Only for the use of Medical Professionals

Aptin® M

Vildagliptin + Metformin Hydrochloride

Description

Aptin® M is a preparation of vildagliptin which is a dipeptidyl peptidase-4 (DPP-4) inhibitor and metformin hydrochloride, a member of the biguanide class. Vildagliptin exerts its actions in patients with type 2 diabetes by slowing the inactivation of incretin hormones. Incretin hormones, including glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP), are released by the intestine throughout the day, and levels are increased in response to a meal. These hormones are rapidly inactivated by the enzyme, DPP-4. The incretins are part of an endogenous system involved in the physiologic regulation of glucose homeostasis. When blood glucose concentrations are normal or elevated, GLP-1 and GIP increase insulin synthesis and release from pancreatic beta cells by intracellular signaling pathways involving cyclic AMP. GLP-1 also lowers glucagon secretion from pancreatic alpha cells, leading to reduced hepatic glucose production. By increasing and prolonging active incretin levels, vildagliptin increases insulin release and decreases glucagon levels in the circulation in a glucose dependent manner. Metformin decreases the glucose level by reducing hepatic glucose production, increases peripheral glucose uptake and utilization by increasing insulin sensitivity of muscle, decreases intestinal absorption of glucose and stimulates intracellular glycogen synthesis by acting on glycogen synthase.

Indication

Aptin® M is indicated 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 & administration

Adults

The recommended dose of vildagliptin plus metformin hydrochloride combination is either 50 mg/500 mg or 50 mg/850 mg 1 tab twice daily. Maximum dose of vildagliptin is 100 mg and metformin hydrochloride is 2000 mg per day. Taking combination of vildagliptin plus metformin hydrochloride with or just after food may reduce gastrointestinal symptoms associated with metformin hydrochloride. There is no clinical experience of vildagliptin plus metformin hydrochloride in triple combination with other antidiabetic agents.

Pediatric use

Combination of vildagliptin plus metformin hydrochloride is not recommended in patients below 18 years of age.

Patients with hepatic impairment

Combination of vildagliptin plus metformin hydrochloride is not recommended in patients with clinical or laboratory evidence of hepatic impairment.

Patients with renal impairment

Combination of vildagliptin plus metformin hydrochloride should not be used in patients with renal failure or renal dysfunction (serum creatinine levels =1.5 mg/dl in males and =1.4 mg/dl in females).

Use in pregnancy & lactation

Pregnancy

There are no adequate and well controlled studies in pregnant women and therefore, vildagliptin plus metformin hydrochloride combination should not be used during pregnancy unless the potential benefit justifies the potential risk to the foetus.

Lactation

It is not known whether vildagliptin plus metformin hydrochloride is excreted in human milk. However, this combination should not be administered to breast feeding women.

Side effects

The most common side effects of this combination are tremor, headache, dizziness, nausea, hypoglycaemia, fatigue, lactic acidosis and hepatic dysfunction. The majority of adverse reactions were mild and transient, not requiring treatment discontinuations.

Contraindications

The combination of vildagliptin plus metformin hydrochloride is contraindicated in patients with known hypersensitivity to vildagliptin or metformin hydrochloride or to any of the excipients. It is also contraindicated in patients with renal disease or renal dysfunction, congestive heart failure, diabetic ketoacidosis, acute myocardial infarction and septicaemia. It should be temporarily discontinued in patients undergoing radiologic studies involving intravascular administration of iodinated contrast materials.

Precautions

Lactic acidosis can occur due to metformin hydrochloride accumulation. If metabolic acidosis is suspected, treatment should be discontinued and the patient should be hospitalized immediately. Serum creatinine should be monitored at least once a year in patients with normal renal function and 2–4 times a year in patients with serum creatinine levels at the upper limit of normal and in elderly patients. Special caution should be exercised in elderly patients where renal function may become impaired (e.g. when initiating antihypertensives, diuretics or NSAIDs). It is recommended that liver function tests (LFTs) are monitored prior to initiation of this drug, at three monthly intervals in the first year and periodically thereafter. If transaminase levels are increased, patients 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 return to normal. Following withdrawal of treatment with vildagliptin plus metformin hydrochloride and LFT normalization, treatment with vildagliptin plus metformin hydrochloride should not be reinitiated. Vildagliptin plus metformin hydrochloride tablets should be discontinued 48 hours before elective surgery with general anaesthesia and should not usually be resumed earlier than 48 hours afterwards.

Drug interaction

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 hydrochloride with no change in renal clearance of metformin hydrochloride.

Overdose

Vildagliptin

Information regarding overdose with vildagliptin is limited. Doses up to 200 mg were well tolerated. In the event of an overdose, supportive management is recommended.

Metformin hydrochloride

If overdosage is suspected, hemodialysis may be useful for removal of accumulated drug from patients. Metformin hydrochloride is dialyzable with a clearance of up to 170 mL/min under good hemodynamic conditions.

Pharmaceutical precautions

Store in a cool (below 25°C) & dry place. Protect from light. Keep out of the reach of children.

Presentation

Aptin® M 50/500 tablet: Each coated tablet contains Vildagliptin INN 50 mg & Metformin Hydrochloride BP 500 mg.
Aptin® M 50/850 tablet: Each coated tablet contains Vildagliptin INN 50 mg & Metformin Hydrochloride BP 850 mg.

Package quantities

Aptin® M 50/500 tablet: Carton of 30 tablets in blister pack.
Aptin® M 50/850 tablet: Carton of 30 tablets in blister pack.

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