Velon®-M
(Vildagliptin + Metformin HCl)
Tablets

50mg/500mg
50mg/850mg
50mg/1000mg

ویلون۔ایم
(ولڈاگلپٹن + میٹ فورمن ہائیڈروکلورائیڈ)
ٹیبلٹس

۵۰ ملی گرام / ۵۰۰ ملی گرام
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QUALITATIVE AND QUANTITATIVE COMPOSITION

Velon®-M Tablets 50mg/500mg
Each film-coated tablet contains:
Vildagliptin.....50mg
Metformin Hydrochloride U.S.P. 500mg
Innovator's Specification

Velon®-M Tablets 50mg/850mg
Each film-coated tablet contains:
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Metformin Hydrochloride U.S.P. 850mg
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Velon®-M Tablets 50mg/1000mg
Each film-coated tablet contains:
Vildagliptin.....50mg
Metformin Hydrochloride U.S.P. 1000mg
Innovator's Specification

WARNINGS: Life threatening lactic acidosis can occur due to accumulation of metformin. The main risk factor is renal impairment, other risk factors include old age associated with reduced renal function and high doses of metformin above 2 g per day.

DESCRIPTION

Velon®-M combines two oral hypoglycaemic agents with complimentary mechanisms of action to improve glycaemic control in patients with type 2 diabetes. Vildagliptin, a member of the islet enhancer class and Metformin, a member of the biguanide class.

CLINICAL PHARMACOLOGY

Mechanism of Action: Vildagliptin: A member of the class that enhances islet cell insulin secretion via an augmented incretin effect is a high affinity dipeptidyl- peptidase-4 (DPP-4) inhibitor that improves glycemic control.
Metformin: Metformin is a biguanide with hypoglycemic effects, lowering both basal and postprandial glucose. It does not stimulate insulin secretion and therefore does not produce hypoglycemia or increased weight gain.
Pharmacodynamics:
Vildagliptin: 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).
Metformin: Metformin may exert its glucose-lowering effect via three 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 utilisation;
- by delaying intestinal glucose absorption.

Pharmacokinetics
Absorption: Vildagliptin: Following oral administration in the fasting state, Vildagliptin is rapidly absorbed with peak plasma concentrations observed at

1.75 hours. Coadministration with food slightly decreases the rate of absorption of Vildagliptin. Metformin Hydrochloride: Studies using single oral doses of metformin hydrochloride tablets 500 mg to 1,500 mg, and 850 mg to 2,550 mg, indicate that there is a lack of dose proportionality with increasing doses, which is due to decreased absorption rather than an alteration in elimination. Food decreases the extent of and slightly delays the absorption of metformin hydrochloride.

Distribution: Vildagliptin: The plasma protein binding of Vildagliptin is low (9.3%), and Vildagliptin distributes equally between plasma and red blood cells. Metformin Hydrochloride: Metformin hydrochloride is negligibly bound to plasma proteins, in contrast to sulfonylureas, which are more than 90% protein bound. Metabolism: Vildagliptin: Metabolism is the major elimination pathway for Vildagliptin in humans. Vildagliptin is not metabolized by cytochrome P450 enzymes to any quantifiable extent. In-vitro studies demonstrated that Vildagliptin does not inhibit or induce cytochrome P450 enzymes. Metformin Hydrochloride: is excreted unchanged in the urine. No metabolites have been identified in humans. Excretion and elimination: **Vildagliptin:** Following oral administration of Vildagliptin, approximately 85% of the dose is excreted into the urine and 15% of the dose is recovered in the faeces. Renal excretion of the unchanged Vildagliptin accounts for 23% of the dose after oral administration. The elimination half-life after oral administration is approximately 3 hours and is independent of dose. Velon®-M. Metformin Hydrochloride: 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.

INDICATIONS

Velon®-M 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 on metformin hydrochloride alone or who are already treated with the combination of vildagliptin and metformin hydrochloride, as separate tablets. Treatment of type 2 diabetes should not be initiated with this fixed-dose combination.

CONTRAINDICATIONS

Hypersensitivity: Velon®-M is contraindicated in patients with known hypersensitivity to vildagliptin or metformin hydrochloride or to any of the excipients.

Renal Disease: Velon®-M is contraindicated in patients with renal disease or renal dysfunction.

Congestive Heart Failure: Velon®-M is contraindicated in patients with congestive heart failure requiring pharmacologic treatment.

Diabetic Ketoacidosis: Velon®-M is contraindicated in patients with acute or chronic metabolic acidosis, including diabetic ketoacidosis, with or without coma. Diabetic ketoacidosis should be treated with insulin.

Radiologic Studies: Velon®-M 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.

INTERACTIONS

Vildagliptin: 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. Metformin Hydrochloride: Furosemide: Furosemide increased Cmax and blood AUC of metformin with no change in renal clearance of metformin. Metformin decreased Cmax, blood AUC of furosemide, with no change in renal clearance of furosemide. Nifedipine: Nifedipine increased absorption, Cmax and AUC

of metformin, and increased excretion of metformin in urine. Metformin had minimal effects on nifedipine. Glyburide: Glyburide produced no changes in metformin PK/PD parameters. Cationic drugs: Cationic drugs (e.g., amiloride, digoxin, morphine, procainamide, quinidine, quinine, ranitidine, triamterene, trimethoprim, or vancomycin) that are eliminated by renal tubular secretion theoretically have the potential for interaction with metformin by competing for common renal tubular transport systems.
Other Certain drugs: tend to produce hyperglycemia and may lead to loss of glycemic control. These drugs include the thiazides and other diuretics, corticosteroids, phenothiazine, thyroid products, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetic, calcium channel blocking drugs, and isoniazid.

USE IN SPECIFIC POPULATION

Pregnancy: Velon®-M should not be used during pregnancy unless the potential benefit justifies the potential risk to the foetus.
Lactation: Velon®-M should not be administered to breast-feeding women.
Pediatric Use: Velon®-M is not recommended for use in children below 18 years of age.
Elderly patient: Velon®-M should only be used in elderly patients with normal renal function.
Hepatic patients: Velon®-M is not recommended in patients with clinical or laboratory evidence of hepatic impairment.
Renal Patients: Velon®-M should not be used in patients with renal failure or renal dysfunction

WARNINGS AND PRECAUTIONS

Lactic acidosis: Lactic acidosis, a very rare but serious metabolic complication, most often occurs at acute worsening of renal function, or cardiorespiratory illness or sepsis. Metformin accumulation occurs at acute worsening of renal function and increases the risk of lactic acidosis. **Administration of iodinated contrast agents:** Intravascular administration of iodinated contrast agents may lead to contrast induced nephropathy, resulting in metformin accumulation and increased risk of lactic acidosis. Metformin should be discontinued prior to or at the time of the imaging procedure and not restarted until at least 48 hours after, provided that renal function has been re-evaluated and found to be stable. Liver enzyme monitoring: Rare cases of hepatic dysfunction (including hepatitis) have been reported with vildagliptin. LFTs should be performed prior to the initiation of treatment with Velon®-M in order to know the patient's baseline value. Liver function should be monitored during treatment with Velon®-M at three-month intervals during the first year and periodically thereafter. Skin disease: In keeping with routine care of the diabetic patient, monitoring for skin disorders, such as blistering or ulceration, is recommended. **Acute pancreatitis:** Use of vildagliptin has been associated with a risk of developing acute pancreatitis. If pancreatitis is suspected, vildagliptin should be discontinued. Hypoglycaemia: Sulphonylureas are known to cause hypoglycaemia. Therefore a lower dose of sulphonylurea may be considered to reduce the risk of hypoglycaemia. **Surgery:** Metformin must be discontinued at the time of surgery under general, spinal or epidural anaesthesia.

ADVERSE REACTIONS

Very common: Nausea, vomiting, diarrhea, abdominal pain, loss of appetite
Common: Tremor, dizziness, headache, metallic taste
Uncommon: Constipation, peripheral odema, decrease of vitamin B12 absorption, lactic acidosis, Liver function test abnormalities, hepatitis, skin reactions such as erythema, pruritus, urticaria

DOSAGE AND ADMINISTRATION

Recommended Dosing: The recommended starting dose of Velon®-M should be based on the patient’s current regimen of vildagliptin and/or met-

formin hydrochloride. Velon®-M should be given with meals to reduce the gastrointestinal side effects associated with metformin hydrochloride. When using Velon®-M the maximum daily dose of vildagliptin (100 mg) should not be exceeded.

Starting dose for patients inadequately controlled on metformin hydrochloride monotherapy: Based on the patient's current dose of metformin hydrochloride, Velon®-M may be initiated at either the 50mg/500 mg, 50mg/850 mg or 50mg/1,000mg tablet strength twice daily.

Starting dose for patients switching from combination therapy of vildagliptin plus metformin hydrochloride as separate tablets: Velon®-M may be initiated with either the 50mg/500mg, 50mg/850mg or 50mg/1,000mg tablet strength based on the dose of vildagliptin or metformin already being taken.

Overdosage:

Vildagliptin: Doses up to 200 mg are well tolerated. At 400mg, cases of muscle pain, and individual cases of mild and transient paraesthesia, fever, oedema and transient increase in lipase levels (2x ULN) may occur. Vildagliptin is not dialyzable, however the major hydrolysis metabolite (LAY151) can be removed by hemodialysis. Metformin HCl: Lactic acidosis has been reported in approximately 32% of metformin hydrochloride overdose cases. Metformin hydrochloride is dialyzable with a clearance of up to 170 mL/min under good haemodynamic conditions. Therefore, haemodialysis may be useful for removal of accumulated drug from patients in whom metformin hydrochloride overdosage is suspected.

INSTRUCTIONS

Dosage as directed by the physician. Store below 30°C. Protect from heat, light and moisture. Keep all medicines out of the reach of children. To be sold on the prescription of a registered medical practitioner only.

PRESENTATION

Velon®-M (Vildagliptin/Metformin HCl) tablets 50mg/500mg are available in 4x7's Alu-Alu blister pack.

Velon®-M (Vildagliptin/Metformin HCl) tablets 50mg/850mg are available in 2x7's Alu-Alu blister pack.

Velon®-M (Vildagliptin/Metformin HCl) tablets 50mg/1000mg are available in 4x7's Alu-Alu blister pack.

ہدایات: خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

روشنی، گرمی اور نمی سے محفوظ رکھیں۔

تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

صرف رجسٹرڈ ڈاکٹر کے نسخہ پر فروخت کریں۔

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