



## Vildagliptin : The Game Changer

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Vildagliptin is a potent and selective, oral hypoglycemic agent that belongs to the class of second-generation dipeptidyl peptidase IV inhibitors (DPP-IV) also known as “incretin enhancers”. The European Medicines Agency (EMA) has given approval for the use of vildagliptin in combination with other hypoglycemic agents including metformin, sulfonylureas, insulin, pioglitazone and thiazolidinediones. Apart from this Eucreas, which is a single tablet formulation of metformin and vildagliptin has also been approved. The drug seems to include disease-modifying effects on patients with type 2 diabetes. Vildagliptin treatment is known for neutral weight and lipid-neutral effects, very low risk of edema and low blood sugar. Moreover, it has been indicated to improve cardiovascular disease in patients with type 2 DM in multiple monotherapies and in combination.

### Mode of action

Glucagon-like peptide-1 (GLP-1) and gastric inhibitor peptide (GIP) are incretins that are released from cells in the gut in response to food. Incretins bind to receptors on pancreatic beta cells, thereby stimulating the release of insulin which is accountable for regulating blood sugar levels. Diabetic patients have impaired incretin function which unables proper regulation of blood sugar levels. Vildagliptin works best by inhibiting DPP-IV, which is an enzyme that breaks down GLP-1. Thus, by slowing up the degradation of GLP-1, vildagliptin enlarges the action of insulin and defeating the release of glucagon which eventually leads to a decrease in the elevated blood glucose level.

### Pharmacological view of vildagliptin

When administered orally, it gets dissolved rapidly with dose-proportional pharmacokinetics. No adjustment in dose is required on the basis of age, gender, body mass index, amount of food, hepatic impairment, and use of any accompanying drugs. Bio-equivalence of the fixed-dose combination of vildagliptin and metformin with the individual components has been shown and the effect of food in decreasing metformin exposure was smaller with the metformin component in the fixed-dose combination than has been reported with metformin alone, and the fixed-dose combination can be administered in the same way as metformin alone.

### Pharmacokinetics

- **Tmax after oral administration:** 1.5-1.7 hours
- **Absolute bioavailability:** 85% which remains unaffected by food.
- **Half-life:** 90 min (maximum inhibition of DPP-4 activity seen at 30 minutes after drug dose and  $\geq 50\%$  inhibition of DPP-4 continuing for  $\geq 10$  hours, making it suitable for once or twice daily.
- **Metabolism:** Extensively metabolized, primarily in the liver via hydrolysis; minimally metabolized by the cytochrome P-450 (CYP) enzyme system Excretion: Mainly in the urine; 18-22% of the excreted drug is unmetabolized.

Thus, Vildagliptin may be used throughout the whole spectrum of T2DM patients and also there remains the assurance of beta-cell protection in the future. The drug profile makes vildagliptin the first-line choice for increasing beta-cell insulin secretion.

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