Gluvan Plus

Vildagliptin + Metformin Hydrochloride

Composition:
Gluvan Plus 500 Tablet: Each film coated tablet contains Vildagliptin INN 50 mg & Metformin Hydrochloride BP 500 mg.
Gluvan Plus 850 Tablet: Each film coated tablet contains Vildagliptin INN 50 mg & Metformin Hydrochloride BP 850 mg.

Pharmacology:
Vildagliptin acts primarily by inhibiting DPP-4, the enzyme responsible for the degradation of the incretin hormones GLP-1 (glucagon-like peptide-1) and GIP (glucose-dependent insulinotropic polypeptide). The administration of Vildagliptin results in a rapid and complete inhibition of DPP-4 activity resulting in increased fasting and postprandial endogenous levels of the incretin hormones GLP-1 and GIP. By increasing the endogenous levels of these incretin hormones, Vildagliptin enhances the sensitivity of beta cells to glucose, resulting in improved glucose-dependent insulin secretion. By increasing endogenous GLP-1 levels, Vildagliptin also enhances the sensitivity of alpha cells to glucose, resulting in more glucose-appropriate glucagon secretion. The enhanced increase in the insulin/glucagon ratio during hyperglycaemia due to increased incretin hormone levels results in a decrease in fasting and postprandial hepatic glucose production, leading to reduced glycaemia.
Metformin lowers both basal and postprandial plasma glucose. It does not stimulate insulin secretion and therefore does not produce hypoglycaemia or increased weight gain. Metformin may exert its glucose-lowering effect via four mechanisms:

- by reduction of hepatic glucose production through inhibition of gluconeogenesis and glycogenolysis;
- in muscle, by modestly increasing insulin sensitivity, improving peripheral glucose uptake and utilization
- by delaying intestinal glucose absorption.
- stimulates intracellular glycogen synthesis by acting on glycogen synthase and increases the transport capacity of glucose transporters (GLUT-1 and GLUT-4).

Indications:
Gluvan Plus is indicated as an adjunct to diet and exercises to improve glycaemic control in patients with type 2 diabetes mellitus whose diabetes is not adequately controlled on Metformin Hydrochloride or Vildagliptin alone or who are already treated with the combination of Vildagliptin and Metformin Hydrochloride, as separate tablets.

Dosage and Administration:
Adults: Based on the patient's current dose of Metformin, **Gluvan Plus** may be initiated at either 50 mg/500 mg or 50 mg/850 mg twice daily, 1 tablet in the morning and the other in the evening. Patients receiving Vildagliptin and Metformin from separate tablets may be switched to **Gluvan Plus** containing the same doses of each component. Doses higher than 100 mg of vildagliptin are not recommended. There is no clinical experience of Vildagliptin and Metformin in triple combination with other antidiabetic agents. Taking Gluvan Plus with or just after food may reduce gastrointestinal symptoms associated with Metformin.

Contraindications:
This combination is contraindicated in patients with known hypersensitivity to Vildagliptin or Metformin Hydrochloride or to any of the excipients. It is contraindicated in patients with renal disease or renal dysfunction, acute myocardial infarction, and septicaemia. It is also contraindicated in patients with congestive heart failure patients and in patients with acute or chronic metabolic acidosis, including diabetic ketoacidosis, with or without coma. It should be temporarily discontinued in patients undergoing radiologic studies involving intravascular administration of iodinated contrast materials, because use of such products may result in acute alteration of renal function.

Side Effects:
The most common side effects are headache, tremor, dizziness, nausea, hypoglycaemia etc.

Use in Special Groups:
Use in pregnancy:
There are no adequate and well controlled studies in pregnant women and therefore, Gluvan Plus should not be used during pregnancy unless the potential benefit justifies the potential risk to the foetus.

Use in lactation:
No studies have been conducted with the components of this combination. As it is not known whether Vildagliptin and/or Metformin Hydrochloride is excreted in human milk this combination should not be administered to breast-feeding women.

Use in pediatric patients:
The safety and effectiveness of this combination in pediatric patients have not been established.Therefore, this combination is not recommended for use in children below 18 years of age.

Use in geriatric patients:
As Metformin is excreted via the kidney, and elderly patients have a tendency to decreased renal function, elderly patients taking this combination should have their renal function monitored regularly.This combination should only be used in elderly patients with normal renal function.

Patients with renal impairment:
This combination should not be used in patients with renal failure or renal dysfunction, e.g. serum creatinine levels ≥ 1.5 mg/dL (>135 micro mol/L) in males and ≥ 1.4 mg/dL (>110 micro mol/L) in females.

Patients with hepatic impairment:
This combination is not recommended in patients with hepatic impairment including patients with a pre-treatment ALT or AST >3 X the upper limit of normal.

Drug Interactions:
No clinically relevant pharmacokinetic interaction was observed when Vildagliptin (100 mg once daily) was co-administered with Metformin Hydrochloride (1,000 mg once daily). Vildagliptin has a low potential for drug interactions. Since Vildagliptin is not a cytochrome P (CYP) 450 enzyme substrate nor does it inhibit nor induces CYP 450 enzymes, it is not likely to interact with co-medications that are substrates, inhibitors or inducers of these enzymes. As a result of these studies no clinically relevant interactions with other oral antidiabetics (glibenclamide, pioglitazone, metformin hydrochloride), amlodipine, digoxin, ramipril, simvastatin, valsartan or warfarin were observed after co-administration with Vildagliptin. On the other hand, furosemide, nifedipine and glyburide increase Cmax and blood AUC of Metformin with no change in renal clearance of Metformin.

Storage:

- Store below 30°C, keep in dry place & protect from light.
- Keep out of the reach of children.

Packing:
Gluvan Plus 500 Tablet: Each box contains 30 tablets in alu-alu blister pack.
Gluvan Plus 850 Tablet: Each box contains 30 tablets in alu-alu blister pack.

Manufactured by:
ARISTOPHARMA LTD.
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