Film coated Tablets

Amarit Plus

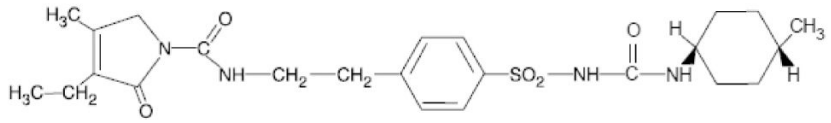
Glimepiride B.P. + Metformin HCl B.P.

ایمارِٹ پلس

گلائی پرائڈ بی۔پی + میٹ فورمین ہائیڈروکلورائڈ بی۔پی

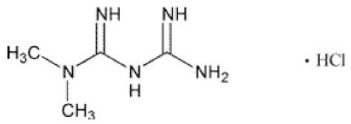
DESCRIPTION

Amarit Plus combines glimepiride and metformin hydrochloride, two anti-hyperglycemic agents with complementary mechanisms of action to improve glycemic control in patients with type 2 diabetes.
Chemically, glimepiride is identified as 1-[[p-[2-(3-ethyl-4-methyl-2-oxo-3-pyrroline-1carboxamido) ethyl] phenyl]sulfonyl]-3-(trans-4-methylcyclohexyl)urea having a molecular Formula: C24H34N4O5S and a structural formula of;



Glimepiride

Chemically, metformin HCl is identified as 1,1-Dimethylbiguanide monohydrochloride having a molecular Formula: C4H11N5·HCl and a structural formula of;



QUALITATIVE & QUANTITATIVE COMOSITION

Amarit Plus (Glimepiride + Metformin HCl) is available for oral administration as;

Each Film coated tablet contains

Glimepiride B.P..... 2mg
Metformin HCl B.P.....500mg
Reko's specs.

CLINICAL PHARMACOLOGY

MECHANISM OF ACTION

Glimepiride is a third generation sulphonylurea. It reduces blood glucose levels by stimulating insulin secretions from the beta cells of pancreas and also known to increase peripheral insulin sensitivity thereby decreasing insulin resistance. There is closing of K+ channels and simultaneously opening of calcium channels giving rise to calcium influx which ultimately results in insulin release from the beta cells of pancreas. Glimepiride also enhances the glucose sensitivity of the beta cells. Glimepiride improves peripheral insulin sensitivity which increases the glucose clearance and also decreases hepatic glucose production.
Metformin acts by improving hepatic and peripheral tissue sensitivity of insulin and thus it acts as an anti hyperglycemic agent. It also has beneficial effect on the serum lipid profile and has even demonstrated to improve fibrinolytic activity. Metformin therapy does not induce weight gain.

INDICATIONS

Amarit Plus (Glimepiride + Metformin HCl) is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes whose diabetes is not adequately controlled with glimepiride or metformin HCl alone, or for those patients who have initially responded to Glimepiride or metformin HCl alone and require additional glycemic control.

DOSAGE AND ADMINISTRATION

The tablet is taken as once daily with meals to a maximum of 4 tablets /day or as directed by the physician. Tablets should be swallowed whole and not crushed or chewed. Dosage must be individualized on the basis of both effectiveness and tolerance. While not exceeding the maximum recommended dose. The maximum daily dose of Metformin is 2000 mg and of Glimepiride is 8mg.

PHARMACOKINETICS

Glimepiride

Glimepiride is rapidly and completely absorbed after oral administration. The oral bioavailability is approximately 100%. More than 99% of the drug is bound to plasma proteins. Glimepiride is completely biotransformed by hepatic oxidative metabolism into cyclohexylhydroxymethyl derivative (M1) which is further metabolized to form a carboxyl derivative (M2) by cytosolic enzymes. After a single dose, the elimination half life (t1/2) of Glimepiride is 5 hours. The urinary excretion of metabolites accounts for 60% of dose, the remainder is found as metabolites in feces.

Metformin HCl

Metformin has absolute oral bioavailability of 50-60%. GIT absorption is complete within 6 hours of ingestion. Metformin is rapidly distributed in body after absorption. The renal elimination of Metformin is biphasic. 95% of the absorbed Metformin is eliminated during primary elimination phase having half-life of 6 hours. Rest of the 5% is eliminated during slow terminal elimination phase with mean half-life of 20 hours. Metformin is not bound to plasma proteins. 40-60% of the dose is recovered as unchanged drug in urine with a further 30% recovered as unchanged drug in feces.

CONTRAINDICATIONS

Insulin-dependent diabetes mellitus, renal or hepatic failure, alcoholism, NIDDM complicated by severe ketosis and acidosis, diabetic pre-coma 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 any of the ingredients.

WARNINGS AND PRECAUTIONS

Hypoglycemia may occur if the patients dietary intake is reduced or after accidental or deliberate overdose or after severe exercise, trauma and stress. Hypoglycemic symptoms can be reduced by prescribing a diabetic meal plan. Immediate intervention should be done if signs and symptoms of hypoglycemia 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.

USAGE IN PREGNANCY AND LACTATION

The drug should not be used in pregnant women and lactating mothers. They should only be used if potential benefit outweights the risk involved.

PEDIATRIC USE

Safety and effectiveness of the drug in children have not been established.

DRUG INTERACTIONS

Glimepiride

The hypoglycemic action of sulfonylurea may be potentiated by certain drugs, including non steroidal anti-inflammatory drugs and other drugs that are highly protein bound, such as salicylates, sulfonamides, monoamine oxidase inhibitors, and beta adrenergic blocking agents; Co-administration of aspirin and Glimepiride led to a 34% decrease in the mean. Glimepiride AUC and, therefore, a 34% increase in the mean CL/f.
The mean Cmax had a decrease of 4%. Blood glucose and serum C-peptide concentrations were unaffected and no hypoglycemic symptoms were reported. Co-administration of either cimetidine (800mg once daily) or ranitidine (150mg bid) with a single 4mg oral dose of Glimepiride did not significantly alter the absorption and disposition of glimepiride. Concomitant administration of propanolol (40mg tid) and Glimepiride significantly increased Cmax, AUC, and t1/2 of Glimepiride by 23%, 22% and 15% respectively, and it decreased CL/f by 18%. Concomitant administration of Glimepiride (4mg once daily) did not alter the pharmacokinetic characteristics of R and S-warfain enantiomers following administration of a single dose (25mg) of racemic warfarin. The responses of serum glucose, insulin, C-peptide, and plasma glucagon to 2mg Glimepiride were unaffected by coadministraton of ramipril (an ACE inhibitor) 5mg once daily.

Metformin HCl

Drug interactions of Metformin are 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, cimetidine and vancomycin). The absorption of Metformin may be reduced by acarbose and guar gum.

ADVERSE REACTIONS

Hyponatremia have been reported with Glimepiride and all other sulfonylurea's, most often in patients who are on other medications or have medical conditions known to cause hyponatremia or increase release of ant diuretic hormone. Change in concentration and / or blurred vision may occur.

OVERDOSAGE AND MANAGEMENT

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

INSTRUCTIONS

Store at a temperature below 30ºC
Protect from heat, sunlight and moisture
Keep all the medicines out of the reach of children.

How supplied

Amarit Plus (Glimepiride + Metformin HCl) Tablets 2mg + 500mg are available in Alu-Alu blister strip pack of 30's.

Please read the contents carefully before use.
This package insert is continually updated from time to time.

REKO

Manufactured by:
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