Galvusmet®

(vildagliptin and metformin HCl fixed combination)

50 mg/500 mg, 50 mg/850 mg
Film-coated Tablets

Product Information

DISETUJUI OLEH BPOM: 16/12/2025 ID REG: EREG10000512500259 - EREG10000512500260

1 Trade name

Galvusmet® 50 mg/500 mg, 50 mg/850 mg tablets

2 Description and composition

Pharmaceutical forms

50 mg/500 mg: light yellow, ovaloid beveled edge, film-coated tablet imprinted with "NVR" on one side and "LLO" on the other side.

50 mg/850 mg: yellow, ovaloid beveled edge, film-coated tablet imprinted with "NVR" on one side and "SEH" on the other side.

Active substances

Vildagliptin

Metformin hydrochloride

Two strengths are available. One tablet of Galvusmet contains:

- 50 mg vildagliptin and 500 mg metformin hydrochloride
- 50 mg vildagliptin and 850 mg metformin hydrochloride

Excipients

Hydroxypropyl cellulose, hypromellose, iron oxide yellow, iron oxide red, macrogol, magnesium stearate, talc and titanium dioxide.

3 Indications

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

Galvusmet is also indicated for use in combination with insulin, when maximal tolerated dose of insulin with maximal tolerated dose of metformin as an adjunct to diet and exercise do not provide adequate glycaemic control.

4 Dosage regimen and administration

Dosage regimen

The use of antihyperglycemic therapy in the management of type 2 diabetes should be individualized on the basis of effectiveness and tolerability. When using Galvusmet, do not exceed the maximum daily dose of vildagliptin (100 mg).

The recommended starting dose of Galvusmet should be based on the patient's condition and/or current regimen of vildagliptin and/or metformin hydrochloride.

Starting dose for patients inadequately controlled on vildagliptin and metformin monotherapy
Based on the patient's current dose of metformin, Galvusmet may be initiated at either the 50 mg/500 mg, 50 mg/850 mg or 50 mg/1000 mg tablet strength twice daily, one tablet in the morning and the other in the evening. The recommended daily dose is 100 mg vildagliptin plus 2000 mg metformin hydrochloride.

Starting dose for patients switching from combination therapy of vildagliptin plus metformin hydrochloride as separate tablets
Patients receiving vildagliptin and metformin from separate tablets may be switched to Galvusmet containing the same doses of each component.

Use in combination with insulin:
The dose of Galvusmet should provide vildagliptin dosed as 50 mg twice daily (100 mg total daily dose) and a dose of metformin similar to the dose already being taken.
Doses higher than 100 mg of vildagliptin are not recommended.

General target population
Adults 18 years of age and above

Special populations

Renal impairment

GFR should be assessed before initiation of treatment with metformin-containing products (such as Galvusmet) and at least annually thereafter. In patients at increased risk of further progression of renal impairment and in the elderly, renal function should be assessed more frequently, e.g. every 3 to 6 months.

The maximum daily dose of metformin should preferably be divided into 2 to 3 daily doses. Factors that may increase the risk of lactic acidosis (see section 6 Warnings and precautions) should be reviewed before considering initiation of metformin-containing products (such as Galvusmet) in patients with GFR < 60 ml/min. Galvusmet is contraindicated in patients with GFR < 30 ml/min because of its metformin component (see section 5 Contraindications).

The following dosing recommendations apply to metformin and vildagliptin, used separately or in combination, in patients with renal impairment. If no adequate strength of Galvusmet is available, individual components should be used instead of the fixed dose combination.

Table 4-1 Dose adjustments in patients with renal impairment

GFR mL/min	Metformin	Vildagliptin
60-89	Maximum daily dose is 3000 mg*. Dose reduction may be considered if renal function declines.	Maximal daily dose is 100 mg.
45-59	Starting dose is 500 mg or 750 mg with a maximum daily dose of 1000 mg*.	Maximal daily dose is 50 mg.
30-44	It is not recommended to initiate metformin, but metformin can be maintained in patients already treated with a maximum daily dose of 1000 mg.	
<30	Metformin is contraindicated.	

*if metformin doses higher than those achievable with Galvusmet alone are considered necessary.

Hepatic impairment
Galvusmet should not be used in patients with hepatic impairment, including those with pre-treatment alanine aminotransferase (ALT) or aspartate aminotransferase (AST) > 3 times the upper limit of normal (ULN).

Geriatric patients (≥ 65 years)
As metformin is excreted via the kidneys, and elderly patients tend to exhibit decreased renal function, elderly patients taking metformin-containing products (such as Galvusmet) should have their renal function monitored regularly (see section 6 Warnings and precautions). Galvusmet has not been studied in patients older than 75 years. Therefore the use of Galvusmet is not recommended in this population.

Paediatric patients (< 18 years)
Galvusmet is not recommended for use in children and adolescents due to a lack of data on safety and efficacy.

Method of administration

For oral use

Galvusmet should be given with meals to reduce the gastrointestinal side effects associated with metformin hydrochloride.

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

5 Contraindications

Hypersensitivity

Galvusmet is contraindicated in patients with known hypersensitivity to vildagliptin or metformin hydrochloride or to any of the excipients (see section 2 Description and composition, sub-section Excipients).

Patients with renal impairment

Galvusmet is contraindicated in patients with severe renal impairment (GFR < 30 mL/min) (see section 4 Dosage regimen and administration and section 6 Warnings and precautions).

Congestive heart failure

Galvusmet is contraindicated in patients with congestive heart failure requiring pharmacologic treatment (see section 6 Warnings and precautions).

Metabolic acidosis

Galvusmet is contraindicated in patients with acute or chronic metabolic acidosis, including lactic acidosis or diabetic ketoacidosis, with or without coma. Diabetic ketoacidosis should be treated with insulin.

Radiologic Studies

Galvusmet should be temporarily discontinued in patients undergoing radiologic studies involving intravascular administration of iodinated contrast materials, because use of such products may result in acute alteration of renal function (see section 6 Warnings and precautions).

Acute conditions with the potential to alter renal function, such as:

- dehydration,
- severe infection,
- shock,
- septicaemia
- intravascular administration of iodinated contrast agents.

Acute or chronic disease which may cause tissue hypoxia, such as:

- cardiac or respiratory failure,
- recent myocardial infarction,
- shock.

Hepatic impairment

Acute alcohol intoxication, alcoholism

Lactation

6 Warnings and precautions

Galvusmet

Galvusmet is not a substitute for insulin in patients requiring insulin. Galvusmet should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

Vildagliptin

Skin disorders

Skin lesions, including blistering and ulceration have been reported with vildagliptin in extremities of monkeys in non-clinical toxicology studies. Although skin lesions were not observed at an increased incidence in clinical trials, there was limited experience in patients with diabetic skin complications. Therefore, in keeping with routine care of the diabetic patient, monitoring for skin disorders, such as blistering or ulceration, is recommended.

Hepatic impairment

A small numerical imbalance of reports of generally asymptomatic elevated transaminases was reported in patients treated with vildagliptin 100 mg daily in controlled clinical trials (see section 7 Adverse drug reactions). Therefore, as per routine clinical practice, it is recommended that liver function tests be performed prior to the initiation of treatment with vildagliptin 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 up thereafter with frequent liver function tests until the abnormality/abnormalities return to normal. Should an increase in AST or ALT of 3x the ULN or greater persist, withdrawal of therapy with vildagliptin is recommended.

Patients with hepatic impairment should not be treated with Galvusmet.

Heart Failure

A clinical study 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 results are inconclusive (see section 12 Clinical studies).

There is no experience of vildagliptin use in clinical studies in patients with NYHA functional class IV and therefore use is not recommended in these patients.

Metformin Hydrochloride

Lactic Acidosis

Lactic acidosis is a very rare but serious metabolic complication that most often occurs with acute worsening of renal function, or cardiorespiratory illness or sepsis. Metformin accumulation occurs with acute worsening of renal function and increases the risk of lactic acidosis.

In case of dehydration (e.g. due to severe diarrhea or vomiting, fever or reduced fluid intake), the patient should stop taking metformin-containing products (such as Galvusmet) and seek immediate medical attention.

Medicinal products that can acutely impair renal function (such as antihypertensives, diuretics and NSAIDs) should be initiated with caution in patients treated with metformin-containing products (such as Galvusmet). Other risk factors for lactic acidosis are excessive alcohol intake, hepatic impairment, inadequately controlled diabetes, ketosis, prolonged fasting and any conditions associated with hypoxia, as well as concomitant use of medicinal products that may cause lactic acidosis (see section 5 Contraindications and section 8 Interactions).

Diagnosis of lactic acidosis

Patients and/or caregivers should be informed of the risk of lactic acidosis. Lactic acidosis is characterized by acidotic dyspnoea, abdominal pain, muscle cramps, asthenia and hypothermia followed by coma. If suspected symptoms occur, the patient should stop taking metformin – containing products (such as Galvusmet) and seek immediate medical attention. Diagnostic laboratory findings are decreased blood pH (< 7.35), increased plasma lactate levels (>5 mmol/L) and an increased anion gap and lactate/pyruvate ratio. If metabolic acidosis is suspected, treatment with metformin-containing products (such as Galvusmet) should be discontinued and the patient should be immediately hospitalised (see section 10 Overdosage).

Cardiac failure

Metformin is contraindicated in patients with heart failure, therefore Galvusmet is contraindicated in this patient population (see section 5 Contraindications).

Patients with known or suspected mitochondrial diseases:

In patients with known mitochondrial diseases such as Mitochondrial Encephalopathy with Lactic Acidosis, and Stroke-like episodes (MELAS) syndrome and Maternal inherited diabetes and deafness (MIDD), metformin is not recommended due to the risk of lactic acidosis exacerbation and neurologic complications which may lead to worsening of the disease.

In case of signs and symptoms suggestive of MELAS syndrome or MIDD, treatment with metformin-containing products (such as Eucreas) should be discontinued immediately and prompt diagnostic evaluation should be performed.

Monitoring of renal function

GFR should be assessed before treatment initiation and regularly thereafter (see section 4 Dosage regimen and administration). Metformin-containing products (such as Galvusmet) are contraindicated in patients with GFR < 30 mL/min and should be temporarily discontinued in the presence of conditions that alter renal function (see section 5 Contraindications).

Metformin hydrochloride is known to be substantially excreted by the kidneys, and the risk of metformin hydrochloride accumulation and lactic acidosis increases with the degree of renal function impairment. Since advancing age is associated with reduced renal function, metformin-containing products (such as Galvusmet) should be carefully titrated in the elderly to establish the minimum dose for adequate glycemic effect, and renal function should be monitored regularly (see section 4 Dosage regimen and administration and section 5 Contraindications).

Renal impairment in elderly patients is frequent and asymptomatic. Special caution should be exercised in situations where renal function may become impaired, for example when initiating antihypertensive or diuretic therapy or when starting treatment with an NSAID.

Interactions

Concomitant medications that may affect renal function or metformin hydrochloride disposition

Concomitant medications that may affect renal function, result in significant haemodynamic change or inhibit renal transport and increase metformin systemic exposure should be used with caution (see section 8 Interactions).

Administration of intravascular iodinated contrast materials

Intravascular administration of iodinated contrast agents may lead to contrast-induced nephropathy, resulting in metformin accumulation and increased risk of lactic acidosis. Metformin-containing products (such as Galvusmet) should be discontinued prior to or at the time of the imaging procedure and not restarted until 48 hours subsequent to the procedure and reinstituted only after renal function has been re-evaluated and found to be stable (see section 4 Dosage regimen and administration, and section 8 Interactions).

Hypoxic states

Cardiovascular collapse (shock), acute congestive heart failure, acute myocardial infarction and other conditions characterized by hypoxaemia have been associated with lactic acidosis and may also cause prerenal azotmeia. If such events occur in patients receiving metformin-containing products (such as Galvusmet), the medication should be promptly discontinued.

Surgical procedures

Metformin-containing products (such as Galvusmet) must be discontinued at the time of surgery under general, spinal or epidural anaesthesia (except minor procedures not associated with restricted intake of food and fluids) and may be restarted no earlier than 48 hours following surgery or until the patient's oral nutrition has resumed and renal function has been re-evaluated and found to be stable.

Alcohol intake

Alcohol is known to potentiate the effect of metformin hydrochloride on lactate metabolism. Patients should be warned against excessive alcohol intake while receiving metformin-containing products (such as Galvusmet).

Alcohol intoxication is associated with an increased risk of lactic acidosis, particularly in cases of fasting, malnutrition or hepatic impairment.

Patients with hepatic impairment

Since impaired hepatic function has been associated with some cases of lactic acidosis, a risk associated with metformin hydrochloride, metformin-containing products (such as Galvusmet) should generally be avoided in patients with clinical or laboratory evidence of hepatic disease.

Vitamin B_{12} levels

Metformin has been associated with a decrease in serum vitamin B_{12} levels without clinical manifestations, in approximately 7% of patients. Such a decrease, is very rarely associated with anaemia and appears to be rapidly reversible with discontinuation of metformin hydrochloride and/or vitamin B_{12} supplementation. Measurement of haematological parameters on at least an annual basis is advised for patients receiving metformin-containing products (such as Galvusmet) and any apparent abnormalities should be appropriately investigated and managed. Certain individuals (e.g., those with inadequate vitamin B_{12} or calcium intake or absorption) appear to be predisposed to developing subnormal vitamin B_{12} levels. In these patients, routine serum vitamin B_{12} measurements at minimally two-to-three-year intervals may be useful.

Change in clinical status of patients with previously controlled type 2 diabetes

A patient with type 2 diabetes previously well-controlled on Galvusmet who develops laboratory abnormalities or clinical illness (especially vague and poorly defined illness) should promptly be evaluated for ketoacidosis and/or lactic acidosis. If acidosis of either form occurs, Galvusmet must be stopped immediately and appropriate measures initiated.

Hypoglycemia

Hypoglycemia does not usually occur in patients receiving Galvusmet alone, but could occur when caloric intake is deficient, when strenuous exercise is not compensated by caloric supplementation, or ethanol use. Elderly, debilitated or malnourished patients and those with adrenal or pituitary insufficiency or alcohol intoxication are susceptible to hypoglycemic effects. Hypoglycemia may be difficult to recognize in the elderly and in people taking beta-adrenergic blocking drugs.

Loss of control of blood glucose

When a patient stabilized on any diabetic regimen is exposed to stress such as fever, trauma, infection, surgery, etc., a temporary loss of glycaemic control may occur. At such times, it may be necessary to withhold Galvusmet and temporarily administer insulin. Galvusmet may be reinstituted after the acute episode is resolved.

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.

7 Adverse drug reactions

Summary of the safety profile

Galvusmet

There have been no therapeutic clinical trials conducted with Galvusmet. However, bioequivalence of Galvusmet with co-administered vildagliptin and metformin has been demonstrated (see section Pharmacokinetics properties). The data presented here relate to the

co-administration of vildagliptin and metformin, where vildagliptin has been added to metformin. There have been no studies of metformin added to vildagliptin.

The majority of adverse reactions 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 ACE inhibitor. The majority of events were mild in severity and resolved with ongoing vildagliptin treatment.

In comparative controlled add-on therapy studies, the incidence of hypoglycemia in patients receiving vildagliptin in combination with metformin was 0.9% and 0.4% in patients receiving placebo and metformin.

Gastrointestinal adverse reactions including diarrhoea and nausea are known to occur very commonly during the introduction of metformin hydrochloride. In the vildagliptin clinical program (n =2,264) the rate of diarrhoea and nausea was 2.5% and 2.6 % respectively as compared to 2.9% for both in the placebo group (n = 347) and 26.2% and 10.3%, respectively, in the metformin hydrochloride group (n = 252).

Overall, gastrointestinal symptoms were reported in 12.9% of patients treated with the combination of vildagliptin and metformin hydrochloride compared to 18.1% of patients treated with metformin hydrochloride alone.

Tabulated summary of adverse drug reactions from clinical trials

Adverse reactions reported in patients who received vildagliptin in double-blind studies as an add-on to metformin and as monotherapy, 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).

Table 7-1 Other adverse reactions reported in patients who received vildagliptin as add-on therapy to metformin compared to placebo plus metformin in double-blind studies (N=441)

Nervous system disorders	
Common	Headache, tremor, dizziness
Uncommon	Fatigue
Gastrointestinal disorders	
Common	Nausea

In controlled clinical trials with the combination of vildagliptin 100 mg daily plus metformin, no withdrawal due to adverse reactions was reported in either the vildagliptin 100 mg daily plus metformin or the placebo plus metformin treatment groups.

In clinical trials, weight did not change from baseline when vildagliptin 100 mg daily was added to metformin (+0.2 kg and -1.0 kg for vildagliptin and placebo, respectively).

Long term clinical studies of up to 2 years in duration did not show any additional safety signals or unforeseen risks when vildagliptin was added on to metformin.

Combination with insulin

In controlled clinical studies using vildagliptin 50 mg twice daily in combination with insulin, with or without concomitant metformin, the overall incidence of withdrawals 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 vs 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 7-2 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

Vildagliptin

Adverse reactions for vildagliptin component from monotherapy double blind studies are presented in Table 7-3.

Table 7-3 Adverse reactions reported in patients who received vildagliptin as monotherapy in double-blind studies (N=2,264)

Nervous system disorders	
Common	Dizziness
Uncommon	Headache
Gastrointestinal disorders	
Common	Constipation
Musculoskeletal and connective tissue disorders	

Common	Arthralgia
Infections and infestations	
Very rare	Upper respiratory tract infection, nasopharyngitis
Vascular disorders	
Uncommon	Oedema peripheral

None of the adverse reactions reported for the vildagliptin monotherapy were observed at clinically significantly higher rates when vildagliptin was administered concomitantly with metformin. In comparative controlled monotherapy studies, hypoglycemia was uncommon in patients receiving vildagliptin as monotherapy (0.4%) and in patients receiving metformin hydrochloride (0.4%). Vildagliptin is weight neutral when administered as monotherapy or in combination with metformin.

In controlled monotherapy trials of up to one year in duration, the incidence of ALT or AST elevations >3 X ULN (classified as present on at least 2 consecutive measurements or at the final on-treatment visit) was 0.3%, 0.9 % and 0.3% for vildagliptin 50 mg once daily, vildagliptin 100 mg daily (administered as single and divided doses) and placebo respectively. These elevations in transaminases were generally asymptomatic, non-progressive in nature and not associated with cholestasis or jaundice.

In clinical trials, weight did not change from baseline when vildagliptin 100 mg daily was administered as monotherapy (-0.3 kg and -1.3 kg for vildagliptin and placebo, respectively).

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

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 Galvusmet 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 6 Warnings and precautions)
- Urticaria, bullous and exfoliative skin lesions, including bullous pemphigoid
- Cutaneous vasculitis
- Pancreatitis
- Arthralgia, sometimes severe
- Cholecystitis

Metformin Hydrochloride

Known adverse reactions for the metformin component are summarized in Table 7-4.

Table 7-4 Known adverse reactions for metformin

Metabolism and Nutrition disorders

	Very common	Decrease appetite
	Very Rare	Lactic acidosis
Nervous system disorders		
	Common	Dysgeusia
Gastrointestinal disorders		
	Very Common	Flatulence, nausea, vomiting, diarrhoea, abdominal pain
Hepatobiliary disorders		
	Very Rare	Hepatitis**
Skin and subcutaneous tissue disorders		
	Very rare	Skin reactions such as erythema, pruritus, urticarial
Investigations		
	Very rare	Decrease of vitamin B_{12} absorption*, Liver function test abnormalities

**A decrease of vitamin B_{12} absorption with decrease of serum levels has very rarely been observed in patients treated long-term with metformin and appears to generally not be of clinical significance. Consideration of such aetiology is recommended if a patient presents with megaloblastic anaemia.*

***Isolated cases of liver function test abnormalities or hepatitis resolving upon metformin discontinuation have been reported.*

Gastrointestinal adverse effects occur most frequently during initiation of therapy and resolve spontaneously in most cases. To prevent them, it is recommended that metformin be taken in 2 daily doses during or after meals. A slow increase in the dose may also improve gastrointestinal tolerability.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:

Pusat Farmakovigilans/MESO Nasional
Direktorat Pengawasan Keamanan, Mutu, dan Ekspor Impor Obat, Narkotika, Psikotropika, Prekursor dan Zat Adiktif
Badan Pengawas Obat dan Makanan
Jl. Percetakan Negara No. 23, Jakarta Pusat, 10560
Email: pv-center@pom.go.id
Phone: +62-21-4244691 Ext.1079
Website: https://e-meso.pom.go.id/ADR

or

Novartis Indonesia
Website: www.novartis.com/report

8 Interactions

Galvusmet

No clinically relevant pharmacokinetic interaction have been observed when vildagliptin (100 mg once daily) was co-administered with metformin hydrochloride (1,000 mg once daily). Drug interactions for each component of Galvusmet has been extensively studied. However, the concomitant use of the active substances in patients in clinical studies and in widespread clinical use has not resulted in any unexpected interactions.

The following statements reflect the information available on the individual active substances (vildagliptin and metformin).

Vildagliptin

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.

Results from clinical trials conducted with the oral antidiabetics pioglitazone, metformin and glyburide in combination with vildagliptin have shown no clinically relevant pharmacokinetic interactions in the target population.

Drug-drug interaction studies with digoxin (P-glycoprotein substrate) and warfarin (CYP2C9 substrate) in healthy subjects have shown no clinically relevant pharmacokinetic interactions after co-administration with vildagliptin.

Drug-drug interaction studies in healthy subjects were conducted with amlodipine, ramipril, valsartan and simvastatin. In these studies, no clinically relevant pharmacokinetic interactions were observed after co-administration with vildagliptin. However, this has not been established in the target population.

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.

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 hydrochloride), amlodipine, digoxin, ramipril, simvastatin, valsartan or warfarin were observed after co-administration with vildagliptin.

Metformin Hydrochloride

The following is known about metformin:

Furosemide – Furosemide increased C_{max} and blood AUC of metformin with no change in renal clearance of metformin. Metformin decreased C_{max}, blood AUC of furosemide, with no change in renal clearance of furosemide.

Nifedipine – Nifedipine increased absorption, C_{max} and AUC of metformin, and increased excretion of metformin in urine. Metformin had minimal effects on nifedipine.

Glyburide – Glyburide produced no changes in metformin PK/PD parameters. Decreases in C_{max}, blood AUC of glyburide were observed, but were highly variable. Therefore the clinical significance of this finding was unclear.

Iodinated contrast agents – Metformin-containing products (such as Galvusmet) must be discontinued prior to or at the time of the imaging procedure and not restarted until at least 48 hours after, provided that renal function has been re-evaluated and found to be stable (see section 4 Dosage regimen and administration, and section 6 Warnings and Precautions).

Drug that reduce metformin cleareance - Concomitant use of drugs that interfere with common renal tubular transport systems involved in the renal elimination of metformin (e.g., organic cationic transporter-2 [OCT2] / multidrug and toxin extrusion [MATE] inhibitors such as ranolazine, vandetanib, dolutegravir, and cimetidine) could increase systemic exposure to metformin.

Other - Some drugs can adversely affect renal function which may increase the risk of lactic acidosis, e.g. NSAIDs, including selective cyclo-oxygenase (COX) II inhibitors, ACE inhibitors, angiotensin II receptor antagonists and diuretics, especially loop diuretics. When starting or using such products in combination with metformin-containing products (such as Galvusmet), close monitoring of renal function is necessary. Certain drugs tend to cause hyperglycaemia and may lead to loss of glycaemic control. These drugs include the thiazides and other diuretics, corticosteroids, phenothiazines, thyroid products, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, calcium channel blocking drugs, and isoniazid. Close monitoring of glycaemic control and metformin dose adjustments are recommended when such drugs are administered or withdrawn for these patients.

There is an increased risk of lactic acidosis in acute alcohol intoxication (particularly in the case of fasting, malnutrition or hepatic impairment) due to metformin. Avoid consumption of alcohol and medicinal products containing alcohol. (see section 6 Warnings and precautions).

Intravascular administration of iodinated contrast media may lead to renal failure, resulting in metformin accumulation with the risk of lactic acidosis. Metformin should be discontinued prior to, or at the time of the test and not reinstituted until 48 hours afterwards, and only after renal function has been re-evaluated and found to be normal.

Combinations requiring precautions for use:
Glucocorticoids, beta-2-agonists, and diuretics have intrinsic hyperglycaemic activity. The patient should be informed and more frequent blood glucose monitoring performed, especially at the beginning of treatment. If necessary, the dosage of Galvusmet may need to be adjusted during concomitant therapy and on its discontinuation.

Angiotensin converting enzyme (ACE) inhibitors may decrease the blood glucose levels. If necessary, the dosage of the antihyperglycaemic medicinal product should be adjusted during therapy with the other medicinal product and on its discontinuation.

9 Pregnancy, lactation, females and males of reproductive potential

9.1 Pregnancy

Risk summary

There are no adequate data from the use of Galvusmet in pregnant women. For vildagliptin studies in animals have shown reproductive toxicity at high doses. For metformin, studies in animals have not shown reproductive toxicity. Studies in animals performed with vildagliptin and metformin have not shown evidence of teratogenicity, but foetotoxic effects at maternotoxic doses (see section 13 Non-clinical safety data). The potential risk for humans is unknown. Galvusmet should not be used during pregnancy.

9.2 Lactation

Risk summary

Studies in animals have shown excretion of both metformin and vildagliptin in milk. It is not known whether vildagliptin is excreted in human milk, but metformin is excreted in human milk in low amounts. Due to both the potential risk of neonate hypoglycemia related to metformin and the lack of human data with vildagliptin, Galvusmet should not be used during lactation.

9.3 Females and males of reproductive potential

No studies on the effect on human fertility have been conducted for Galvusmet. Fertility studies have been performed with vildagliptin in rats at doses producing exposures equivalent to up to 200 times the human dose and have revealed no evidence of impaired fertility or early embryonic development due to vildagliptin.

10 Overdosage

Signs and symptoms

Vildagliptin

In healthy subjects (seven to fourteen subjects per treatment group), vildagliptin 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 hands and feet, 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

The most effective method of removing metformin is haemodialysis. However, vildagliptin cannot be removed by haemodialysis, although the major hydrolysis metabolite (LAY 151) can. Supportive management is recommended.

Metformin Hydrochloride

Overdose of metformin hydrochloride has occurred, including ingestion of amounts greater than 50 grams. Hypoglycemia was reported in approximately 10% of cases, but no causal association with metformin hydrochloride has been established. Lactic acidosis has been reported in approximately 32% of metformin hydrochloride overdose cases. Metformin hydrochloride is dialyzable with a clearance of up to 170 ml/min under good haemodynamic conditions. Therefore, haemodialysis may be useful for removal of the accumulated drug from patients in whom metformin hydrochloride overdosage is suspected.

In the event of overdosage, appropriate supportive treatment should be initiated according to patient's clinical signs and symptoms.

11 Clinical pharmacology

Pharmacotherapeutic group, ATC code

Drugs used in diabetes, combinations of oral blood glucose lowering drugs. ATC code: A10BD08.

Mechanism of action (MOA)

Galvusmet combines two antihyperglycemic agents with different mechanisms of action to improve glycemic control in patients with type 2 diabetes: vildagliptin, a member of the DPP-4 (dipeptidyl-peptidase-4) inhibitor class and metformin hydrochloride, a member of the biguanide class.

Vildagliptin, a member of the islet enhancer class, is a potent and selective dipeptidylpeptidase-4 (DPP-4) inhibitor that improves glycemic 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).

Metformin hydrochloride decreases hepatic glucose production, decreases intestinal absorption of glucose and improves insulin sensitivity by increasing peripheral glucose uptake and utilization. Metformin hydrochloride stimulates intracellular glycogen synthesis by acting on glycogen synthase and increase the transport capacity of specific types of membrane glucose transporters (GLUT-1 and GLUT).

Pharmacodynamics (PD)

Galvusmet

The efficacy and safety of the separate components have been previously established and the co-administration of the separate components have been evaluated for efficacy and safety in clinical studies. These clinical studies established an added benefit of vildagliptin in patients with inadequately controlled type 2 diabetes while on metformin hydrochloride therapy (see section 12 Clinical studies).

Vildagliptin

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 and GIP.

By increasing endogenous GLP-1 levels, vildagliptin also enhances the sensitivity of alpha cells to glucose, resulting in more glucose-appropriate glucagon secretion.

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 delaying gastric emptying is not observed with vildagliptin treatment.

Metformin Hydrochloride

Metformin is a biguanide with antihyperglycaemic effects, lowering both basal and postprandial plasma glucose. It does not stimulate insulin secretion and therefore does not produce hypoglycemia or increased weight gain.

In humans, metformin has favourable effects on lipid metabolism, independently of its action on glycaemia. This has been shown at therapeutic doses in controlled, medium-term or long-term clinical studies: metformin reduces serum levels of total cholesterol, LDL cholesterol and triglycerides.

The prospective randomized UKPDS (UK Prospective Diabetes Study) study has established the longterm benefit of intensive blood glucose control in type 2 diabetes. Analysis of the results for overweight patients treated with metformin after failure of diet alone showed:

- a significant reduction in the absolute risk of any diabetes-related complication in the metformin group (29.8 events/1,000 patient-years) versus diet alone (43.3 events/1,000 patient-years), p=0.0023, and versus the combined sulphonylurea and insulin monotherapy groups (40.1 events/1,000 patient-years), p=0.0034;
- a significant reduction in the absolute risk of diabetes-related mortality: metformin 7.5 events/1,000 patient-years, diet alone 12.7 events/1,000 patient-years, p=0.017;
- a significant reduction in the absolute risk of overall mortality: metformin 13.5 events/1,000 patient-years versus diet alone 20.6 events/1,000 patient-years (p=0.011), and versus the combined sulphonylurea and insulin monotherapy groups 18.9 events/1,000 patientyears (p=0.021);
- a significant reduction in the absolute risk of myocardial infarction: metformin 11 events/1,000 patient-years, diet alone 18 events/1,000 patient-years (p=0.01).

Pharmacokinetics (PK)

Galvusmet

Absorption

Bioequivalence has been demonstrated between Galvusmet at three dose strengths (50 mg/500 mg, 50 mg/850 mg and 50 mg/1000 mg) versus free combination of vildagliptin and metformin hydrochloride tablets at the corresponding doses.

Food does not affect the extent and rate of absorption of vildagliptin from Galvusmet. The rate and extent of absorption of metformin from Galvusmet 50 mg/1000 mg were decreased when given with food as reflected by the decrease in C_{max} by 26%, AUC by 7% and delayed T_{max} (2.0 to 4.0 h).

The following statements reflect the pharmacokinetic properties of the individual active substances of Galvusmet.

Vildagliptin

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%) compared to dosing in the fasting state. 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 (Vss) 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 (LAY 151) 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 dose). DPP-4 contributes partially to the hydrolysis of vildagliptin based on an *in vivo* study using DPP-4 deficient rats. Vildagliptin is not metabolised by CYP 450 enzymes to any quantifiable extent, and accordingly the metabolic clearance of vildagliptin is not anticipated to be affected by comedications that are CYP 450 inhibitors and/or inducers. *In vitro* studies demonstrated that vildagliptin does not inhibit/induce CYP 450 enzymes. 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 [14C] vildagliptin, approximately 85% of the dose was excreted into the urine and 15% of the dose was recovered in the faeces. Renal excretion of the unchanged vildagliptin accounted 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.

Linearity / non-linearity
The C_{max} for vildagliptin and the area under the plasma concentrations versus time curves (AUC) increased in an approximately dose proportional manner over the therapeutic dose range.

Special populations

Gender: No clinically relevant differences in the pharmacokinetics of vildagliptin were observed between male and female healthy subjects within a wide range of age and body mass index (BMI). DPP-4 inhibition by vildagliptin is not affected by gender.

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

Hepatic impairment: In subjects with mild, moderate or severe hepatic impairment (Child-Pugh A-C) there were no clinically significant changes (maximum ~30%) in exposure to vildagliptin.

Renal impairment: In subjects with mild, moderate, and severe renal impairment systemic exposure to vildagliptin was increased (C_{max} 8% to 66%; AUC 32% to 134%) compared to subjects with normal renal function.

Ethnic group: Limited data suggest that race does not have any major influence on vildagliptin pharmacokinetics.

Metformin Hydrochloride

Absorption
After an oral dose of metformin, the maximum plasma concentration (C_{max}) is achieved after about 2.5 h. Absolute bioavailability of a 500 mg metformin tablet is approximately 50-60% in healthy subjects. After an oral dose, the non-absorbed fraction recovered in faeces was 20-30%.

After oral administration, metformin absorption is saturable and incomplete. It is assumed that the pharmacokinetics of metformin absorption are non-linear. At the usual metformin doses and dosing schedules, steady state plasma concentrations are reached within 24-48 h and are generally less than 1 µg/ml. In controlled clinical trials, maximum metformin plasma levels (C_{max}) did not exceed 4 µg/ml, even at maximum doses.

Food slightly delays and decreases the extent of the absorption of metformin. Following administration of a dose of 850 mg, the plasma peak concentration was 40% lower, AUC was decreased by 25% and time to peak plasma concentration was prolonged by 35 minutes. The clinical relevance of this decrease is unknown.

Distribution
Plasma protein binding is negligible. Metformin partitions into erythrocytes. The mean volume of distribution (Vd) ranged between 63-276 liters.

Biotransformation/Metabolism

Metformin is excreted unchanged in the urine. No metabolites have been identified in humans.

Elimination

Metformin is eliminated by renal excretion. Renal clearance of metformin is > 400 ml/min, indicating that metformin is eliminated by glomerular filtration and tubular secretion. Following an oral dose, the apparent terminal elimination half-life is approximately 6.5 h. When renal function is impaired, renal clearance is decreased in proportion to that of creatinine and thus the elimination half-life is prolonged, leading to increased levels of metformin in plasma.

12 Clinical studies

Vildagliptin added to patients whose glycaemic control was not satisfactory despite treatment with metformin monotherapy resulted after 6-month treatment in additional statistically significant mean reductions in HbA1c compared to placebo (between group differences of -0.7% to -1.1% for vildagliptin 50 mg and 100 mg, respectively). The proportion of patients who achieved a decrease in HbA1c of ≥ 0.7% from baseline was statistically significantly higher in both vildagliptin plus metformin groups (46% and 60%, respectively) versus the metformin plus placebo group (20%).

In a 24 week study (LAF2354) vildagliptin (50 mg bid) was compared to pioglitazone (30 mg qd) in patients inadequately controlled with metformin. Mean reductions from baseline HbA1c of 8.4% were -0.9% with vildagliptin added to metformin and -1.0% with pioglitazone added to metformin. The decrease in HbA1c 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, HbA1c reductions and the body weight differences were maintained.

In a long-term study 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 1-year mean reductions in HbA1c 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 HbA1c was similar to baseline values in both treatment groups and the body weight changes and hypoglycemia differences were maintained.

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 a 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.

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 duration (mean exposure 50 weeks for vildagliptin and 49 weeks for comparators) was performed and showed that vildagliptin treatment was not associated with an increase in cardiovascular risk versus comparators. The composite endpoint of adjudicated major adverse cardiovascular events (MACE) including acute myocardial infarction, stroke or cardiovascular death was similar for vildagliptin versus combined active and placebo comparators [Mantel–Haenszel risk ratio (M-H RR) 0.82 (95% CI 0.61-1.11)]. A MACE occurred in 83 out of 9,599 (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 heart failure (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 M-H RR 1.08 (95% CI 0.68-1.70).

13 Non-clinical safety data

Animal studies of up to 13-weeks in duration have been conducted with the combined active substances of Galvusmet. No new toxicities associated with the combination were identified. The following data are findings from studies performed with vildagliptin or metformin individually.

Vildagliptin
Intra-cardiac impulse conduction delays were observed in dogs with a no-effect dose of 15 mg/kg (7-fold human exposure based on C_{max}).

Accumulation of foamy alveolar macrophages in the lung was observed in rats and mice. The noeffect dose in rats was 25 mg/kg (5-fold human exposure based on AUC) and in mice 750 mg/kg (142-fold human exposure).

Gastrointestinal symptoms, particularly soft faeces, mucoid faeces, diarrhoea and, at higher doses, faecal blood were observed in dogs. A no-effect level was not established.

Vildagliptin was not mutagenic in conventional *in vitro* and *in vivo* tests for genotoxicity.

A fertility and early embryonic development study in rats revealed no evidence of impaired fertility, reproductive performance or early embryonic development due to vildagliptin. Embryofoetal toxicity was evaluated in rats and rabbits. An increased incidence of wavy ribs was observed in rats in association with reduced maternal body weight parameters, with a no-effect dose of 75 mg/kg (10-fold human exposure). In rabbits, decreased foetal weight and skeletal variations indicative of developmental delays were noted only in the presence of severe maternal toxicity, with a no-effect dose of 50 mg/kg (9-fold human exposure). A pre- and postnatal development study was performed in rats. Findings were only observed in association with maternal toxicity at ≥ 150 mg/kg and included a transient decrease in body weight and reduced motor activity in the F1 generation.

A two-year carcinogenicity study was conducted in rats at oral doses of up to 900 mg/kg (approximately 200 times human exposure at the maximum recommended dose). No increases

in tumour incidence attributable to vildagliptin were observed. Another two-year carcinogenicity study was conducted in mice at oral doses of up to 1000 mg/kg. An increased incidence of mammary adenocarcinomas and haemangiosarcomas was observed with a no-effect dose of 500 mg/kg (59-fold human exposure) and 100 mg/kg (16-fold human exposure), respectively. The increased incidence of these tumours in mice is considered not to represent a significant risk to humans based on the lack of genotoxicity of vildagliptin and its principal metabolite, the occurrence of tumours only in one species, and the high systemic exposure ratios at which tumours were observed.

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. Skin lesions were not reversible in the monkeys treated at 160 mg/kg/day during a 4-week recovery period.

Metformin Hydrochloride
Non-clinical data on metformin reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction.

14 Pharmaceutical information

Incompatibilities

Not applicable.

Special precautions for storage

Do not store above 30°C, store in the original package in order to protect from moisture.

Galvusmet must be kept out of the reach and sight of children.

Nature and contents of container

Alu/Alu strip packs.

Instructions for use and handling, and disposal

No special requirements.

Package
Box, 3 strip @ 10 film-coated tablets

Galvusmet 50/500 mg film-coated tablets	Reg. No. DKL1930413117A1
Galvusmet 50/850 mg film-coated tablets	Reg. No. DKL1930413117B1

HARUS DENGAN RESEP DOKTER

To be dispensed only on the prescription of a physician.

Manufactured by Novartis Pharma Produktions GmbH, Wehr, Germany for Novartis Pharma AG, Basel, Switzerland.

Packaged and imported by PT Novartis Indonesia, Jakarta, Indonesia.

Product Information based on CDS v4.3 18-Jun-2025

GALVUSMET®

(kombinasi dosis tetap vildagliptin dan metformin HCl)

Tablet salut selaput 50 mg/500 mg, 50 mg/850 mg

Informasi Produk untuk Pasien

DISETUJUI OLEH BPOM: 16/12/2025 ID REG: EREG10000512500259 - EREG10000512500260

Bacalah brosur ini dengan saksama sebelum Anda mengonsumsi Galvusmet

Mohon simpan brosur ini. Anda mungkin akan membutuhkan brosur ini untuk dibaca kembali.

Apabila Anda memiliki pertanyaan lebih lanjut, mohon hubungi dokter, apoteker atau tenaga kesehatan Anda.

Obat ini diresepkan untuk Anda. Mohon jangan berikan obat ini kepada orang lain. Obat ini mungkin dapat membahayakan, meskipun mereka memiliki gejala penyakit yang serupa dengan Anda. Jangan menggunakan obat ini untuk mengobati penyakit lain.

Jika Anda mengalami efek samping yang serius, atau jika anda mengalami efek samping yang tidak tertera pada brosur ini, mohon informasikan kepada dokter, apoteker atau tenaga kesehatan Anda.

Daftar isi

1 Apa itu Galvusmet dan apa kegunaannya

Apa itu Galvusmet

Galvusmet tersedia dalam bentuk tablet. Tiap tabletnya, Galvusmet mengandung 2 zat aktif: *vildagliptin* dan *metformin hydrochloride*. Kedua zat tersebut tergolong dalam obat antidiabetes oral.

Galvusmet tersedia dalam 2 kekuatan (*vildagliptin*/*metformin hydrochloride*) 50 mg/500 mg dan 50 mg/850 mg.

Apa kegunaan Galvusmet

Galvusmet merupakan obat yang digunakan dalam pengobatan diabetes tipe 2. Obat ini membantu mengontrol kadar gula dalam darah. Obat ini diresepkan sebagai tambahan dari diet dan olahraga pada pasien diabetes yang tidak cukup terkontrol dengan pengobatan bentuk tunggal dari *metformin hydrochloride* atau *vildagliptin;* atau pada pasien-pasien yang sebelumnya telah menerima pengobatan *vildagliptin* dan *metformin hydrochloride* secara terpisah.

Galvusmet juga diresepkan sebagai kombinasi dengan insulin, ditambah diet dan olahraga, pada pasien yang masih mengalami kontrol glikemik yang kurang baik ketika sudah diberikan dosis insulin dan metformin (yang dapat ditoleransi) secara maksimal.

Bagaimana cara kerja Galvusmet

Diabetes tipe 2 terjadi apabila tubuh kita tidak dapat memproduksi insulin yang cukup atau insulin yang diproduksi oleh tubuh kita 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 memicu proses produksi gula oleh hati, yang kemudian akan menyebabkan kenaikan kadar gula dalam darah. Pankreas merupakan organ yang memproduksi kedua zat tersebut.

Galvusmet bekerja dengan membuat pankreas memproduksi lebih banyak insulin dan lebih sedikit glukagon (efek dari *vildagliptin*) dan juga membantu tubuh bekerja lebih baik dalam penggunaan insulin yang telah diproduksi oleh tubuh (efek dari *metformin hydrochloride*). Galvusmet membantu mengontrol kadar gula dalam darah.

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

Apabila Anda masih memiliki pertanyaan terkait mengapa obat ini diresepkan untuk Anda, silakan tanyakan kepada dokter Anda.

2 Apa yang perlu Anda ketahui sebelum dan selama mengonsumsi Galvusmet

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

Jangan mengonsumsi Galvusmet

- Apabila Anda alergi (hipersensitif) terhadap *vildagliptin*, *metformin hydrochloride* atau terhadap kandungan zat lain yang terdapat pada Galvusmet (tercantum pada bagian 6 Informasi lain).

Jika Anda merasa bahwa Anda mungkin alergi, mintalah nasihat dokter Anda.

- Apabila Anda mengalami penurunan fungsi ginjal yang berat (berdasarkan pada keputusan dokter Anda).
- Apabila Anda baru saja terkena serangan jantung, gagal jantung, atau apabila Anda memiliki masalah serius dengan sirkulasi darah, termasuk syok, atau kesulitan bernapas.
- Apabila Anda pernah atau masih mengalami komplikasi serius pada penyakit diabetes Anda, seperti diabetes ketoasidosis (merupakan komplikasi diabetes termasuk turunnya berat badan secara drastis, mual atau muntah) atau koma diabetes.

Apabila Anda mengalami hal-hal diatas, jangan mengonsumsi Galvusmet dan hubungi dokter Anda.

Perhatian khusus saat mengonsumsi Galvusmet

Apabila Anda mengalami hal-hal berikut, hubungi dokter, apoteker atau tenaga kesehatan Anda sebelum mengonsumsi Galvusmet.

- Galvusmet bukanlah pengganti insulin. Anda seharusnya tidak mengonsumsi Galvusmet sebagai pengobatan diabetes tipe 1 (contohnya jika tubuh Anda tidak memproduksi insulin sama sekali) atau untuk pengobatan diabetes ketoasidosis.
- Apabila Anda akan menjalani operasi dengan anastesi total, Anda harus berhenti mengonsumsi Galvusmet untuk beberapa hari sebelum dan sesudah menjalani operasi. Dokter Anda akan memutuskan kapan Anda harus menghentikan dan kapan Anda dapat memulai kembali pengobatan Anda dengan Galvusmet.
- Apabila Anda akan menjalani prosedur sinar X kontras (tipe spesifik sinar X yang melibatkan tinta yang diinjeksikan ke dalam tubuh), Anda harus menghentikan penggunaan Galvusmet sebelum atau pada saat menjalani prosedur tersebut dan beberapa hari setelahnya.
- Apabila Anda mengonsumsi obat apapun yang digunakan untuk mengobati angina/nyeri dada, infeksi HIV, atau kanker tiroid (tipe meduler).
- Apabila Anda mengonsumsi alkohol secara berlebihan, baik setiap hari atau hanya dalam periode waktu tertentu saja.
- Apabila Anda memiliki masalah dengan hati atau ginjal.
- Apabila Anda diketahui menderita penyakit bawaan genetik yang memengaruhi mitokondria (komponen penghasil energi dalam sel), seperti sindrom MELAS (*Mitochondrial Encephalopathy, Myopathy, Lactic Acidosis, and Stroke-like episodes*) atau diabetes dan gangguan pendengaran yang diwariskan secara maternal (MIDD).

Apabila Anda mengalami hal-hal berikut saat menjalani pengobatan dengan Galvusmet, segera hubungi dokter, apoteker atau tenaga kesehatan Anda.

- Apabila Anda mengalami salah satu atau lebih gejala berikut ini: demam dan tidak enak badan, nyeri otot, mengantuk, mual atau muntah yang berat, nyeri perut, pusing, detak jantung yang tidak beraturan, atau napas pendek. Asidosis laktat (kondisi dimana terlalu banyak kandungan asam laktat dalam darah) merupakan kejadian yang sangat jarang terjadi pada pasien yang mengonsumsi metformin (salah satu zat aktif Galvusmet). Kejadian ini sangat mungkin terjadi pada pasien dimana organ ginjalnya tidak berkerja dengan baik.
- Apabila Anda mengalami satu atau lebih gejala dari sindrom MELAS dan MIDD berikut ini: kejang, penurunan kemampuan kognitif, kesulitan dalam pergerakan tubuh, gejala yang menunjukkan kerusakan saraf (misalnya nyeri atau mati rasa), migrain, dan gangguan pendengaran.
- Apabila Anda mengalami mual, berkeringat, lemah, pusing, gemetar, sakit kepala (tanda-tanda rendahnya kadar gula darah), yang dapat juga disebabkan oleh kekurangan asupan makanan, olahraga terlalu berat yang tidak diimbangi dengan asupan makanan yang cukup,

atau asupan alkohol yang berlebih (biasanya tidak terjadi pada pengobatan dengan Galvusmet saja).
- Apabila penyakit diabetes Anda memburuk secara tiba-tiba, atau apabila Anda memiliki hasil uji kadar gula yang tidak normal atau merasa tidak sehat, hubungi dokter Anda.

Pemantauan selama pengobatan dengan Galvusmet

Dokter Anda sebaiknya memastikan pemeriksaan di bawah ini telah dilakukan:
- Kadar gula dalam darah dan urin secara teratur
- Pemeriksaan fungsi ginjal:
  - pada saat awal pengobatan
  - setidaknya sekali dalam setahun ketika Anda masih dalam pengobatan
  - lebih sering apabila Anda merupakan pasien usia lanjut atau apabila fungsi ginjal Anda mulai mengalami penurunan
- 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 Galvusmet dikarenakan adanya masalah hati, Anda sebaiknya tidak mengonsumsi Galvusmet lagi.
- Tes darah secara keseluruhan setidaknya sekali dalam setahun
- Pemeriksaan kadar vitamin B12 dapat juga dilakukan setidaknya setiap 2-3 tahun

Pasien anak-anak dan remaja (dibawah usia 18 tahun)

Tidak ada informasi yang tersedia untuk penggunaan Galvusmet pada anak-anak dan remaja (dibawah usia 18 tahun). Penggunaan Galvusmet pada pasien ini tidak direkomendasikan.

Pasien usia lanjut (usia 65 tahun keatas)

Dokter Anda akan memeriksa kinerja ginjal Anda. Anda mungkin memerlukan pemeriksaan yang lebih sering apabila Anda memiliki masalah dengan ginjal.

Penggunaan obat lain

Sebelum mengonsumsi Galvusmet, informasikan kepada dokter atau apoteker atau tenaga kesehatan Anda apabila Anda sedang atau baru saja mengonsumsi obat-obatan lainnya, termasuk obat-obat tanpa resep dokter.

Secara khusus, hal tersebut mencakup antara lain obat-obat sebagai berikut:
- obat-obatan tertentu untuk pengobatan inflamasi (contohnya kortikosteroid)
- obat-obatan tertentu untuk pengobatan tekanan darah tinggi (contohnya *nifedipine*, *enalapril, losartan, diuretics*)
- obat-obatan tertentu untuk mengurangi nyeri (contohnya *diclofenac*)
- obat-obatan tertentu untuk mengobati angina/nyeri dada (contohnya *ranolazine*)

- obat-obatan tertentu untuk mengobati infeksi HIV (contohnya *dolutegravir*)
- obat-obatan tertentu untuk mengobati kanker tiroid tertentu (tipe meduler) (contohnya *vandetanib*)
- obat-obatan tertentu untuk pengobatan gangguan perut (contohnya *cimetidine*)
- obat-obatan tertentu untuk pengobatan pada gangguan psikiatrik (contohnya *phenothiazine*)
- obat-obatan tertentu untuk pengobatan gangguan tiroid
- kontrasepsi oral, obat-obatan tertentu untuk mengurangi gejala pada wanita menopause atau osteoporosis (contohnya *estrogen*)

Apabila Anda membutuhkan injeksi media kontras yang mengandung *iodine* ke dalam aliran darah Anda, seperti contohnya prosedur *X-ray* atau *scan*, Anda harus menghentikan penggunaan Galvusmet sebelum atau pada saat pemberian injeksi. Dokter Anda akan menentukan kapan Anda harus berhenti dan kapan Anda harus memulai kembali pengobatan Anda menggunakan Galvusmet.

Anda tidak diperbolehkan mengonsumsi alkohol berlebihan atau mengonsumsi obat-obatan yang mengandung alkohol ketika mengonsumsi Galvusmet.

Tanyakan kepada dokter atau apoteker Anda jika Anda tidak yakin apakah obat-obat lain yang Anda konsumsi termasuk kedalam jenis obat yang disebutkan diatas.

Penggunaan Galvusmet bersama makanan dan minuman

Anda direkomendasikan untuk mengonsumsi tablet bersamaan dengan atau setelah makan. Hal ini akan mengurangi kemungkinan bahwa Anda akan mengalami gangguan perut.

Wanita hamil dan menyusui

Informasikan kepada dokter Anda jika Anda sedang hamil, berpikir bahwa Anda mungkin hamil atau sedang merencanakan kehamilan. Dokter Anda akan berdiskusi dengan Anda mengenai potensi risiko jika Anda menggunakan Galvusmet selama kehamilan.

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

Jangan menyusui selama menjalani pengobatan dengan Galvusmet.

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

Mengemudi dan menggunakan mesin

Apabila Anda merasa pusing ketika mengonsumsi Galvusmet, jangan mengemudikan kendaraan atau menggunakan alat atau mesin sampai Anda dalam kondisi normal kembali.

3 Bagaimana cara mengonsumsi Galvusmet

Ikuti semua instruksi yang diberikan oleh dokter atau apoteker Anda dengan saksama. Cek kembali dengan dokter atau apoteker atau tenaga kesehatan apabila Anda tidak yakin dengan instruksinya.

Anda tidak diperbolehkan mengonsumsi Galvusmet lebih dari yang diresepkan dokter Anda.

Berapa banyak Galvusmet yang perlu Anda konsumsi

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

Dosis yang umum digunakan untuk Galvusmet adalah 1 atau 2 tablet per hari. Jangan mengonsumsi lebih dari 2 tablet sehari.

Dokter Anda dapat menyarankan dosis yang lebih tinggi atau lebih rendah tergantung bagaimana respon Anda terhadap pengobatan.

Apabila Anda mengalami penurunan fungsi ginjal, dokter Anda akan meresepkan obat ini dengan dosis yang lebih rendah. Dokter Anda akan melakukan hal yang sama apabila Anda mengonsumsi obat anti diabetes yang dikenal dengan *sulphonylurea*.

Dokter Anda dapat meresepkan Galvusmet saja atau dikombinasikan dengan obat anti diabetes lainnya, tergantung dari kondisi Anda.

Bagaimana dan kapan Anda mengonsumsi Galvusmet

Galvusmet sebaiknya dikonsumsi pada pagi dan/atau malam hari. Anda direkomendasikan untuk mengonsumsi Galvusmet bersamaan dengan atau setelah makan. Hal ini akan mengurangi kemungkinan Anda mengalami gangguan perut.

Tablet Galvusmet harus ditelan secara utuh bersama dengan segelas air.

Berapa lama Anda mengonsumsi Galvusmet

Tetap konsumsi Galvusmet setiap hari selama dokter Anda masih menyarankan penggunaannya. Anda mungkin perlu melanjutkan pengobatan ini untuk periode waktu yang panjang. Dokter Anda akan memantau kondisi Anda secara teratur untuk memastikan efek pengobatan yang diharapkan.

Apabila dokter meminta Anda untuk menghentikan pengobatan Galvusmet dikarenakan adanya masalah pada organ hati, Anda sebaiknya tidak menggunakan Galvusmet lagi.

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

Apabila Anda mengonsumsi Galvusmet lebih dari yang seharusnya

Apabila Anda tidak sengaja mengonsumsi Galvusmet 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.

Apabila Anda lupa mengonsumsi Galvusmet

Anda direkomendasikan untuk mengonsumsi Galvusmet pada waktu yang sama setiap harinya. Apabila Anda lupa mengonsumsi Galvusmet, mohon konsumsi dosis yang terlewat sesegera mungkin saat Anda ingat. Kemudian konsumsi dosis berikutnya sesuai jadwal seperti biasa. Namun, apabila jadwal minum obat yang terlewat sudah terlalu dekat dengan jadwal berikutnya, lanjutkan dengan dosis selanjutnya saja. Jangan meminum dosis ganda untuk menutupi dosis yang telah Anda lewatkan.

4 Efek samping yang mungkin terjadi

Seperti obat-obatan lain, Galvusmet dapat menimbulkan efek samping walaupun tidak semua orang mengalaminya.

Beberapa pasien dapat mengalami efek samping berikut ketika mengonsumsi Galvusmet.

Beberapa efek samping yang mungkin serius

Anda sebaiknya **berhenti mengonsumsi Galvusmet dan carilah pertolongan medis segera** apabila Anda mengalami gejala berikut ini:

- Demam dan tidak enak badan, nyeri otot, mengantuk, mual atau muntah berat, nyeri perut bagian atas, berat badan turun, pusing, detak jantung yang tidak beraturan, atau napas pendek (gejala asidosis laktat). Apabila hal ini terjadi, Anda **harus berhenti mengonsumsi Galvusmet dan segera hubungi dokter atau kunjungi rumah sakit terdekat**, karena asidosis laktat dapat menyebabkan koma.
- Pembengkakan pada wajah, lidah atau tenggorokan, kesulitan menelan, kesulitan bernapas, tiba-tiba timbul ruam atau gatal-gatal (gejala reaksi alergi berat 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’).

Apabila Anda mengalami efek samping yang serius, **berhenti mengonsumsi Galvusmet dan segera hubungi dokter Anda.**

Beberapa efek samping yang sangat umum terjadi *(terjadi pada > 1 dari 10 pasien)*

- Mual, muntah, diare, nyeri perut, kehilangan nafsu makan.

Beberapa efek samping yang umum terjadi *(terjadi pada < 1 dari 10 pasien)*

- Pusing, sakit kepala, gemetar, adanya rasa seperti logam (metal) di mulut.

Beberapa efek samping yang tidak umum terjadi *(terjadi pada < 1 dari 100 pasien)*

- Konstipasi, pembengkakan pada tangan, kaki atau pergelangan kaki (edema).

Beberapa efek samping yang sangat tidak umum terjadi *(terjadi pada < 1 dari 10.000 pasien)*

- Kulit kemerahan, gatal, penurunan kadar vitamin B12 dalam darah, hasil tes yang menunjukkan adanya gangguan fungsi hati.

Apabila Anda mengalami efek samping seperti diatas yang serius, **berhenti mengonsumsi Galvusmet dan segera hubungi dokter Anda.**

Efek samping lainnya

Efek samping yang umum terjadi (terjadi pada < 1 dari 10 pasien).
Efek samping yang tidak umum terjadi (terjadi pada < 1 dari 100 pasien).

Beberapa pasien pernah mengalami efek samping berikut ini **ketika mengonsumsi Galvusmet dan insulin:**

- Umum terjadi: Sakit kepala, menggigil, mual, rasa panas pada dada, penurunan gula darah.
- Tidak umum terjadi: Diare, perut kembung.

Beberapa pasien pernah mengalami efek samping berikut ini **ketika mengonsumsi Galvusmet dan sulfonylurea:**

- Umum terjadi: Pusing, gemetar, lemah, produksi keringat berlebih.

Beberapa pasien pernah mengalami efek samping lainnya **ketika mengonsumsi Galvusmet saja atau dikombinasikan dengan obat-obatan antidiabetes lainnya:**

- Ruam yang juga menimbulkan rasa gatal, timbulnya area kulit yang terkelupas atau melepuh, nyeri sendi, radang kantong empedu.

Apabila Anda mengalami salah satu efek seperti diatas yang serius, **hubungi dokter Anda.**

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

Pelaporan efek samping

Apabila ada keluhan efek samping atau kondisi tidak nyaman selama dan setelah penggunaan obat, konsultasikan ke dokter, apoteker, atau perawat. Anda dapat juga melaporkan keluhan efek samping atau kondisi tidak nyaman tersebut secara langsung ke Industri Farmasi melalui kontak berikut:

Novartis Indonesia
Website: www.novartis.com/report

Dengan melaporkan efek samping, Anda dapat membantu memberikan informasi lebih lanjut mengenai keamanan obat ini.

5 Cara penyimpanan Galvusmet

- Jauhkan obat dari jangkauan dan penglihatan anak-anak.
- Jangan menggunakan obat setelah tanggal kedaluwarsa yang tercantum pada kemasan obat.
- Simpan obat di dalam kemasannya.
- Jangan menggunakan Galvusmet jika kemasannya rusak atau menunjukkan adanya cacat.
- Simpan pada suhu tidak lebih dari 30°C.

6 Informasi lain

Kandungan Galvusmet

Tiap tablet Galvusmet mengandung 2 zat aktif: vildagliptin dan *metformin hydrochloride*.

Kekuatan yang tersedia:

- Satu tablet mengandung 50 mg vildagliptin dan 500 mg *metformin hydrochloride*.
- Satu tablet mengandung 50 mg vildagliptin dan 850 mg *metformin hydrochloride*.

Komposisi lain (zat tambahan/eksipien) Galvusmet:

hydroxypropyl cellulose, hypromellose, ironoxide yellow, iron oxide red, macrogol, magnesium stearate, talc and titanium dioxide.

Bagaimana bentuk dari Galvusmet

Galvusmet dijual dalam bentuk tablet. Berikut deskripsi fisik Galvusmet tablet:

- Galvusmet 50 mg/500 mg: berwarna kuning terang, berbentuk oval bertepi miring, tablet salut selaput yang dicetak dengan "NVR" pada salah satu sisi dan "LLO" pada sisi lainnya.
- Galvusmet 50 mg/850 mg: berwarna kuning, berbentuk oval bertepi miring, tablet salut selaput yang dicetak dengan "NVR" pada salah satu sisi dan "SEH" pada sisi lainnya.

Kemasan

Dus, 3 strip @ 10 tablet salut selaput

Galvusmet 50/500 mg tablet salut selaput	No. Reg. DKL1930413117A1
Galvusmet 50/850 mg tablet salut selaput	No. Reg. DKL1930413117B1

HARUS DENGAN RESEP DOKTER

Pemegang Nomor Ijin Edar

PT Novartis Indonesia

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

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