Galvus
Eucreas
(Vildagliptin)

Presentation: Tablets containing 50mg vildagliptin.
Indications: Treatment of type 2 diabetes mellitus 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.

Dosage: 100mg daily when used in dual combination with metformin or a thiazolidinedione administered as one dose of 50 mg given in the morning and one dose of 50mg in the evening. Give 50mg once daily in the morning when used in dual combination with a sulphonylurea. Vildagliptin may be taken with or without a meal. No dosage adjustment is required in the elderly, or in patients with mild renal impairment. Vildagliptin is not recommended in moderate to severe renal impairment or hepatic impairment including patients with pre-treatment ALT or AST >3xULN. Vildagliptin is not recommended for use in children and adolescents.

Contra-indications:

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

Precautions:

Caution should be exercised in patients aged 75 years and older due to limited clinical experience. 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. Due to limited experience, Vildagliptin is not recommended in patients with

moderate to severe renal impairment or in patients with ESRD on haemodialysis. It is recommended that LFTs are monitored prior to initiation of Vildagliptin, 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 (ies) return (s) to normal. If AST or ALT persists at 3xULN, vildagliptin treatment should be stopped. Patients who develop jaundice or other signs of liver dysfunction should discontinue vildagliptin. Following withdrawal of treatment with vildagliptin and LFT normalisation, treatment with vildagliptin should not be reinitiated. Due to limited clinical experience, use with caution in patients with congestive heart failure of NYHA functional class I-II, and use is not recommended in patients with NYHA functional class III-IV. In keeping with routine care of the diabetic patient, monitoring for skin disorders, such as blistering or ulceration, is recommended. The tablets contain lactose; patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product. Vildagliptin should not be used in pregnancy or lactation. Patients who experience dizziness as a side effect should avoid driving vehicles or using machines.

Drug interactions:

Vildagliptin has a low potential for interactions with co-administered medicinal products, including drugs that are substrates, inhibitors or inducers of CYP450 enzymes. In pharmacokinetic studies, no inter - actions were seen with pioglitazone, metformin, glibenclamide, digoxin, warfarin, amlodipine, ramipril, valsartan or simvastatin. As with other oral anti-diabetic medicinal products the hypoglycaemic effect of vildagliptin may be reduced by certain active substances, including thiazides, corticosteroids, thyroid products and sympathomimetics.

Side-effects:

The majority of adverse reactions were mild and transient, not requiring treatment discontinuations.
General: rare cases of hepatic dysfunction (including hepatitis). ALT or AST elevations ≥3xULN for vildagliptin 50mg od (0.2%), vildagliptin 50mg bd (0.3%) compared to 0.2% with comparators in clinical trials. Rare cases of angioedema at similar rates to controls.

When used in combination with metformin
Common: tremor, headache, dizziness, nausea, hypoglycaemia;
Uncommon: fatigue.
When used in combination with a sulphonlyurea.
Common: tremor, headache, dizziness, asthenia, hypoglycaemia;
Uncommon: constipation;
Very rare: nasopharyngitis.
When used in combination with a thiazolidinedione
Common: weight increase, peripheral oedema;
Uncommon: headache, asthenia, hypoglycaemia. Monotherapy dizziness, headache, peripheral oedema, constipation, nasopharyngitis, upper respiratory tract infection, arthralgia were reported in greater incidence than placebo.
Uncommon: hypoglycaemia.

Abstract

There is increasing evidence that glycemic disorders such as rapid glucose fluctuations over a daily period might play an important role on diabetic complications. We evaluated the efficacy of Sitagliptin 100 mg once daily vs. vildagliptin 50 mg twice daily on daily blood glucose fluctuations in patients with type 2 diabetes that was inadequately controlled by metformin.

Forty-eight-hour continuous subcutaneous glucose monitoring (CSGM) was performed in patients treated with metformin plus vildagliptin (n=18) or Sitagliptin (n=20) over a period of 3 months. The mean amplitude of glycemic excursions (MAGE) was used for assessing glucose fluctuations

during the day. During a standardized meal, glucagon-like peptide-1 (GLP-1), glucagon, and insulin were measured.

CSGM shows large MAGE decrements in the vildagliptin group compared with the Sitagliptin group ($P<.01$). A marked increase in GLP-1 occurred during interprandial period in vildagliptin bid-treated toward Sitagliptin 100 mg once daily ($P<.01$). Glucagon was more suppressed during interprandial period in subjects receiving vildagliptin compared to those receiving sitagliptin ($P<.01$). Since MAGE is associated with an activation of oxidative stress, our data suggest that dipeptidyl peptidase IV inhibition therapy should target not only reducing HbA1c but also flattening acute glucose fluctuations over a daily period.