfactorily controlled, while keeping to steps of at least 14 days between successive levels, and with close monitoring of blood glucose.	
Other patients at particular risk: In patients who are malnourished or showing markedly poor general state of health, or whose calorie intake is irregular, or whose kidney or liver function is impaired, treatment should be begun at the lowest dose. The stepwise increases in dosage must be scrupulously adhered to in order to avoid a hypoglycaemic reaction.	
Patients treated with other oral hypoglycaemic agents: As with any sulfonylurea, this medicinal product can be used as follow-on from another antidiabetic drug, without any transitional period being needed. When patients change to this medication from a sulfonylurea with a longer half-life (such as chlorpropamide), they must be closely monitored (for several weeks). This is to avoid the possible occurrence of hypoglycaemia due to an overlapping of effects from the two treatments. <i><u>Paediatric population</u></i> The safety and efficacy of Gliclazide in children and adolescents have not been established. No data are available.	
Route of Administration For oral use.	
Contraindication This medicinal product is contraindicated in cases of: • Hypersensitivity to gliclazide, or to any of the excipients, other sulphonylureas or sulphonamides. • Type 1 diabetes • Diabetic pre-coma and coma, diabetic keto-acidosis, • Severe hepatic or renal insufficiency: in these cases, the use of insulin is recommended • Treatment with miconazole • Lactation.	
Warning and Precautions Hypoglycaemia This medication should be prescribed only to patients who are able to feed themselves regularly (including having breakfast).It is important to consume carbohydrates regularly, in view of the increased risk of hypoglycaemia if meals are taken late, if food intake is inadequate or if there is an imbalance in carbohydrates. Hypoglycaemia is all the more likely to occur when the patient's diet is low in calories, following major or prolonged exercise, following ingestion of alcohol or when a combination of hypoglycaemic agents is being administered. Hypoglycaemia can occur following administration of sulfonylureas. Some episodes can be severe and prolonged. Admission to hospital may then be necessary, and glucose administration may need to be carried out for several days. To reduce the risk of hypoglycaemia, the patient must be carefully selected, the posology must be carefully matched to the patient, and the patient must be given appropriate information. Factors which increase the risk of hypoglycaemia: • Patient refuses or is unable to co-operate (particularly in elderly subjects) • Malnutrition, irregular mealtimes, skipping meals, periods of fasting or dietary changes. • Imbalance between physical exercise and carbohydrate intake. • Renal insufficiency. • Severe hepatic insufficiency. • Overdose of DIABEND - Gliclazide Tablets BP 80mg • Certain endocrine disorders: thyroid disorders hypopituitarism and adrenal insufficiency. • Concomitant administration of certain other medicines.	
Renal and hepatic insufficiency The pharmacokinetics and/or pharmacodynamics of gliclazide may be altered in patients with insufficiency or severe renal failure. If hypoglycaemia occurs in such patients, it can be prolonged so appropriate management should be initiated.	
Information for the patient The risks of hypoglycaemia, together with its symptoms, treatment, and conditions that predispose to its development, should be explained to patients and to family members. They must be informed of the importance of keeping to an appropriate diet, undertaking regular physical exercise, and of regular monitoring of blood glucose levels.	
Blood sugar imbalance Blood glucose control in a patient receiving oral antidiabetic treatment may be affected by any of the following: St. John's Wort (<i>Hypericum perforatum</i>) preparations, fever, injury, infection or surgery. In some cases, it may be necessary to administer insulin. The hypoglycaemic efficacy of any oral antidiabetic agent, including gliclazide, 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.	
Dysglycaemia Disturbances in blood glucose, including hypoglycaemia and hyperglycaemia have been reported in diabetic patients receiving concomitant treatment with fluoroquinolones, especially in elderly patients. Indeed, careful monitoring of blood glucose is recommended in all patients receiving at the same time DIABEND - Gliclazide Tablets BP 80mg and a fluoroquinolone.	
Laboratory tests Measurement of glycated haemoglobin levels (or fasting venous plasma glucose) is recommended in assessing blood glucose control. Blood glucose self-monitoring may also be useful. Treatment of patients with G6PD-deficiency (glucose-6-phosphate dehydrogenase deficiency) with sulfonylurea agents can lead to haemolytic anaemia. Since gliclazide belongs to the chemical class of sulfonylurea drugs, caution should be used in patients with G6PD-deficiency and a non-sulfonylurea alternative should be considered.	
Porphyric patients: Cases of acute porphyria have been described with some other sulfonylurea drugs, in patients who have porphyria.	
Excipients This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.	
Interactions with Other Medicaments <i>The following substances can increase hypoglycaemia:</i> Combination contraindicated Miconazole (systemic route, oromucosal gel): Increase the hypoglycaemic effect with possible onset of hypoglycaemic symptoms, or even coma.	
Combinations which are not recommended Phenylbutazone (systemic route): Increase in the hypoglycaemic effect of sulphonylureas (displaces their binding to plasma proteins and/or reduces their elimination).	

It is preferable to use a different anti-inflammatory agent, or else warm the patient and emphasise the self-monitoring. Where necessary adjust the dose during and after treatment with the anti-inflammatory agent.

Alcohol: "Antabuse effect", in particular with chlorpropamide, glibenclamide, glipizide and tolbutamine
Increases hypoglycaemic reaction (due to inhibiting compensating reactions), that can lead to the onset of hypoglycaemic coma.
Consumption of alcoholic drinks and of medicinal products containing alcohol should be avoided.

Combinations requiring precautions for use

Potentialiation of the blood glucose lowering effect and thus, in some instances, hypoglycaemia may occur when one of the following drugs is taken:
Other antidiabetic agents (insulin, acarbose, metformin, thiazolidinediones, dipeptidyl peptidase-4 inhibitors, GLP-1 receptor agonists), beta-blockers, fluconazole, angiotensin converting enzyme inhibitors (captopril, enalapril), H2-receptor antagonists, MAOIs, sulfonamides, clarithromycin and nonsteroidal anti-inflammatory agents.

The following products may cause an increase in blood glucose levels :

Combination which is not recommended

Danazol: diabetogenic effect of danazol
If the use of this active substance cannot be avoided, warn the patient and emphasise the importance of urine and blood glucose monitoring.
It may be necessary to adjust the dose of the antidiabetic agent during and after treatment with danazol.

Combinations requiring precautions during use
Chlorpromazine (neuroleptics agent)
High doses (>100 mg per day of chlorpromazine): increase blood glucose levels (reduced insulin release). Warn the patient and emphasise the importance of blood glucose monitoring.
It may be necessary to adjust the dose of the antidiabetic active substance during and after treatment with the neuroleptic agent.

•Glucocorticoids (systemic route and local route: intraarticular use, cutaneous or rectal preparations) and tetracosactide
Increase in blood glucose levels with sometimes ketosis (reduced tolerance to carbohydrates due to corticosteroids).
Warn the patient and emphasise the blood glucose monitoring, particularly at the start of treatment. It may be necessary to adjust the dose of the antidiabetic active substance during and after treatment with glucocorticoids.

•Ritodrine, salbutamol, terbutaline (I.V. route)
Increased blood glucose levels due to beta-2-agonist effects.
Emphasise the importance of monitoring blood glucose levels.
If necessary, switch to insulin.

Saint John's Wort (*Hypericum perforatum*) preparations:
Gliclazide exposure is decreased by Saint John's Wort (*Hypericum perforatum*).
Emphasise the importance of blood glucose levels monitoring.

The following products may cause dysglycaemia:
Combinations requiring precautions during use
Fluoroquinolones:
In case of concomitant use of DIABEND - Gliclazide Tablets BP 80mg and a fluoroquinolone, the patient should be warned of the risk of dysglycaemia, and the importance of blood glucose monitoring should be emphasised.

Combinations which must be taken into account

• Anticoagulant therapy (warfarin ...)
Sulfonylureas may lead to potentiation of anticoagulation during treatment.
Adjustment of the anticoagulant posology may be necessary.

Pregnancy and Lactation
Pregnancy
There is no or limited amount of data (less than 300 pregnancy outcomes) from the use of gliclazide in pregnant women, even though there are few data with other sulfonylurea.
In animal, gliclazide is not teratogenic.
As a precautionary measure, it is preferable to avoid the use of gliclazide during pregnancy.
Control of diabetes should be obtained before the time of conception to reduce the risk of congenital abnormalities due to uncontrolled diabetes.
Oral hypoglycaemic agents are not suitable, insulin is the first choice for the treatment of diabetes during pregnancy. It is recommended that oral hypoglycaemic therapy is changed to insulin before a pregnancy is attempted, or as soon as pregnancy is discovered.

Breast-feeding
It is not known whether gliclazide or its metabolites are excreted in breast milk. Given the risk of neonatal hypoglycaemia, gliclazide is contra-indicated in breast-feeding mother.
A risk to the newborns/infants cannot be excluded.

Fertility
No effect on fertility or reproductive performance was noted in male and female rats.

Side Effects
Based on the clinical experience with gliclazide, the following undesirable effects have been reported:

Hypoglycaemia
The most frequent adverse reaction with gliclazide is hypoglycaemia.
As for other sulfonylureas, treatment with Diamicon can cause hypoglycaemia, in particular if mealtimes are irregular and, 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.

Other undesirable effects
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 a meal or by splitting the doses.
The following undesirable effects have been more rarely reported:

Skin and subcutaneous tissue disorders: rash, pruritus, urticaria, angioedema, erythema, maculopapular rash, bullous reactions (such as Stevens-Johnson syndrome and toxic epidermal necrolysis and autoimmune bullous disorders) and exceptionally, drug rash with eosinophilia and systemic symptoms (DRESS).

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 liverenzyme 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.

Symptoms and Treatment of Overdose
An overdose of hypoglycaemic sulphonylureas may lead to hypoglycaemia.
Moderate symptoms of hypoglycaemia, without any loss of consciousness or neurological signs, must be corrected by the administration of carbohydrate intake, dose adjustment and/or change of diet. Strict monitoring should be continued until the doctor is sure that the patient is out of danger.
Severe hypoglycaemic reactions, with coma, convulsions or other neurological disorders are possible and must be treated as a medical emergency, requiring immediate hospitalisation.
If hypoglycaemic coma is diagnosed or suspected, the patient should be given a rapid I.V. injection of 50mL of a concentrated glucose solution (20% to 30%). This should be followed by a continuous infusion of a more dilute glucose solution (10 %) at a rate that will maintain blood glucose levels above 1g/L. Patients should be monitored closely and, depending on the patient's condition after this time, the doctor will decide if further monitoring is necessary.
Dialysis is of no benefit to patients due to the strong binding of gliclazide to proteins.

Effects on Ability to Drive and Use Machine
DIABEND - Gliclazide Tablets BP 80 mg has no or negligible influence on the ability to drive and use machines. However, patients should be made aware of the symptoms of hypoglycaemia and should be careful if driving or operating machinery, especially at the beginning of treatment.

Instruction for Use
The dose may need to be titrated if Patient has been switched from a different brand of product containing Gliclazide.

Storage Condition:
Store below 30°C. Protect from Moisture.
Keep medicine out of reach of children.

Shelf Life
24 months

Packaging Available:
Each carton contains 10 x 10's Alu PVC Blister pack for Gliclazide Tablets BP 80mg

Date of Revision: 18th November 2023.

Product registration holder:
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