HOSPIMAX
Maximising Life

HosVilda-M™

Vildagliptin 50 mg + Metformin 500 mg Tablets

Complete Command Over Diabetes

Product Description-

- **Hosvilda M: -**Each film coated tablet contains Vildagliptin 50mg with Metformin 500mg

General Information

Vildagliptin is an orally active antihyperglycemic agent that selectively inhibits the dipeptidyl peptidase-4 (DPP-4) enzyme. It is used to manage type II diabetes mellitus, where GLP-1 secretion and insulinotropic effects are impaired. By inhibiting DPP-4, vildagliptin prevents the degradation of glucagon-like peptide 1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP), which are incretin hormones that promote insulin secretion and regulate blood glucose levels. Elevated levels of GLP-1 and GIP consequently results in improved glycaemic control. In clinical trials, vildagliptin has a relatively low risk of hypoglycaemia.

Metformin is an antihyperglycemic agent of the *biguanide* class, used for the management of type II diabetes). Currently, metformin is the first drug of choice for the management of type II diabetes and is prescribed to at least 120 million people worldwide

Oral vildagliptin was approved by the European Medicines Agency in 2008 for the treatment of type II diabetes mellitus in adults as monotherapy & in combination with metformin in patients with inadequate glycaemic control following monotherapy.

Indication & Usage: -

HosVilda-Mis indicated in adults with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control:

- as initial therapy when diabetes is not adequately controlled by diet and exercise alone
- as therapy in patients inadequately controlled with metformin hydrochloride or vildagliptin alone or who are already treated with the combination of vildagliptin and metformin hydrochloride, as separate tablets
- as combination therapy- in combination with other medicinal products, including insulin, when these do not provide adequate glycemic control

Dosage & Administration

- The recommended dose of vildagliptin with metformin is twice daily, 1 tablet in the morning & 1 in the evening.

Mechanism Of Action: -

Vildagliptin exerts its blood glucose-lowering effects by selectively inhibiting dipeptidyl peptidase-4 (DPP-4), an enzyme that rapidly truncates and inactivates GLP-1 and GIP upon their release from the intestinal cells. DPP-4 cleaves oligopeptides after the second amino acid from the N-terminal end. Inhibition of DPP-4 substantially prolongs the half-life of GLP-1 and GIP, increasing the levels of active circulating incretin hormones. The duration of DPP-4 inhibition by vildagliptin is dose-dependent. Vildagliptin reduces fasting and prandial glucose and HbA1c. It enhances the glucose sensitivity of alpha- and beta-cells and augments glucose-dependent insulin secretion. Fasting and postprandial glucose levels are decreased, and postprandial lipid and lipoprotein metabolism are also improved.

Metformin's mechanisms of action are unique from other classes of oral antihyperglycemic drugs. Metformin decreases blood glucose levels by decreasing hepatic glucose production (gluconeogenesis), decreasing the intestinal absorption of glucose, and increasing insulin sensitivity by increasing peripheral glucose uptake and utilization. It is well established that metformin inhibits mitochondrial complex I activity, and it has since been generally postulated that its potent antidiabetic effects occur through this mechanism . The above processes lead to a decrease in blood glucose, managing type II diabetes and exerting positive effects on glycemic control

Absorption

In a fasting state, vildagliptin is rapidly absorbed following oral administration. Peak plasma concentrations are observed at 1.7 hours following administration. Plasma concentrations of vildagliptin increase in an approximately dose-proportional manner.

The absolute bioavailability of a metformin 500 mg tablet administered in the fasting state is about 50%-60%. Single-dose clinical studies using oral doses of metformin 500 to 1500 mg and 850 to 2550 mg show that there is a lack of dose proportionality with an increase in metformin dose, attributed to decreased absorption rather than changes in elimination

Distribution

The mean volume of distribution of vildagliptin at steady state after intravenous administration is 71 L, suggesting extravascular distribution

The apparent volume of distribution (V/F) of metformin after one oral dose of metformin 850 mg averaged at 654 ± 358 L

Metabolism

About 69% of orally administered vildagliptin is eliminated via metabolism not mediated by cytochrome P450 enzymes. Based on the findings of a rat study, DPP-4 contributes partially to the hydrolysis of vildagliptin. Vildagliptin is metabolized to pharmacologically inactive cyano (57%) and amide (4%) hydrolysis products in the kidney.LAY 151 (M20.7) is a major inactive metabolite and a carboxylic acid that is formed via hydrolysis of the cyano moiety: it accounts for 57% of the dose. Other circulating metabolites reported are an N-glucuronide (M20.2), an N-amide hydrolysis product (M15.3), two oxidation products, M21.6 and M20.

Intravenous studies using a single dose of metformin in normal subjects show that metformin is excreted as unchanged drug in the urine and does not undergo hepatic metabolism (no metabolites have been identified in humans) nor biliary excretion

Route of elimination

Vildagliptin is eliminated via metabolism. Following oral administration, approximately 85% of the radiolabelled vildagliptin dose was excreted in urine and about 15% of the dose was recovered in feces. Of the recovered dose in urine, about 23% accounted for the unchanged parent compound.

Metformin is substantially excreted by the kidney. Following oral administration, approximately 90% of the absorbed drug is eliminated via the renal route within the first 24 hours, with a plasma elimination half-life of approximately 6.2 hours. In blood, the elimination half-life is approximately 17.6 hours, suggesting that the erythrocyte mass may be a compartment of distribution.

Overdose

There is limited information regarding overdose with vildagliptin. In one study, patients experienced muscle pain, mild and transient paraesthesia, fever, oedema, and a transient increase in lipase levels at a dose of 400 mg. At 600 mg, one subject experienced oedema of the feet and hands and increases in creatine phosphokinase (CPK), aspartate aminotransferase (AST), C-reactive protein (CRP) and myoglobin levels. Supportive management is recommended in case of an overdose. There is no known antidote, and vildagliptin and its major metabolite cannot be removed via haemodialysis.

Use in specific population

Renal impairment–

- **Vildagliptin:**No dose adjustment is required in patients with mild renal impairment (creatinine clearance ≥ 50 ml/min). In patients with moderate or severe renal impairment or with end-stage renal disease (ESRD), the recommended dose of Vildagliptin is 50 mg once daily.
- **Metformin:**In patients with decreased renal function (based on measured creatinine clearance), the plasma and blood half-life of metformin hydrochloride is prolonged and the renal clearance is decreased in proportion to the decrease in creatinine clearance.

Hepatic impairment-

- **Vildagliptin:** should not be used in patients with hepatic impairment, including patients with pre-treatment alanine aminotransferase (ALT) or aspartate aminotransferase (AST) > 3x the upper limit of normal (ULN).
- No pharmacokinetic studies of metformin hydrochloride have been conducted in subjects with hepatic impairment.

- **Elderly (≥ 65 years)** -No dose adjustments are necessary in elderly patients

- **Paediatric population** Vildagliptin is not recommended for use in children and adolescents (< 18 years). The safety and efficacy of Vildagliptin in children and adolescents (< 18 years) have not been established. No data are available.
- **Pregnancy** -There are no adequate data from the use of vildagliptin in pregnant women.Should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus.
- **Lactation** -It is unknown whether vildagliptin is excreted in human milk or not.Should not be administered to breast-feeding women.

Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section.

Special warnings and precautions

- **General**-HosVilda-M is not a substitute for insulin in insulin-requiring patients. Vildagliptin should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.
- **Renal impairment**-Metformin-containing products are contraindicated in patients with GFR < 30 mL/min and should be temporarily discontinued in the presence of conditions that alter renal function
- **Hepatic impairment** Vildagliptin should not be used in patients with hepatic impairment, including patients with pre-treatment ALT or AST > 3x ULN.
- **Liver enzyme monitoring-** Patients may develop jaundice or other signs suggestive of liver dysfunction should discontinue vildagliptin.
- **Acute pancreatitis** Use of vildagliptin has been associated with a risk of developing acute pancreatitis. Patients should be informed of the characteristic symptom of acute pancreatitis.

Adverse Reaction:

Vildagliptin

- **Common:**Hypoglycaemia , Headache, chills , Nausea, Gastro-oesophageal reflux disease, , Dizziness, tremor , Hyperhidrosis , Asthenia, Weight increase , Oedema peripheral
- **Uncommon:** Diarrhoea, Flatulence , Oedema peripheral , Constipation , Arthralgia , Hypoglycaemia
- Headache , Asthenia
- **Very Rare:** Upper respiratory tract infection , Nasopharyngitis

Meformin HCL

- **Very Common:**Decreased appetite**,** Flatulence, Nausea, Vomiting, Diarrhea, Abdominal pain
- **Common:**Dysgeusia
- **Very Rare:** Lactic acidosis, Hepatitis, Skin reactions such as erythema, pruritus, urticarial