GALVUS

(vildagliptin)

50 mg Tablet

Leaflet

DISETUJUI OLEH BPOM : 23/03/2022 ID REG : EREG100005VR12200025

Trade Name

Galvus 50 mg tablet

Description and composition

Active substance(s)

Vildagliptin
One tablet of Galvus contains 50 mg of vildagliptin.

Pharmaceutical form

Galvus 50 mg: white to light yellowish, round flat faced with beveled edges, unscored tablet. One side is debossed with "NVR", and the other side with "FB".

Active moiety

Vildagliptin

Excipients

Lactose anhydrous, microcrystalline cellulose, sodium starch glycolate, magnesium stearate.

Indications

Galvus is indicated as an adjunct to diet and exercise to improve glycaemic control in patients with type 2 diabetes mellitus (T2DM).

- **as monotherapy.**
- **in dual combination** with metformin, a sulphonylurea (SU), a thiazolidinedione (TZD) when diet, exercise and a single antidiabetic agent do not result in adequate glycaemic control.
- **in triple combination**

  In patients with uncontrolled use of sulphonylurea (at submaximal dose) and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control.

  It is not recommended as initial therapy.

Galvus is also indicated for use in combination with insulin (with or without metformin), when maximal tolerated dose of insulin (without metformin or with maximal tolerated dose of metformin) as an adjunct to diet and exercise do not provide adequate glycemic control.

Dosage and administration

The management of antidiabetic therapy should be individualized.

Monotherapy:

The recommended dose of Galvus is 50 mg or 100 mg daily. The 50 mg dose should be administered once daily in the morning. The 100 mg dose should be administered as two divided doses of 50 mg given in the morning and evening.

Combination therapy:

Combination therapy with other antidiabetic drugs such metformin, an SU, a TZD or insulin may be given if a tighter glycaemic control is required on the top of the maximum recommended daily dose of 100 mg Galvus monotherapy.

The recommended dose of Galvus is 50 mg or 100 mg daily in dual combination with metformin, or a TZD or insulin. The 50 mg dose should be administered once daily in the morning. The 100 mg dose should be administered as two divided dose of 50 mg given in the morning and evening.

The recommended dose of Galvus is 50 mg bid for triple combination with metformin and a SU.

When used in dual combination with a sulphonylurea, the recommended dose of vildagliptin is 50 mg once daily administered in the morning. In this patient population, vildagliptin 100 mg daily was no more effective than vildagliptin 50 mg once daily.

Special populations

Hepatic impairment

Galvus is not recommended in patients with hepatic impairment including patients with a pre-treatment ALT or AST >2.5x the upper limit of normal (ULN) (see section Clinical pharmacology for Pharmacokinetics under Special Populations).

No dosage adjustment of Galvus is required in patients with mild renal impairment. In patients with moderate or severe renal impairment, the recommended dose of Galvus is 50 mg once daily (see section Clinical pharmacology for Pharmacokinetics under Special Populations).

Renal impairment

Galvus is, however, not recommended in patients with End Stage Renal Disease (ESRD) on haemodialysis due to limited experience in patients with End Stage Renal Disease (ESRD) on haemodialysis (see also sections Warnings and Precautions and section Clinical pharmacology for Pharmacokinetics under Special Populations).

There is limited data on the use of combination therapy in patients with renal and hepatic impairment. Therefore, the use of Galvus in combination therapy is not recommended in these patients.

Geriatrics

In patients treated with Galvus ≥65 years of age and ≥75 years of age, no differences were observed in the overall safety, tolerability, or efficacy between this elderly population and younger patients. No dosage adjustments are therefore necessary in the elderly patients (see section Clinical pharmacology for Pharmacokinetics under Special Populations).

Paediatric patients

Galvus has not been studied in patients under 18 years of age; therefore, the use of Galvus in paediatric patients is not recommended (see section Clinical pharmacology for Pharmacokinetics under Special Populations).

Method of administration

For oral use.

Galvus can be administered with or without meal.

If a dose of Galvus is missed, it should be taken as soon as the patient remembers. A double dose should not be taken on the same day.

Contraindications

Galvus is contraindicated in patients with known hypersensitivity to vildagliptin or to any of the excipients (see section Description and composition under subsection Excipients).

Warnings and precautions

General

Galvus is not a substitute for insulin in patient requiring insulin. Galvus 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 End Stage Renal Disease (ESRD) on haemodialysis. Therefore, the use of Galvus is not recommended in these patients.

Hepatic impairment

Galvus is not recommended in patients with hepatic impairment, including patients with a pre-treatment ALT or AST >2.5x ULN.

Hepatic enzyme monitoring

Rare cases of hepatic dysfunction (including hepatitis) have been reported. In these cases, the patients were generally asymptomatic without clinical sequelae and liver function tests (LFTs) returned to normal after discontinuation of treatment. LFTs should be performed prior to the initiation of treatment with Galvus. Galvus is not recommended in patients with a pre-treatment ALT or AST >2.5X the upper limit of normal. LFTs should be monitored during

Galvus treatment 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 to normal. Should an increase in AST or ALT of 3x ULN or greater persist, withdrawal of therapy with Galvus is recommended. Patients who develop jaundice or other signs suggestive of liver dysfunction should discontinue Galvus and contact their physician immediately. Following withdrawal of treatment with Galvus and LFT normalisation, vildagliptin treatment should not be reinitiated.

Heart 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. Clinical experience in patients with NYHA functional class III treated with vildagliptin is still limited and the results are inconclusive (see section Pharmacodynamics and Clinical studies).

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.

Other

Galvus tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Interactions

Vildagliptin has low potential for drug interactions. Since vildagliptin is not a cytochrome P (CYP) 450 enzyme substrate nor does it inhibit or induce CYP 450 enzymes, it is not likely to interact with co-medications that are substrates, inhibitors or inducers of these enzymes.

Furthermore, vildagliptin does not affect metabolic clearance of co-medications metabolised by CYP 1A2, CYP 2C8, CYP 2C9, CYP 2C19, CYP 2D6, CYP 2E1, and CYP 3A4/5. Drug-drug interaction studies were conducted with commonly co-prescribed medications for patients with type 2 diabetes or medications with a narrow therapeutic window. As a result of these studies, no clinically relevant interactions with other oral antidiabetics (glibenclamide, pioglitazone, metformin), amlodipine, digoxin, ramipril, simvastatin, valsartan or warfarin were observed after co-administration with vildagliptin.

Pregnancy, lactation, females and males of reproductive potential

Pregnancy

Risk summary

Vildagliptin was not teratogenic in either rats or rabbits. There is insufficient experience with Galvus in pregnant women. Therefore, Galvus should not be used during pregnancy unless the benefit to the mother outweighs the potential risk to the foetus.

Animal studies are not always predictive of human response. Because current information strongly suggests that abnormal blood glucose levels during pregnancy are associated with a higher incidence of congenital anomalies as well as increased neonatal morbidity and mortality, most experts recommend that insulin monotherapy be used during pregnancy to maintain blood glucose levels as close to normal as possible.

Lactation

Risk summary

As it is not known whether vildagliptin is excreted in human milk Galvus should not be administered to breastfeeding women.

Females and males of reproductive potential

No studies of the effect on human fertility have been conducted for Galvus. Fertility studies have been performed in rats at doses up to 200 times the human dose and have revealed no evidence of impaired fertility or early embryonic development due to 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 may experience dizziness should therefore avoid driving vehicles or using machines.

Adverse Drug Reactions

Summary of the safety profile

The safety and tolerability of vildagliptin (50 mg qd, 50 mg bid and 100 mg qd) have been assessed by pooling data from more than 11,000 patients from 36 Phase II and III studies (including 3 open label studies) ranging in duration from 12 to more than 104 weeks. The studies used in this pooled analysis have assessed vildagliptin as monotherapy, add-on therapy to other oral anti-diabetic agents (metformin, TZD, SU and insulin). Patients not receiving vildagliptin (all comparators group) were taking only placebo or metformin, TZD, SU, acarbose or insulin. For the calculation of frequency of adverse drug reactions for the individual indications, safety data from a subset of pivotal controlled trials of at least 12 week's duration was considered. Safety data were obtained from patients exposed to vildagliptin at a daily dose of 50 mg (once daily) or 100 mg (50 mg twice daily or 100 mg once daily) who received vildagliptin as monotherapy or in combination with another agent.

The majority of adverse reactions in these trials were mild and transient, not requiring treatment discontinuations. No association was found between adverse reactions and age, ethnicity, duration of exposure or daily dose.

Rare cases of angioedema have been reported on vildagliptin at a similar rate to controls. A greater proportion of cases were reported when vildagliptin was administered in combination with an angiotensin converting enzyme inhibitor (ACE-Inhibitor). The majority of events were mild in severity and resolved with ongoing vildagliptin treatment.

Rare cases of hepatic dysfunction (including hepatitis) have been reported. In these cases, the patients were generally asymptomatic without clinical sequelae and liver function tests (LFTs) returned to normal after discontinuation of treatment. In data from controlled monotherapy and add-on therapy trials up to 24 weeks in duration, the incidence of ALT or AST elevations >= 3x ULN (classified as present on at least 2 consecutive measurements or at the final on-treatment visit) was 0.2%, 0.3% and 0.2% for vildagliptin 50 mg daily, vildagliptin 50 mg twice daily and all comparators, respectively. These elevations in transaminases were generally asymptomatic, non-progressive in nature and not associated with cholestasis or jaundice.

Tabulated summary of adverse drug reactions from clinical trials

Adverse reactions reported in patients who received Galvus in double-blind studies as monotherapy and add-on therapies, are listed below, for each indication, by MedDRA system organ class and absolute frequency. Within each system organ class, the adverse drug reactions are ranked by frequency, with the most frequent reactions first. Within each frequency grouping, adverse drug reactions are presented in order of decreasing seriousness. In addition, the corresponding frequency category for each adverse drug reaction is based on the following convention (CIOMS III): very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000).

Monotherapy

The overall incidence of withdrawals from monotherapy trials due to adverse reactions was no greater for patients treated with vildagliptin at a dose of 50 mg once daily (0.2%) or vildagliptin at a dose of 50 mg twice daily (0.1%) than for placebo (0.6%) or comparators (0.5%).

In monotherapy studies, hypoglycaemia was uncommon, reported in 0.5% (2 of 409) of patients treated with vildagliptin 50 mg once daily and 0.3% (4 of 1,373) of patients treated with vildagliptin 50 mg twice daily compared to 0.2% (2 of 1,082) of patients in the groups treated with an active comparator or placebo, with no serious or severe events reported.

Galvus is weight neutral when administered as monotherapy.

Table 1 Adverse reactions reported in patients who received Galvus 50 mg once daily (n=409) or 50 mg twice daily (n=1373) as monotherapy in double-blind studies

Nervous system disorders	
Common	Dizziness

Uncommon	Headache
Gastrointestinal disorders	
Uncommon	Constipation, nausea, diarrhea
General disorders and administration site conditions	
Uncommon	Oedema peripheral
Infection and infestation	
Common	Nasopharyngitis
Cardiovascular disorders	
Common	Hypertension

Long term clinical trials of up to 2 years did not show any additional safety signals or unforeseen risks with vildagliptin monotherapy.

Combination with metformin

In clinical trials with the combination of vildagliptin + metformin, 0.4% of patients withdrew due to adverse reactions in the vildagliptin 50 mg once daily + metformin treatment group, and no withdrawal due to adverse reactions was reported in either the vildagliptin 50 mg twice daily + metformin or the placebo + metformin treatment groups.

In clinical trials, the incidence of hypoglycaemia was uncommon in patients receiving vildagliptin 50 mg once daily in combination with metformin (0.9%), patients receiving vildagliptin 50 mg twice daily in combination with metformin (0.5%) and in patients receiving placebo+metformin (0.4%). No severe hypoglycaemic events were reported in the vildagliptin arms.

Galvus is weight neutral when administered in combination with metformin.

Table 2 Adverse reactions reported in patients who received Galvus 50 mg once daily (n=233) or 50 mg twice daily (n=183) in combination with metformin in double-blind studies

GALVUS IN DUAL ORAL THERAPY WITH METFORMIN	
Nervous system disorders	
Common	Tremor, dizziness, headache

Long term clinical trials of up to more than 2 years did not show any additional safety signal or unforeseen risks when vildagliptin was added on to metformin.

Combination with a sulphonylurea

In clinical trials with the combination of vildagliptin 50 mg + glimepiride, the overall incidence of withdrawals due to adverse reactions was 0.6% in the vildagliptin 50 mg + glimepiride treatment group versus 0% in the placebo + glimepiride treatment group.

In clinical trials, the incidence of hypoglycemia when vildagliptin 50 mg once daily was added to glimepiride was 1.2% versus 0.6% for placebo+glimepiride. No severe hypoglycaemic events were reported in the vildagliptin arms.

At the recommended dose of 50 mg, Galvus is weight neutral when administered in combination with glimepiride.

Table 3 **Adverse reactions reported in patients who received Galvus 50 mg once daily in combination with a sulphonylurea in double-blind studies (n=170)**

Nervous system disorders	
Common	Tremor, headache, dizziness
General disorders and administration site conditions	
Common	Asthenia

Combination with a thiazolidinedione

In clinical trials with the combination of vildagliptin and a thiazolidinedione, 0.7% of patients withdrew for adverse reactions in the vildagliptin 50 mg once daily + pioglitazone group, and there were no withdrawals due to adverse reactions reported in either the vildagliptin 50 mg twice daily + pioglitazone or the placebo + pioglitazone treatment groups.

In clinical trials, no hypoglycaemia events were reported in patients receiving vildagliptin 50 mg once daily + pioglitazone 45 mg, hypoglycaemia was uncommon in patients receiving vildagliptin 50 mg twice daily + pioglitazone 45 mg (0.6%) but common in patients receiving placebo + pioglitazone 45 mg (1.9%). No severe hypoglycaemic events were reported in the vildagliptin arms.

In the pioglitazone add-on study, the change in body weight compared to placebo was +0.1 kg and +1.3 kg for Galvus 50 mg daily and Galvus 50 mg twice daily, respectively.

The incidence of peripheral oedema when vildagliptin was added to a maximum dose of background pioglitazone (45 mg once daily) was 8.2% as 50 mg once daily and 7.0%, as 50 mg twice daily compared to 2.5% for background pioglitazone alone. The incidence of oedema when vildagliptin was added to pioglitazone as dual initial therapy in drug naïve patients was, however, less than for pioglitazone alone (50 mg once daily 3.5%, 50 mg twice daily 6.1% vs. pioglitazone 30 mg 9.3%).

Table 4 **Adverse reactions reported in patients who received Galvus 50 mg once daily (n= 146) or 50 mg twice daily (n=158) in combination with a thiazolidinedione in double-blind studies**

Investigations	
Common	Weight increase
General disorders and administration site conditions	
Common	Oedema peripheral

Combination with insulin

In controlled clinical trials using vildagliptin 50 mg twice daily in combination with insulin, with or without concomitant metformin, the overall incidence of withdrawal due to adverse reactions was 0.3% in the vildagliptin treatment group and there were no cases of withdrawal in the placebo group.

The incidence of hypoglycemia was similar in both treatment groups (14.0% in the vildagliptin group versus 16.4% in the placebo group). Two patients reported severe hypoglycemic events in the vildagliptin group, and 6 patients - in the placebo group.

At the end of the study, the effect on mean body weight was neutral (+ 0.6 kg change from baseline in the vildagliptin group and no weight change in the placebo group).

Table 5 Adverse reactions reported in patients who received Galvus 50 mg twice daily in combination with insulin (with or without metformin (n=371))

Nervous system disorders	
Common	Headache
Gastrointestinal disorders	
Common	Nausea, gastrooesophageal reflux disease
Uncommon	Diarrhoea, flatulence
General disorders and administration site conditions	
Common	Chills
Investigations	
Common	Blood glucose decreased

Combination with metformin and SU

There were no cases of withdrawal reported due to adverse reactions in the vildagliptin + metformin + glimepiride treatment group versus 0.6% in the placebo + metformin + glimepiride treatment group.

The incidence of hypoglycemia was common in both treatment groups (5.1% for the vildagliptin + metformin + glimepiride vs. 1.9 % for the placebo + metformin + glimepiride). One severe hypoglycemic event was reported in the vildagliptin group.

At the end of the study, the effect on mean body weight was neutral (+ 0.6 kg in the vildagliptin group and -0.1 kg in the placebo group).

Table 6 Adverse reactions reported in patients who received Galvus 50 mg twice daily in combination with metformin and SU (n=157)

Nervous system disorders	
Common	Dizziness, tremor
General disorders and administration site condition	
Common	Asthenia
Metabolism and nutritional disorders	
Common	Hypoglycemia
Skin and subcutaneous tissue disorders	
Common	Hyperhidrosis

Adverse drug reactions from spontaneous reports and literature cases - Post-marketing Experience (frequency not known)

The following adverse drug reactions have been derived from post-marketing experience with Galvus via spontaneous case reports and literature cases. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency, which is therefore categorized as not known.

- Hepatitis reversible upon drug discontinuation (see also section Warnings and precautions)
- Urticaria, bullous and exfoliative skin lesions, including bullous pemphigoid.
- Pancreatitis.
- Arthralgia, sometimes severe

Overdose

Signs and symptoms

In healthy subjects (seven to fourteen subjects per treatment group), Galvus was administered in once-daily doses of 25, 50, 100, 200, 400, and 600 mg for up to 10 consecutive days. Doses up to 200 mg were well tolerated. At 400 mg, there were three cases of muscle pain, and individual cases of mild and transient paraesthesia, fever, oedema and transient increase in lipase levels (2x ULN). At 600 mg, one subject experienced oedema of the feet and hands, and an excessive increase in creatine phosphokinase (CPK) levels, accompanied by elevations of aspartate aminotransferase (AST), C-reactive protein, and myoglobin. Three additional subjects in this dose group presented with oedema of both feet, accompanied by paraesthesia in two cases. All symptoms and laboratory abnormalities resolved after study drug discontinuation.

Management

Galvus is not dialyzable, however the major hydrolysis metabolite (LAY151) can be removed by haemodialysis.

Clinical Pharmacology

Pharmacotherapeutic group, ATC code

Drugs used in diabetes, dipeptidyl peptidase 4 (DPP-4) inhibitors, ATC code: A10BH02

Mechanism of actions (MOA)

Vildagliptin, a member of the islet enhancer class, is a potent and selective dipeptidyl-peptidase-4 (DPP-4) inhibitor that improves glycaemic control. Vildagliptin inhibition of DPP-4 results in increased fasting and postprandial endogenous levels of the incretin hormones GLP-1 (glucagon-like peptide 1) and GIP (glucose-dependent insulinotropic polypeptide).

Pharmacodynamics (PD)

The administration of vildagliptin results in rapid and complete inhibition of DPP-4 activity. In patients with type 2 diabetes, administration of vildagliptin led to inhibition of DPP-4 enzyme activity for a 24-hour period.

By increasing the endogenous levels of these incretin hormones, vildagliptin enhances the sensitivity of beta cells to glucose resulting in improved glucose-dependent insulin secretion. Treatment with 50 to 100 mg daily in patients with type 2 diabetes significantly improved markers of beta cell function. The degree of improvement in beta-cell function is dependent on the initial degree of impairment; in non-diabetic (normal glycaemic) individuals, vildagliptin does not stimulate insulin secretion or reduce glucose levels.

By increasing endogenous GLP-1 levels, vildagliptin enhances the sensitivity of alpha cells to glucose, resulting in more glucose-appropriate glucagon secretion. The reduction in inappropriate glucagon during meals in turn attenuates insulin resistance.

The enhanced increase in the insulin/glucagon ratio during hyperglycaemia due to increased incretin hormone levels results in a decrease in fasting and postprandial hepatic glucose production, leading to reduced glycaemia.

The known effect of increased GLP-1 levels to delay gastric emptying is not observed with vildagliptin treatment. In addition, a reduction in postprandial lipaemia that is not associated with vildagliptin's incretin mediated effect to improve islet function, has been observed.

Pharmacokinetics (PK)

Absorption

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, as characterized by a 19% decrease in peak concentrations, and a delay in the time to peak plasma concentration to 2.5 hours. There is no change in the extent of absorption, and food does not alter the overall exposure (AUC).

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 liters, suggesting extravascular distribution.

Biotransformation/ Metabolism

Metabolism is the major elimination pathway for vildagliptin in humans, accounting for 69% of the dose. The major metabolite, LAY151, is pharmacologically inactive and is the hydrolysis product of the cyano moiety, accounting for 57% of the dose, followed by the amide hydrolysis product (4% of the dose). DPP-4 contributes partially to the hydrolysis of vildagliptin as shown in an in-vivo study using DPP-4 deficient rats. 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.

Elimination

Following oral administration of [^{14}C]-vildagliptin, approximately 85% of the dose is excreted into the urine and 15% of the dose is recovered in the faeces. Renal excretion of unchanged vildagliptin accounts for 23% of the dose after oral administration. After intravenous administration to healthy subjects, the total plasma and renal clearances of vildagliptin are 41 liters/hour and 13 liters/hour, respectively. The mean elimination half-life after intravenous

administration is approximately 2 hours. The elimination half-life after oral administration is approximately 3 hours and is independent of the dose.

Linearity

Vildagliptin is rapidly absorbed with an absolute oral bioavailability of 85%. Peak plasma concentrations for vildagliptin and the area under the plasma concentration versus time curve (AUC) increased in an approximately dose-proportional manner over the therapeutic dose range.

Special Populations

Pediatric patients (below 18 years)

No pharmacokinetic data available.

Geriatric patients (65 years or above)

In otherwise healthy elderly subjects (≥ 70 years), the overall exposure to vidagliptin (100 mg once daily) was increased by 32% with an 18% increase in peak plasma concentration compared to younger healthy subjects (18 to 40 years). These changes are not considered to be clinically relevant. DPP-4 inhibition by vildagliptin is not affected by age in the age groups studied.

Gender

No differences in the pharmacokinetics of vildagliptin were observed between male and female subjects with a diverse range of age and body mass index (BMI). DPP-4 inhibition by vildagliptin was unaffected by gender.

Obesity

BMI does not show any impact on the pharmacokinetic parameters of vildagliptin. DPP-4 inhibition by vildagliptin was unaffected by BMI.

Ethnicity

There was no evidence that ethnicity affects the pharmacokinetics of vildagliptin.

Renal Impairment

The AUC of vildagliptin increased on average 1.4, 1.7 and 2-fold in patients with mild, moderate and severe renal impairment, respectively, compared to normal healthy subjects. The AUC of the metabolites LAY151increased 1.6, 3.2 and 7.3-fold and that of BQS867 increased 1.4, 2.7 and 7.3-fold in patients with mild, moderate and severe renal impairment, respectively, compared to healthy volunteers. Limited data from patients with end stage renal disease (ESRD) indicate that vildagliptin exposure is similar to that in patients with severe renal impairment. LAY151 concentrations in ESRD patients were approximately 2 to 3-fold higher than in patients with severe renal impairment. Dosage adjustment may be required in patients with renal impairment (see section Dosage regimen and administration).

Vildagliptin was removed by hemodialysis to a limited extent (3% over a 3 to 4 hour hemodialysis session starting 4 hours post dose).

Hepatic Impairment

The effect of impaired hepatic function on the pharmacokinetics of vildagliptin was studied in subjects with mild, moderate, and severe hepatic impairment based on the Child-Pugh scores (ranging from 6 for mild to 12 for severe) in comparison to subjects with normal hepatic function. The exposure to vildagliptin (100 mg) after a single dose in subjects with mild and moderate hepatic impairment was decreased (20% and 8%, respectively), while the exposure to vildagliptin for subjects with severe impairment was increased by 22%. The maximum change (increase or decrease) in the exposure to vildagliptin is ~30%, which is not considered to be clinically relevant. There was no correlation between the severity of hepatic function impairment and changes in exposure to vildagliptin.

The use of vildagliptin is not recommended in patients with hepatic impairment including patients with a pre-treatment ALT or AST >2.5x the ULN.

Clinical Studies

More than 15,000 patients with type 2 diabetes participated in double-blind, placebo- or active-controlled clinical trials of up to more than 2 years of treatment duration. In these studies, vildagliptin was administered to more than 9,000 patients at daily doses of 50 mg once daily, 50 mg twice daily or 100 mg once daily. More than 5,000 male and more than 4,000 female patients received vildagliptin 50 mg once daily or 100 mg daily. More than 1,900 patients receiving vildagliptin 50 mg once daily or 100 mg daily were ≥65 years of age. In these trials, vildagliptin was administered as monotherapy in drug-naïve patients with type 2 diabetes or in combination in patients not adequately controlled by other antidiabetic medicinal products.

Overall, vildagliptin improved glycaemic control when given as monotherapy or when used in combination with metformin, a sulphonylurea, and a thiazolidinedione, as measured by clinically relevant reductions in HbA_{1c} from baseline at the study endpoint (see Table 5).

In clinical trials, the magnitude of HbA_{1c} reductions with vildagliptin was greater in patients with higher baseline HbA_{1c}.

In a 52-week trial (LAF2309), vildagliptin (100 mg/day) reduced baseline HbA_{1c} by -1% compared to -1.4% for metformin (titrated to 2 g/day). Patients treated with vildagliptin reported significantly lower incidences of gastrointestinal adverse reactions versus those treated with metformin.

In a 24-week trial (LAF2327), vildagliptin (100 mg/day) was compared to rosiglitazone (8 mg once daily). Mean reductions were -1.1% with vildagliptin and -1.3% with rosiglitazone in patients with mean baseline HbA_{1c} of 8.7%. Patients receiving rosiglitazone experienced a mean increase in weight (+1.6 kg) while those receiving vildagliptin experienced no weight gain (-0.3 kg). The incidence of peripheral oedema was lower in the vildagliptin group than in the rosiglitazone group (2.1% vs. 4.1%, respectively).

In a 24 week trial (LAF2354) vildagliptin (50 mg bid) was compared to pioglitazone (30 mg qd) in patients inadequately controlled with metformin. Mean reductions from baseline HbA_{1c} of 8.4% were -0.9% with vildagliptin added to metformin and -1.0% with pioglitazone added to metformin. The decrease in HbA_{1c} from baseline >9.0% was greater (-1.5%) in both treatment groups. Patients receiving pioglitazone in addition to metformin experienced an increase in weight of 1.9 kg. Patients receiving vildagliptin in addition to metformin experienced an increase in weight of 0.3 kg. In a 28 week extension, HbA_{1c} reductions and the body weight differences were maintained.

In a long-term trial of up to 2 years (LAF2308), vildagliptin (100 mg/day) was compared to glimepiride (up to 6 mg/day) in patients treated with metformin. After one year mean reductions in HbA_{1c} were -0.4% with vildagliptin added to metformin and -0.5% with glimepiride added to metformin. Body weight change with vildagliptin was -0.2 kg vs +1.6 kg with glimepiride. The incidence of hypoglycemia was significantly lower in the vildagliptin group (1.7%) than in the glimepiride group (16.2%). At the end of study (2 years), the HbA_{1c} was similar to baseline values in both treatment groups and the body weight changes and the differences in hypoglycemia were maintained.

In a long-term trial of 2 years (LAF2310), vildagliptin (50 mg twice daily was compared to gliclazide (up to 320 mg/day). After two years, mean reduction in HbA_{1c} was -0.5% for vildagliptin and 0.6% for gliclazide. At similar levels of glycemic control vildagliptin had less of a weight gain (0.75 kg) and fewer hypoglycemic events (0.7%) than gliclazide (1.6 kg and 1.7%, respectively).

A 24-week randomized, double blind, placebo-controlled study was conducted in 318 patients to evaluate the efficacy and safety of vildagliptin (50 mg twice daily) in combination with metformin (≥1,500 mg daily) and glimepiride (≥4 mg daily). Vildagliptin in combination with metformin and glimepiride significantly decreased HbA1c compared with placebo: the placebo-adjusted mean reduction from mean baseline HbA1c 8.8% was -0.76%.

A 24-week randomized, double-blind, placebo-controlled trial was conducted in 449 patients to evaluate the efficacy and safety of vildagliptin (50 mg twice daily) in combination with a stable dose of basal or premixed insulin (mean daily dose 41 U), with (N = 276) or without (N = 173) concomitant metformin. Vildagliptin in combination with insulin significantly decreased HbA1c compared with placebo: in the overall population, the placebo-adjusted mean reduction from mean baseline HbA1c 8.8% was -0.72%. In the subgroups treated with insulin with or without concomitant metformin the placebo-adjusted mean reduction in HbA1c was -0.63% and -0.84%, respectively. The incidence of hypoglycemia in the overall population was 8.4% and 7.2% in the vildagliptin and placebo groups, respectively. Changes in weight were +0.2 kg and -0.7 kg in the vildagliptin and placebo groups, respectively.

Table 7 **Key efficacy results of vildagliptin in placebo-controlled monotherapy trials and in add-on combination therapy trials (primary efficacy ITT population)**

Monotherapy placebo controlled studies	**Mean baseline HbA_{1c} (%)**	**Mean change from baseline in HbA_{1c} (%) at week 24**	**Placebo-corrected mean change in HbA_{1c} (%) at week 24 (95%CI)**
Study 2301: Vildagliptin 50 mg once daily (N=104)	8.2	-0.8	-0.5* (-0.8, -0.1)
Study 2301: Vildagliptin 50 mg twice daily (N=90)	8.6	-0.8	-0.5* (-0.8, -0.1)
Study 2384: Vildagliptin 50 mg once daily (N=84)	8.3	-0.5	-0.5* (-0.9, -0.1)
Study 2384: Vildagliptin 50 mg twice daily (N=79)	8.4	-0.7	-0.7* (-1.1, -0.4)
		* p < 0.05 for comparison versus placebo	
Add-on / Combination studies			
Study 2303: Vildagliptin 50 mg once daily + metformin (N=143)	8.4	-0.5	-0.7* (-1.0, -0.5)
Study 2303: Vildagliptin 50 mg twice daily + metformin (N=143)	8.4	-0.9	-1.1* (-1.4, -0.8)
Study 2305: Vildagliptin 50 mg daily + glimepiride (N=132)	8.5	-0.6	-0.6* (-0.9, -0.4)
Study 2304: Vildagliptin 50 mg daily + pioglitazone (N=124)	8.6	-0.8	-0.5* (-0.7, -0.2)
Study 2304: Vildagliptin 50 mg twice daily + pioglitazone (N=136)	8.7	-1.0	-0.7* (-0.9, -0.4)
Study 23152: vildagliptin 50 mg twice daily + metformin + glimepiride (N=152)	8.8	-1.0	-0.8 (-1.0, -0.5)
Study 2311: Vildagliptin 50 mg twice daily + insulin (N=125)	8.5	-0.5	-0.3* (-0.5, -0.0)
Study 23135: Vildagliptin 50 mg twice daily + insulin	8.8	-0.8	-0.7* (-0.9, -0.5)
		* p < 0.05 for comparison versus placebo + background therapy	

A 52-week multi-center, randomized, double-blind trial was conducted in patients with type 2 diabetes and congestive heart failure (CHF) (NYHA class I - III) to evaluate the effect of vildagliptin 50 mg bid (N=128) compared to placebo (N=126) on left ventricular ejection functionfraction (LVEF). Vildagliptin was not associated with a change in left-ventricular function or worsening of pre-existing CHF. Adjudicated cardiovascular events were overall balanced. There were slightly more cardiac events in vildagliptin-treated patients with NYHA class III heart failure compared to placebo. However there were imbalances in baseline CV risk favoring placebo and the number of events was low, precluding firm conclusions. Vildagliptin significantly decreased HbA1c compared with placebo (difference of 0.6%) from

a mean baseline of 7.8%. The incidence of hypoglycemia in the overall population was 4.7% and 5.6% in the vildagliptin and placebo groups, respectively.

Cardiovascular risk

A meta-analysis of independently and prospectively adjudicated cardiovascular events from 37 phase III and IV monotherapy and combination therapy clinical studies of up to more than 2 years in duration was performed. It involved 9599 patients with type 2 diabetes treated with vildagliptin 50 mg qd or 50 mg bid and showed that vildagliptin treatment was not associated with an increase in cardiovascular risk. The composite endpoint of adjudicated major adverse cardio-vascular events (MACE) including acute myocardial infarction, stroke or CV death was similar for vildagliptin versus combined active and placebo comparators [Mantel–Haenszel risk ratio (M-H RR) 0.82 (95% confidence interval 0.61-1.11)] supporting the cardiovascular safety of vildagliptin. A MACE occurred in 83 out of 9599 (0.86%) vildagliptin treated patients and in 85 out of 7,102 (1.20%) comparator treated patients. Assessment of each individual MACE component showed no increased risk (similar M-H RR). Confirmed HF events defined as HF requiring hospitalization or new onset of HF were reported in 41 (0.43%) vildagliptin-treated patients and 32 (0.45%) comparator-treated patients, with MH RR 1.08 (95% CI 0.68-1.70) showing no increased risk of HF in vildagliptin treated patients.

Nonclinical safety data

A two-year carcinogenicity study was conducted in rats at oral doses up to 900 mg/kg (approximately 200 times the human exposure at the maximum recommended dose). No increases in tumour incidence attributable to vildagliptin were observed. A two-year carcinogenicity study was conducted in mice at oral doses up to 1000 mg/kg (up to 240 times the human exposure at the maximum recommended dose). Mammary tumour incidence was increased in female mice at approximately 150 times the maximum anticipated human exposure to vildagliptin; it was not increased at approximately 60 times the maximum human exposure. The incidence of haemangiosarcoma was increased in male mice treated at 42 to 240 times the maximum human exposure to vildagliptin and in female mice at 150 times the maximum human exposure. No significant increases in haemangiosarcoma incidences were observed at approximately 16 times the maximum human exposure to vildagliptin in males and approximately 60 times the maximum human exposure in females.

Vildagliptin was not mutagenic in a number of mutagenicity tests including a bacterial reverse mutation Ames assay and a human lymphocyte chromosomal aberration assay. Oral bone marrow micronucleus tests in both rats and mice did not reveal clastogenic or aneugenic potential up to 2,000 mg/kg or approximately 400 times the maximum human exposure. An in-vivo mouse liver comet assay using the same dose was also negative.

In a 13-week toxicology study in cynomolgus monkeys, skin lesions have been recorded at doses ≥ 5 mg/kg/day. These were consistently located on the extremities (hands, feet, ears and tail). At 5 mg/kg/day (approximately equivalent to human AUC exposure at the 100 mg dose), only blisters were observed. They were reversible despite continued treatment and were not associated with histopathological abnormalities. Flaking skin, peeling skin, scabs and tail sores with correlating histopathological changes were noted at doses ≥ 20 mg/kg/day

(approximately 3 times human AUC exposure at the 100 mg dose). Necrotic lesions of the tail were observed at ≥ 80 mg/kg/day. It should be noted that vildagliptin exhibits a significantly higher pharmacological potency in monkeys compared with humans. Skin lesions were not reversible in the monkeys treated at 160 mg/kg/day during a 4-week recovery period. Skin lesions have not been observed in other animal species or in humans treated with vildagliptin.

Pharmaceutical information

Incompatibilities

Not applicable.

Special precautions for storage

Do not store above 30°C, protect from moisture.
Store in the original package. Galvus must be kept out of the reach and sight of children.

Nature and contents of container

Alu/Alu blister packs.

Instructions for use and handling <and disposal>

No special requirements.

Package

Galvus® 50 mg Tablet: Box, 2 Blister @ 14 Tablets; Reg.No.:

HARUS DENGAN RESEP DOKTER

To be dispensed only on the prescription of a physician.

Manufactured by Siegfried Barbera S.L., Barberà del Vallès, Spain for Novartis Pharma AG, Basel, Switzerland. Imported by PT Novartis Indonesia, Jakarta, Indonesia.

Leaflet version: CDS 28-Nov-2016_Siegfried

NOVARTIS

GALVUS®

(vildagliptin)

Tablet 50 mg

Informasi Produk untuk Pasien

DISETUJUI OLEH BPOM : 23/03/2022 ID REG : EREG100005VR12200025

Mohon brosur dibaca dengan saksama sebelum Anda menggunakan Galvus

Mohon agar brosur ini disimpan. Anda mungkin akan membutuhkan brosur ini untuk dibaca kembali.

Jika Anda ingin bertanya lebih lanjut, mohon hubungi dokter atau apoteker Anda.

Obat ini diresepkan untuk Anda. Mohon jangan berikan obat ini kepada orang lain meskipun mereka memiliki gejala penyakit yang serupa dengan Anda.

Jika Anda mengalami efek samping yang berat, atau jika Anda mengalami efek samping yang tidak tertera pada brosur ini, mohon informasikan kepada dokter ataupun apoteker Anda.

Daftar isi

1 Apakah Galvus dan apa kegunaannya

Tiap tabletnya, Galvus mengandung 50 mg vildagliptin.

Galvus merupakan obat yang digunakan untuk mengobati pasien dengan diabetes tipe 2 yang kondisinya tidak dapat dikontrol oleh diet dan olahraga saja. Obat ini membantu mengontrol kadar gula dalam darah. Obat-obatan seperti ini dikenal dengan obat antidiabetes oral.

Diabetes tipe 2 terjadi apabila tubuh kita tidak dapat memproduksi insulin yang cukup atau insulin yang diproduksi oleh tubuh tidak bekerja sebagaimana mestinya. Penyakit ini juga dapat terjadi apabila tubuh kita memproduksi glukagon dalam jumlah yang terlalu besar.

Insulin merupakan zat yang dapat membantu menurunkan kadar gula dalam darah, khususnya setelah makan. Glukagon merupakan zat yang dapat mencetuskan proses produksi gula oleh hati, yang kemudian akan menyebabkan kenaikan kadar gula dalam darah. Pankreas merupakan organ yang memproduksi kedua zat tersebut.

Galvus bekerja dengan cara membuat pankreas memproduksi lebih banyak insulin dan lebih sedikit glukagon. Galvus membantu mengontrol kadar gula dalam darah.

Dokter Anda akan meresepkan Galvus saja ataupun kombinasi dengan obat antidiabetes lainnya berdasarkan kondisi Anda.

Penting bagi Anda untuk melanjutkan diet dan/atau olahraga yang telah direkomendasikan walaupun Anda sudah menjalani pengobatan dengan Galvus.

Apabila Anda masih memiliki pertanyaan terkait mengapa obat ini diresepkan untuk Anda, mohon tanyakan pada dokter Anda.

2 Sebelum mengonsumsi Galvus

Ikuti semua petunjuk yang diberikan dokter atau apoteker Anda dengan saksama walaupun informasi tersebut dapat saja berbeda dengan informasi yang tercantum pada brosur ini.

Tidak diperbolehkan mengonsumsi Galvus

Apabila Anda alergi (hipersensitif) terhadap vildagliptin atau terhadap kandungan zat lain yang terdapat pada Galvus.

Perhatian khusus saat mengonsumsi Galvus

- Apabila Anda sedang hamil atau berencana untuk hamil
- Apabila Anda sedang menyusui
- Apabila Anda memiliki masalah dengan ginjal
- Apabila Anda memiliki masalah dengan hati
- Apabila Anda mengalami gagal jantung, dokter akan memutuskan apakah Anda akan diresepkan Galvus atau tidak tergantung pada tingkat keparahan kondisi Anda
- Galvus bukanlah pengganti insulin. Anda sebaiknya tidak mengonsumsi Galvus sebagai pengobatan diabetes tipe 1 (contohnya jika tubuh Anda tidak memproduksi insulin sama sekali) atau untuk pengobatan diabetes ketoasidosis.

Apabila Anda mengalami hal-hal di atas, **mohon hubungi kepada dokter sebelum Anda mengonsumsi Galvus.**

Pemantauan terhadap pengobatan menggunakan Galvus

Dokter Anda sebaiknya memastikan pemeriksaan di bawah ini telah dilakukan:

- Kadar gula dalam darah dan urin secara teratur
- Pemeriksaan fungsi hati:
  - pada saat awal pengobatan
  - setiap 3 bulan selama tahun pertama pengobatan dan secara teratur pada tahun selanjutnya
  - apabila dokter meminta Anda untuk menghentikan pengobatan Galvus dikarenakan adanya masalah hati, Anda sebaiknya tidak menggunakan Galvus lagi.

Penggunaan Galvus bersama makanan dan minuman

Galvus dapat dikonsumsi dengan atau tanpa makanan.

Galvus dan pasien usia lanjut

Galvus dapat dikonsumsi oleh pasien usia lanjut.

Galvus dan pasien anak-anak dan remaja

Tidak ada informasi yang tersedia untuk penggunaan Galvus pada anak-anak dan remaja (di bawah umur 18 tahun). Penggunaan Galvus pada pasien ini tidak direkomendasikan.

Wanita hamil

- Informasikan kepada dokter Anda jika Anda sedang hamil atau kemungkinan mengalami kehamilan atau merencanakan suatu kehamilan. Dokter Anda akan menjelaskan kepada Anda mengenai potensi risiko jika Anda menggunakan Galvus selama kehamilan.

- Mohon konsultasikan dengan dokter atau apoteker Anda sebelum menggunakan obat apapun selama kehamilan.

Ibu menyusui

Anda tidak diperbolehkan menyusui selama menjalani pengobatan dengan Galvus.

Mohon konsultasikan dengan dokter atau apoteker Anda sebelum menggunakan obat apapun selama menyusui.

Mengemudi dan menggunakan mesin

Pasien yang mengalami pusing tidak diperbolehkan mengemudi kendaraan atau menggunakan mesin.

Informasi penting mengenai kandungan Galvus

Galvus mengandung laktosa (gula susu). Apabila Anda mengalami intoleransi laktosa yang berat, intoleransi galaktosa, atau malabsorpsi glukosa-galaktosa, informasikan kepada dokter Anda sebelum mengonsumsi Galvus.

Mengonsumsi obat lain

Informasikan ke dokter atau apoteker apabila Anda sedang atau baru saja mengonsumsi obat-obatan lainnya. Juga termasuk obat-obatan yang tidak diresepkan oleh dokter.

3 Bagaimana mengonsumsi Galvus

Ikuti semua instruksi yang diberikan oleh dokter atau apoteker Anda secara saksama, walaupun informasi tersebut dapat saja berbeda dengan informasi yang tercantum pada brosur ini. Anda tidak diperbolehkan mengonsumsi Galvus lebih dari yang diresepkan dokter Anda.

Berapa banyak Galvus yang dikonsumsi

Dokter Anda akan memberikan informasi kepada Anda berapa jumlah tablet Galvus yang harus Anda konsumsi.

Dosis yang umum digunakan untuk Galvus adalah 50 mg atau 100 mg per hari. Dosis 50 mg sebaiknya diminum 50 mg sekali sehari (pagi hari). Dosis 100 mg sebaiknya diminum 50 mg dua kali sehari (pagi dan malam hari). Dokter Anda akan menyarankan dosis yang lebih tinggi atau lebih rendah tergantung dari respon Anda terhadap pengobatan.

Dokter Anda akan meresepkan Galvus saja atau kombinasi dengan obat anti diabetes lainnya, tergantung dari kondisi Anda.

Bagaimana dan kapan mengonsumsi Galvus

Galvus sebaiknya diminum pada pagi hari (50 mg sehari sekali), atau pada pagi dan malam hari (50 mg dua kali sehari).

Tablet sebaiknya diminum bersama dengan segelas air.

Berapa lama mengonsumsi Galvus

Mohon tetap lanjutkan penggunaan Galvus setiap hari selama dokter Anda masih menyarankan penggunaannya. Anda dapat melanjutkan pengobatan ini untuk periode waktu

yang panjang. Dokter Anda akan memantau kondisi Anda secara teratur untuk memastikan efek pengobatan yang diharapkan.

Apabila dokter telah meminta Anda untuk menghentikan pengobatan Galvus dikarenakan adanya masalah hati, Anda sebaiknya tidak menggunakan Galvus lagi.

Apabila Anda memiliki pertanyaan berapa lama Anda perlu mengonsumsi Galvus, mohon hubungi dokter atau apoteker Anda.

Apabila Anda lupa mengonsumi Galvus

Apabila Anda lupa mengonsumsi Galvus, mohon agar sesegera mungkin mengonsumsi saat Anda ingat, kemudian konsumsi dosis berikutnya sesuai jadwal seperti biasa. Akan tetapi, apabila jadwal minum obat yang terlewat sudah terlalu dekat dengan jadwal berikutnya, lanjutkan dengan dosis selanjutnya saja.

Anda tidak diperbolehkan meminum dosis yang digandakan untuk menutupi dosis yang telah Anda lewatkan.

Apabila Anda mengonsumsi Galvus lebih dari yang seharusnya

Apabila Anda tidak sengaja mengonsumsi Galvus berlebihan, atau seseorang telah mengonsumsi obat Anda, **segera hubungi dokter Anda**. Anda mungkin membutuhkan tindakan medis. Mohon agar menunjukkan kemasan obat kepada dokter, apabila memungkinkan.

4 Efek samping yang mungkin terjadi

Sama halnya dengan obat-obat lainnya, pasien yang sedang menjalani terapi dengan Galvus dapat mengalami efek samping, meskipun tidak semua orang mengalaminya.

Beberapa pasien dapat mengalami efek samping berikut ketika mengonsumsi Galvus saja atau kombinasi dengan pengobatan antidiabetes lainnya:

Beberapa gejala yang segera membutuhkan perhatian medis:

Anda sebaiknya **berhenti mengonsumsi Galvus dan secepatnya menemui dokter Anda** apabila Anda mengalami gejala berikut ini:

- Pembengkakan pada wajah, lidah atau tenggorokan, kesulitan menelan, kesulitan bernapas, tiba-tiba timbul ruam atau gatal-gatal (gejala reaksi alergi berat yang dapat menyebabkan pembengkakan yang disebut ‘angiodema’).
- Timbul warna kekuningan pada kulit dan/atau mata, mual, hilangnya rasa lapar, urin berwarna gelap (menunjukkan kemungkinan gejala adanya masalah pada hati).
- Nyeri perut bagian atas yang berat (kemungkinan gejala radang pankreas).
- Sakit kepala, mengantuk, lemah, pusing, perasaan bingung, sensitif (cepat marah), timbul rasa lapar, jantung berdetak cepat, berkeringat, gelisah (kemungkinan gejala rendahnya kadar gula dalam darah yang dikenal dengan ‘hipoglikemia’)

Efek samping lainnya

Efek samping yang sering (terjadi pada < 1 dari 10 pasien).

Efek samping yang tidak sering (terjadi pada < 1 dari 100 pasien).

Beberapa pasien pernah mengalami efek samping berikut ini **ketika mengonsumsi Galvus saja**:

- Sering: pusing
- Tidak sering: sakit kepala, konstipasi, pembengkakan pada tangan, pergelangan atau pada kaki (edema).

Beberapa pasien pernah mengalami efek samping berikut ini **ketika mengonsumsi Galvus dan metformin:**

- Sering: gemetar, sakit kepala, pusing.

Beberapa pasien pernah mengalami beberapa efek samping berikut ini **ketika mengonsumsi Galvus dan sulfonilurea:**

- Sering: gemetar, sakit kepala, pusing, lemah.

Beberapa pasien pernah mengalami efek samping berikut ini **ketika mengonsumsi galvus dan glitazon:**

- Sering: kenaikan berat badan, pembengkakan pada tangan, pergelangan kaki atau kaki (edema).
- Tidak sering: sakit kepala.

Beberapa pasien pernah mengalami efek samping berikut ini **ketika mengonsumsi Galvus dan insulin (dengan atau tanpa metformin):**

- Sering: sakit kepala, menggigil, mual, penurunan gula darah, rasa panas pada dada.
- Tidak sering: diare, perut kembung.

Beberapa pasien pernah mengalami beberapa efek samping **ketika mengonsumsi Galvus dengan metformin dan sulfonilurea:**

- Sering: Pusing, gemetar, lemah, produksi keringat berlebih.

Apabila Anda mengalami salah satu efek seperti di atas yang berat, **hubungi dokter Anda.**

Beberapa pasien pernah mengalami efek samping lainnya **ketika mengonsumsi Galvus saja atau kombinasi dengan pengobatan antidiabetes lainnya:**

- Ruam yang juga menimbulkan rasa gatal, timbulnya área kulit yang terkelupas atau melepuh, nyeri sendi.

Apabila Anda mengalami salah satu efek seperti di atas yang berat, **hubungi dokter Anda.**

Apabila Anda mengenali adanya efek samping lainnya yang tidak tertera pada brosur ini, harap menginformasikannya dengan dokter atau apoteker Anda.

5 Penyimpanan Galvus

- Mohon tidak menggunakan obat setelah tanggal kadaluarsa yang tercantum pada dus obat.
- Simpan obat di dalam kemasannya.
- Mohon tidak menggunakan Galvus jika kemasannya rusak atau menunjukkan adanya cacat.
- Disimpan pada suhu tidak lebih dari 30°C.

- Mohon jauhkan obat ini dari jangkauan anak-anak.

6 Informasi lebih lanjut

Kandungan Galvus

Zat aktif Galvus adalah vildagliptin.

Kandungan lainnya adalah *lactose anhydrous*, *microcrystalline cellulose*, *sodium starch glycolate*, *magnesium stearate*.

Bagaimana bentuk dari Galvus

Galvus dijual dalam bentuk tablet.

Tabletnya berwarna putih hingga kekuningan dan berbentuk bulat bertepi, dengan permukaan datar, serta tidak memiliki garis bagi. Satu sisi dicetak "NVR", dan pada sisi lain dicetak "FB".

Tiap tablet mengandung zat aktif 50 mg vildagliptin.

Kemasan

Galvus 50 mg Tablet: Dus, 2 blister @ 14 tablet No. Reg.:

HARUS DENGAN RESEP DOKTER

Pemegang Nomor Ijin Edar

PT. Novartis Indonesia

Pabrik pembuat

Dibuat oleh Siegfried Barbera S.L., Barberà del Vallès, Spanyol untuk Novartis Pharma AG, Basel, Swiss. Diimpor oleh PT. Novartis Indonesia, Jakarta, Indonesia.

Apabila Anda memiliki pertanyaan mengenai obat ini, mohon hubungi dokter atau apoteker Anda.

PIL based on BPL 28-Nov-2016_Siegfried