Glypin®MET (Tablets)

1346
Ref. No.:INS346/12.18

Glimepiride and Metformin Hydrochloride
Sulfonyl Urea
Biguanide

GLYPIN® MET 2:500MG TABLETS (FILM COATED)

PRESENTATION:
Glypin® MET 2:500mg Film Coated Tablets: White, oblong shaped film coated tablets embossed COSMOS on one side and PLAIN on the other side. Each film coated tablet contains: Glimepiride 2 mg, Metformin Hydrochloride 500 mg, Lactose and other excipients.

CLINICAL PHARMACOLOGY:
Glypin® MET combines two antihyperglycaemic agents with complimentary mechanisms of action to improve glycemic control in patients with type 2 diabetes: Glimepiride, a member of the Sulfonylurea class, and Metformin hydrochloride, a member of the Biguanide class.
Glimepiride
Glimepiride reduces blood glucose levels by correcting both defective insulin secretion and peripheral insulin resistance. It interacts with specific receptors at the plasma membrane of the insulin releasing pancreatic beta- cells where it inhibits ATP- sensitive K+ channels resulting in depolarization of the cell membrane, opening of voltage sensitive Ca2+ channels, increase in intracellular calcium levels and subsequent insulin release.
Metformin
Metformin acts as an antihyperglycaemic agent by improving hepatic and peripheral tissue sensitivity to insulin. It also appears to have beneficial effect on serum lipid levels and so on fibrinolytic activity. Metformin therapy is not associated with increase in body weight. Metformin decreases glucose production, decreases intestinal absorption of glucose and improves insulin sensitivity by increasing peripheral glucose uptake and utilization.

Pharmacokinetics:
Glimepiride: Glimepiride is completely absorbed from the gastrointestinal tract. Peak plasma concentrations occur in 2 to 3 hours, and it is highly protein bound. The drug is extensively metabolised in the liver to two main metabolites. The cytochrome P450 isoenzyme CYP2C9 is involved in the formation of a hydroxyl derivative, which is further metabolised to a carboxy derivative by cytosolic enzymes.
The half-life after multiple doses is about 9 hours. About 60% of a dose is eliminated in the urine and 40% in the faeces.
Metformin: Metformin Hydrochloride is slowly and incompletely absorbed from the gastrointestinal tract; the absolute bioavailability of a single 500mg dose is reported to be about 50 to 60%, although this is reduced somewhat if taken with food. Protein binding in plasma is negligible.
Metformin is excreted unchanged in the urine. The plasma elimination half -life is reported to range from about 2 to 6 hours. Metformin crosses the placenta and is distributed into breast milk in small amounts.

USES:
Glypin® MET is indicated in the treatment of type 2 diabetes mellitus.
It is indicated in the treatment of adult patients who are unable to achieve sufficient glycemic control at their maximally tolerated dose of oral metformin alone or who are already treated with the combination of glimepiride and metformin as separate tablets.
- It is indicated in combination with a sulphonylurea (i.e. triple combination therapy) as an adjunct to diet and exercise in adult patients inadequately controlled with metformin and a sulphonylurea.
- It is indicated in triple combination therapy with insulin as an adjunct to diet and exercise to improve glycemic control in adult patients when insulin at a stable dose and metformin alone do not provide adequate glycemic control.

DOSAGE AND ADMINISTRATION:
The recommended dose is 1-2 tablets once daily to a maximum of 4 tablets/day. Glypin® MET is not recommended for use in children below 18 years of age.

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CONTRA-INDICATIONS AND WARNINGS:
Glypin® MET should be used with caution in patients with: Insulin-dependent diabetes mellitus, renal or hepatic failure, alcoholism, NIDDM complicated by severe ketosis and acidosis, diabetic precoma and coma, patients undergoing surgery, after severe trauma or during infections, chronic obstructive pulmonary disease, coronary heart disease, cardiac failure, peripheral vascular disease, pregnancy, known hypersensitivity to the drug.

Precautions:
Hypoglycaemia may occur if the patient's dietary intake is reduced or after accidental or deliberate overdose or after severe exercise, trauma and stress. Hypoglycaemic symptoms can be reduced by prescribing a diabetic meal plan. Immediate intervention should be done if signs and symptoms of hypoglycaemia occur. Adjust dose of drug according to blood and urinary glucose levels during the first few months. However, there have been few reports of lactic acidosis with Metformin in patients of renal or liver disease.

Adverse Effects
Vomiting, gastrointestinal pain and diarrhoea have been reported, but the incidence in placebo controlled trials was less than 1%. Isolated transaminase elevations have been reported. Cholestatic jaundice has been reported to occur rarely with sulfonylureas. Allergic skin reactions, e.g., pruritus, erythema, urticaria, and morbilliform or maculopapular eruptions, occur in less than 1% of treated patients. Cases of hyponatremia have been reported with Glimepiride and all other sulfonylureas, most often in patients who are on other medications or have medical conditions known to cause hyponatremia or increase release of antidiuretic hormone.
Change in accommodation and / or blurred vision may occur. Nausea, diarrhoea, gastric pain, constipation, vomiting, metallic taste in mouth. Rash, pruritus, urticaria, erythema and flushing Headache and dizziness Impaired gastrointestinal absorption of vitamin B_{12} and folic acid has been associated with long-term metformin therapy. Measurement of serum vitamin B_{12} level is advised on an annual basis as metformin interferes with B_{12} absorption from intrinsic factor complex.

Overdosage
Hypoglycaemia may occur in case of an overdosage. In the event of an overdosage, gastric lavage should be performed and correction of hypoglycaemia should be attempted by intravenous administration of hypertonic glucose (10 or 30%) with continued monitoring of the patient's blood glucose levels.

Interactions
Glimepiride
The hypoglycemic action of sulfonylureas may be potentiated by certain drugs, including nonsteroidal anti-inflammatory drugs and other drugs that are highly protein bound, such as salicylates, sulfonamides, monoamine oxidase inhibitors, and beta adrenergic blocking agents. Coadministration of aspirin and Glimepiride led to a 34% decrease in the mean Glimepiride AUC and, therefore, a 34% increase in the mean CL/f.
Metformin
A drug interaction of metformin is seen with phenprocoumon, hyperglycemic agent (e.g. - thiazides, corticosteroids and others), alcohol, furosemide, nifedipine and cationic drugs (amiloride, digoxin, morphine, procainamide, quinidine, quinine, ranitidine, triamterene, trimethoprim and cimetidine, vancomycin). The absorption of metformin may be reduced by acarbose and guar gum.

Pregnancy and Breastfeeding
Glypin® MET is not recommended during pregnancy and breastfeeding.

PHARMACEUTICAL PRECAUTIONS:
Store in a dry place below 30ºC. Protect from light. Keep all medicines out of the reach of children.

LEGAL CATEGORY:
Prescription Only Medicine (POM)

®Regd. TM

COSMOS

Cosmos Limited,
Rangwe Rd; Off Lunga Lunga Rd,
Nairobi, Kenya