

Glibenclamide

Introduction: Glibenclamide is a popular anti-diabetic drug, belonging to class of sulfonylureas. The drug is widely used for treating type II diabetes.

Mechanism of action: The drug works by inhibiting ATP-sensitive potassium channels in pancreatic beta cells. This inhibition causes cell membrane depolarization, opening of voltage-dependent calcium channels, thus triggering an increase in intracellular calcium into the beta cell which stimulates insulin release.

Indications: It is used in the treatment of type II diabetes.

Dosage: Dosage should be adapted to each individual patient and is determined by results of medical examinations. In general the initial dose is 2,5 mg daily (half a Glibenclamide tablet). The daily dose can then be raised gradually in steps of half tablets, but only after repeating medical examination. Raising the dose beyond three tablets daily does not produce any increased response. When changing over from another oral antidiabetic preparation, with a similar mode of action, the dosage of Glibenclamide is determined by the amount of the previously administered dose and the medical examination. It may be considered that the effect of 1 g tolbutamide or glycodiazine, 0,5 g carbutamide or 250 mg chlorpropamide corresponds roughly to that of 5 mg Glibenclamide (1 tablet). In combination therapy with a biguanide, there may be a greater risk of cardiovascular mortality than with the use of gliclazide alone.

Side effects: Side-effects include nausea, vomiting, epigastric pain, dizziness, headache, weakness, and paraesthesia. Sensitivity reactions with fever, eosinophilia skin rashes, jaundice and blood disorders, including leucopenia, thrombocytopenia, aplastic anaemia, and agranulocytosis has occurred. Intolerance to alcohol, characterised by facial flushing, may also occur. Hypoglycaemic reactions may occur.

Precautions:

Hypoglycemia: All sulfonylureas are capable of producing severe hypoglycemia. Proper patient selection and dosage and instructions are important to avoid hypoglycemic episodes. Renal or hepatic insufficiency may cause elevated drug levels of Glibenclamide and the latter may also diminish gluconeogenic capacity, both of which increase the risk of serious hypoglycemic reactions. Elderly, debilitated or malnourished patients, and those with adrenal or pituitary insufficiency, are particularly susceptible to the hypoglycemic action of glucose-lowering drugs. Hypoglycemia may be difficult to recognize in the elderly and in people who are taking beta-adrenergic blocking drugs. Hypoglycemia is more likely to occur when caloric intake is deficient, after severe or wering drug is used. The risk of hypoglycemia may be increased with combination therapy.

Loss of Control of Blood Glucose: When a patient stabilized 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 discontinue Glibenclamide and administer insulin. The

effectiveness of any hypoglycemic drug, including Glibenclamide, in lowering blood glucose to a desired level decreases in many patients over a period of time which may be due to progression of the severity of diabetes or to diminished responsiveness to the drug. This phenomenon is known as secondary failure, to distinguish it from primary failure in which the drug is ineffective in an individual patient when Glibenclamide is first given. Adequate adjustment of dose and adherence to diet should be assessed before classifying a patient as a secondary failure.

Pregnancy: Teratogenic Effects: *Pregnancy Category B:* Because recent information suggests that abnormal blood glucose levels during pregnancy are associated with a higher incidence of congenital abnormalities, many experts recommend that insulin be used during pregnancy to maintain blood glucose as close to normal as possible.

Nursing Mothers: Although it is not known whether Glibenclamide is excreted in human milk, some sulfonylurea drugs are known to be excreted in human milk. Because the potential for hypoglycemia in nursing infants may exist, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. If the drug is discontinued, and if diet alone is inadequate for controlling blood glucose, insulin therapy should be considered.

Pediatric Use: Safety and effectiveness in pediatric patients have not been established.

Geriatric Use: Elderly patients are particularly susceptible to the hypoglycemic action of glucose lowering drugs. Hypoglycemia may be difficult to recognize in the elderly. The initial and maintenance dosing should be conservative to avoid hypoglycemic reactions. Elderly patients are prone to develop renal insufficiency, which may put them at risk of hypoglycemia. Dose selection should include assessment of renal function.

Contraindications: Glibenclamide Tablets are contraindicated in patients with:

- Known hypersensitivity or allergy to the drug.
- Diabetic ketoacidosis, with or without coma. This condition should be treated with insulin.
- Type I diabetes mellitus.

How supplied: Customized as per request.