Glimitus M

Glimepiride BP & Metformin Hydrochloride BP

Composition:
Glimitus M 1/500 mg: Each film coated bilayered tablet contains Glimepiride BP 1 mg & Metformin Hydrochloride BP 500 mg (in sustained release form).
Glimitus M 2/500 mg: Each film coated bilayered tablet contains Glimepiride BP 2 mg & Metformin Hydrochloride BP 500 mg (in sustained release form).

Pharmacology:
Glimepiride primarily lowers the blood glucose level by stimulating the release of insulin from pancreatic beta cells.
Metformin is an antihyperglycemic medicine which enhances glucose tolerance in patients with type-2 diabetes mellitus, lowering both basal and postprandial plasma glucose. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization. With metformin therapy insulin secretion remains unchanged while fasting insulin levels and day-long plasma insulin response may decrease.

Indication:
Glimitus M is indicated as an adjunct to diet and exercise to improve glycemic control in patients with Type 2 Diabetes Mellitus, whose hyperglycemia cannot be controlled with diet and exercise alone. **Glimitus M** can be used as a monotherapy, or in combination with Metformin when diet, exercise and Metformin alone cannot control the blood sugar level of the patient. **Glimitus M** may also be used in combination with insulin in patients with high blood sugar levels that cannot be controlled adequately with diet, exercise and the administration of an oral hypoglycemic agent.

Dosage and Administration:
The initial and maintenance dose of **Glimitus M** should be determined by frequent monitoring of glucose in blood or urine. The initial recommended starting dose of **Glimitus M** is 1/500 mg tablet once daily with breakfast or first main meal of the day, and gradually titrated after assessing the therapetic response. Patients with increased risk of hypoglycemia (elderly or patients with renal impairment) should be started with 1/500 mg once daily. The maximum recommended dose is 8/2000 mg once daily.

Contraindication:
For Glimepiride:
- Type 1 Diabetes or Diabetic Ketoacidosis
- Hypersensitivity to Glimepiride
- Hypersensitivity to Sulfonylureas and Sulfonamide derivatives

For Metformin:
- Renal disease or dysfunction which may also result from conditions such as cardiovascular collapse (shock), acute MI & septicemia
- Patients undergoing radiologic studies involving parenteral administration of iodinated contrast meals

Warning and Precaution:
* Hypoglycemia: All sulfonylureas including Glimepiride can cause Hypoglycemia. Caution should be maintained while initiating and increasing the dose of Glimepiride in patients who are most susceptible to hypoglycemia (e.g. the elderly, the patients with renal impairment, and patients on other anti-diabetic medications). Debilitated or malnourished patients, and those with adrenal, pituitary, or hepatic impairment are particularly susceptible to the hypoglycemic action of glucose-lowering medications. Hypoglycemia is also more likely to occur when caloric intake is deficient, after severe or prolonged exercise, or when alcohol is ingested.
* Hemolytic anemia: Sulfonylureas cause hemolytic anemia in Glucose-6-Phosphate Dehydrogenase (G6PD) deficient patients. Use of non-sulfonylurea medication is recommended in those cases.
* In Renal Impairment: Glimepiride metabolites may accumulate in patients with renal impairment. Use of Glimepiride is not recommended in patients with Chronic Kidney Disease (Stage 4 or 5), due to the risk of severe hypoglycemia. Glimepiride is not recommended in individuals with Glomerular Filtration Rate (GFR) < 30 ml/min.
* *Hypoxic states:* Cardiovascular collapse (shock), acute CHF, acute MI and other conditions characterized by hypoxemia have been associated with lactic acidosis and may also cause prerenal azotemia. If such events occur, Metformin must be discontinued.
* *Vitamin B_{12} levels:* Certain individuals with inadequate Vitamin B_{12} or calcium intake or absorption may be predisposed to developing subnormal Vitamin B_{12} levels. In these patients, routine serum Vitamin B_{12} measurements as 2 or 3-year intervals may be useful.

Side effects:
Hypoglycemia, headache, dizziness, nausea, vomiting, diarrhea, flu-like syndrome, allergic skin reactions such as pruritis, erythema and urticaria, weight gain and elevated serum ALT levels may be reported.

Use in Pregnancy and Lactation:
During Pregnancy: There is insufficient data available for the use of Glimepiride in pregnant individuals. However, sulfonylureas (including Glimepiride) cross the placenta and cause hypoglycemia in neonates. Therefore, Glimitus should not be administered to pregnant women.
During Lactation: It is not known whether Glimepiride is excreted in human milk. However, studies on animals have shown that Glimepiride is present in rat milk. Therefore, Glimitus should not be administered to breast-feeding women due to the risk of hypoglycemia in the infant.
In both cases, switching to insulin therapy for the duration of pregnancy or lactation is recommended.

Use in Children and Adolescents:
Glimitus M is not recommended for use in children because of its adverse effects on body weight and hypoglycemia.

Drug interactions:
For Glimepiride: The susceptibility to hypoglycemia can be increased by co-administration of certain drugs with Glimitus M, such as other oral anti-diabetic medications, pramlintide acetate, insulin, angiotensin converting enzyme (ACE) inhibitors, H2 receptor antagonists, fibrates, propoxyphene, pentoxifylline, somatostatin analogs, anabolic steroids and androgens, cyclophosphamide, phenyramidol, guanethidine, fluconazole, sulfinpyrazone, tetracyclines, clarithromycin, disopyramide, quinolones, and those drugs that are highly protein-bound, such as fluoxetine, nonsteroidal anti-inflammatory drugs, salicylates, sulfonamides, chloramphenicol, coumarins, probenecid and monoamine oxidase inhibitors. The glucose-lowering effect of Glimitus is reduced by certain drugs leading to uncontrolled blood glucose levels, such as danazol, glucagon, somatropin, protease inhibitors, atypical antipsychotic medications (e.g., olanzapine and clozapine), barbiturates, diazoxide, laxatives, rifampin, thiazides and other diuretics, corticosteroids, phenothiazines, thyroid hormones, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics (e.g., epinephrine, albuterol, terbutaline), and isoniazid. Beta-blockers, clonidine, reserpine and acute or chronic alcohol intake may contribute to either potentiation or weakening of Glimepiride's glucose-lowering action.
For Metformin: Miconazole can cause severe hypoglycemia when co-administered with Glimitus. Colesevelam can reduce the maximum plasma concentration and total exposure of Glimitus when the two are co-administered. Drugs that may affect Metformin include Alcohol, Cationic drugs, Cimetidine, Furosemide, Iodinated contrast material and Nifedipine. Drugs that may be affected by Metformin include Glyburide and Furosemide. Certain drugs tend to produce hyperglycemia and may lead to loss of glycemic control such as Thiazide and other diuretics, Corticosteroids, Phenothiazines, Thyroid products, Estrogens, Oral contraceptives, Phenytoin, Nicotinic acid, Sympathomimetics, Calcium channel blockers, Isoniazide and Beta-adrenergic blockers.

Overdose:
Overdosage of sulfonylureas, including Glimepiride, can produce hypoglycaemic. Mild hypoglycaemic symptoms without loss of consciousness or neurologic findings should be treated aggressively with oral glucose and adjustments in drug dosage or meal patterns. Close monitoring should continue untill the physician is assured that the patient is out of danger. Severe hypoglycaemic reactions with coma, seizure of other neurological impairment occur infrequently, but constitute medical emergencies requiring immediate hospitalization. If hypoglycaemic 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 solution at a rate that will maintain the blood glucose at a level above 100 mg/dl. Patients should be closely monitored for a minimum of 24 to 46 hours, because hypoglycaemia may recur after apparent clinical recovery. overdose of Metformin may lead to lactic aacidosis. Remove Metrormin by haemodialysis.

Storage:
Do not store above 30°C. Protect from light. Keep all medicines out of the reach of children.

Packaging:
Glimitus M 1/500 mg: Each box contains 3x10's tablets in blister pack.
Glimitus M 2/500 mg: Each box contains 3x10's tablets in blister pack.

Manufactured by

ZISKA PHARMA

Ziska Pharmaceuticals Ltd.
Kaliakoir, Gazipur, Bangladesh