Insutol Tablets

(Vildagliptin)

انسوٹول گولیاں

(ولڈاگلپٹن)

COMPOSITION:
Each tablet contains:
Vildagliptin ... 50mg
[Innovator's Specs.]

INDICATIONS:
Insutol Tablet is indicated in the treatment of type 2 diabetes mellitus in adults.
As monotherapy: - In patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance.
As dual oral therapy: - In combination with metformin, in patients with insufficient glycaemic control despite maximal tolerated dose of monotherapy with metformin.
- A sulphonylurea, in patients with insufficient glycaemic control despite maximal tolerated dose of a sulphonylurea and for whom metformin is inappropriate due to contraindications or intolerance.
- A thiazolidinedione, in patients with insufficient glycaemic control and for whom the use of a thiazolidinedione is appropriate.
As triple oral therapy: - In combination with: a sulphonylurea and metformin when diet and exercise plus dual therapy with these medicinal products do not provide adequate glycaemic control. Vildagliptin is also indicated for use in combination with insulin (with or without metformin) when diet and exercise plus a stable dose of insulin do not provide adequate glycaemic control.

PHARMACODYNAMICS: Mechanism of Action: 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 (glucagon-like peptide 1) and GIP (glucose-dependent insulinotropic polypeptide).

PHARMACOKINETICS: Absorption: Following oral administration in the fasting state, Vildagliptin is rapidly absorbed, with peak plasma concentrations observed at 1.7 hours. Food slightly delays the time to peak plasma concentration to 2.5 hours, but does not alter the overall exposure (AUC). Administration of Vildagliptin with food resulted in a decreased C_{max} (19%). However, the magnitude of change is not clinically significant, so that Vildagliptin can be given with or without food. The absolute bioavailability is 85%.
Distribution: The plasma protein binding of Vildagliptin is low (9.3%) and Vildagliptin distributes equally between plasma and red blood cells. The mean volume of distribution of Vildagliptin at steady-state after intravenous administration (V_{ss}) is 71 litres, suggesting extravascular distribution.
Biotransformation: Metabolism is the major elimination pathway for Vildagliptin in humans, accounting for 69% of the dose. The major metabolite (LAY 151) is pharmacologically inactive and is the hydrolysis product of the cyano moiety, accounting for 57% of the dose, followed by the glucuronide (BQS867) and the amide hydrolysis products (4% of dose). Accordingly, the metabolic clearance of Vildagliptin is not anticipated to be affected by co-medications that are CYP 450 inhibitors and/or inducers. Therefore, Vildagliptin is not likely to affect metabolic clearance of co-medications metabolised by CYP 1A2, CYP 2C8, CYP 2C9, CYP 2C19, CYP 2D6, CYP 2E1 or CYP 3A4/5.
Elimination: Following oral administration of [^{14}C] Vildagliptin, approximately 85% of the dose was excreted into the urine and 15% of the dose is recovered in the faeces. Renal excretion of the unchanged Vildagliptin accounted for 23% of the dose after oral administration. The elimination half-life after oral administration is approximately 3 hours.

DOSAGE AND ADMINISTRATION: Insutol can be administered orally with or without a meal. As monotherapy, in combination with metformin, in combination with thiazolidinedione, in combination with metformin and a sulphonylurea, or in combination with insulin (with or without metformin), the recommended daily dose of Vildagliptin is 100mg, administered as one dose of 50mg in the morning and one dose of 50mg in the evening.
In dual combination with a sulphonylurea, the recommended dose of Vildagliptin is 50mg once daily administered in the morning. In this patient population, Vildagliptin 100mg daily was no more effective than Vildagliptin 50 mg once daily. In combination with a sulphonylurea, a lower dose of the sulphonylurea may be considered to reduce the risk of hypoglycaemia. Doses higher than 100mg are not recommended.

SPECIAL POPULATIONS:
Elderly (≥ 65 years): No dose adjustments are necessary in elderly patients.
Renal impairment: No dose adjustment is required in patients with mild renal impairment (creatinine clearance ≥ 50ml/min). In patients with moderate or severe renal impairment or with end-stage renal disease (ESRD), the recommended dose of Insutol is 50mg once daily.
Hepatic impairment: Insutol 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).
Paediatric population: Insutol is not recommended for use in children and adolescents (< 18 years). The safety and efficacy of Insutol in children and adolescents (< 18 years) have not been established.

Rev: 07-21/0

OVERDOSAGE: At 400mg, there were three cases of muscle pain, and individual cases of mild and transient paraesthesia, fever, oedema and a transient increase in lipase levels. At 600mg, 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. Three other subjects experienced oedema of the feet, with paraesthesia in two cases. All symptoms and laboratory abnormalities resolved without treatment after discontinuation of the medicinal product.

CONTRAINDICATIONS: Hypersensitivity to the active substance or to any of the excipients.

WARNINGS & PRECAUTIONS: General: Vildagliptin 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: There is limited experience in patients with ESRD on haemodialysis. Therefore, Vildagliptin should be used with caution in these patients.
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: Liver function tests should be performed prior to the initiation of treatment with Vildagliptin in order to know the patient's baseline value. Liver function should be monitored during treatment with Vildagliptin at three-month intervals during the first year and periodically thereafter. Patients who develop increased transaminase levels should be monitored with a second liver function evaluation to confirm the finding and be followed thereafter with frequent liver function tests until the abnormality(ies) return(s) to normal. Patients who develop jaundice or other signs suggestive of liver dysfunction should discontinue Vildagliptin. Following withdrawal of treatment with Vildagliptin and LFT normalisation, treatment with Vildagliptin should not be reinitiated.
Cardiac failure: A clinical trial of Vildagliptin in patients with New York Heart Association (NYHA) functional class I-III showed that treatment with Vildagliptin was not associated with a change in left-ventricular function or worsening of pre-existing congestive heart failure (CHF) versus placebo. There is no experience of Vildagliptin use in clinical trials in patients with NYHA functional class IV and therefore use is not recommended in these patients.
Skin disorders: There have been post-marketing reports of bullous and exfoliative skin lesions. Therefore, in keeping with routine care of the diabetic patient, monitoring for skin disorders, such as blistering or ulceration, is recommended.
Acute pancreatitis: Patients should be informed of the characteristic symptom of acute pancreatitis. If pancreatitis is suspected, Vildagliptin should be discontinued; if acute pancreatitis is confirmed, Vildagliptin should not be restarted. Caution should be exercised in patients with a history of acute pancreatitis.
Hypoglycemia: Sulphonylureas are known to cause hypoglycemia. Patients receiving Vildagliptin in combination with a sulphonylurea may be at risk for hypoglycemia. Therefore, a lower dose of sulphonylurea may be considered to reduce the risk of hypoglycemia.

INTERACTIONS: Vildagliptin has a low potential for interactions with co-administered medicinal products. Since, Vildagliptin is not a cytochrome P (CYP) 450 enzyme substrate and does not inhibit or induce CYP 450 enzymes, it is not likely to interact with active substances that are substrates, inhibitors or inducers of these enzymes. There may be an increased risk of angioedema in patients concomitantly taking ACE-inhibitors. As with other oral antidiabetic medicinal products the hypoglycaemic effect of Vildagliptin may be reduced by certain active substances, including thiazides, corticosteroids, thyroid products and sympathomimetics.

FERTILITY, PREGNANCY AND LACTATION: Pregnancy: There are no adequate data from the use of Vildagliptin in pregnant women.
Breast-feeding: Vildagliptin should not be used during breast-feeding.
Fertility: No studies on the effect on human fertility have been conducted for Vildagliptin.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES: No studies on the effects on the ability to drive and use machines have been performed. Patients who experience dizziness as an adverse reaction should avoid driving vehicles or using machines.

SIDE EFFECTS: Metabolism and nutrition disorders: Common: Hypoglycaemia.
Nervous system disorders: Common: Dizziness.
Uncommon: Headache.
Gastrointestinal disorders: Uncommon: Constipation.
Infections and infestations: Very rare: Upper respiratory tract infection and nasopharyngitis.
Vascular disorders: Uncommon: Oedema peripheral.
Musculoskeletal and connective tissue disorders: Uncommon: Arthralgia.

INSTRUCTIONS: Store below 30°C. Protect from heat, light and moisture. Keep out of the reach of children.

PRESENTATION: Insutol 50mg Tablets is available in the pack size of 10's.

ہدایات: ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ گرمی، روشنی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔

Manufactured by:
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