Galvecta® Plus

(Vildagliptin + Metformin HCl)

گیلویکٹا پلس

COMPOSITION

Galvecta Plus 50/500 mg Tablet
Each film coated tablet contains:
Vildagliptin.....50mg
Metformin HCl...500mg
(Manufacturer's Specs.)

Galvecta Plus 50/850 mg Tablet
Each film coated tablet contains:
Vildagliptin.....50mg
Metformin HCl...850mg
(Manufacturer's Specs.)

Galvecta Plus 50/1000 mg Tablet
Each film coated tablet contains:
Vildagliptin.....50mg
Metformin HCl...1000mg
(Manufacturer's Specs.)

Life threatening lactic acidosis can occur due to accumulation of metformin. The main risk factor is renal impairment; other risk factors include old age associated with reduced renal function, sepsis, hepatic insufficiency, acute congestive heart failure and high doses of metformin above 2 g per day. Discontinue metformin containing products, if acidosis is suspected.

DESCRIPTION

Galvecta Plus is a combination of Vildagliptin and Metformin hydrochloride.

Vildagliptin belongs to dipeptidyl peptidase-4 (DPP-4) inhibitor class of drugs. The designated chemical name of Vildagliptin is (S)-1-[2-(3-Hydroxy-adamantan- 1-ylamino)acetyl]-pyrrolidine- 2(S)-carbonitrile and it has a molecular formula of $C_{17}H_{25}N_3O_2$

Metformin belongs to Biguanide class of drugs. The designated chemical name of Metformin hydrochloride is Imidodicarbinimidic, N,N-dimethyl-, monohydrochloride and it has a molecular formula of $C_4H_{11}N_5.HCl$

The combination product is used as an oral hypoglycemic in Type II diabetes mellitus.

CLINICAL PHARMACOLOGY

Mechanism of Action
Galvecta Plus combines two antihyperglycaemic agents with different mechanisms of action to improve glycemic control in patients with Type II diabetes: vildagliptin, a member of the DPP-4 (dipeptidyl-peptidase-4) inhibitor class and metformin hydrochloride, a member of the Biguanide class.

Pharmacodynamics

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 (glucagon-like peptide 1) and GIP (glucose-dependent insulinotropic polypeptide). 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. 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 insulin/glucagon ratio during hyperglycemia due to increased incretin hormone levels results in a decrease in fasting and postprandial hepatic glucose production, leading to improved glycemic control.

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.

Metformin may act via 3 mechanisms,

- Reduction of hepatic glucose production by inhibiting gluconeogenesis and glycogenolysis.
- Effects in muscle, by increasing insulin sensitivity, improving peripheral glucose uptake and utilization.
- Delaying of intestinal glucose absorption.

Metformin stimulates intracellular glycogen synthesis by acting on glycogen synthase. Metformin increases the transport capacity of all types of membrane glucose transporters (GLUTs) known to date.

Pharmacokinetics

Absorption

Vildagliptin

Following oral administration in the fasting state, vildagliptin is rapidly absorbed with peak plasma concentrations observed at 1.75 hours. Co-administration 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).

Metformin Hydrochloride

The absolute bioavailability of a 500 mg metformin hydrochloride oral formulation given under fasting conditions is approximately 50 to 60%. Food decreases the extent of and slightly delays the absorption of metformin hydrochloride, as shown by approximately a 40% lower mean peak plasma concentration (Cmax), a 25% lower area under the plasma concentration versus time curve, and a 35 minute prolongation of time to peak plasma concentration (Tmax) following administration of a single 850 mg tablet of metformin hydrochloride with food, compared to the same tablet strength administered with fasting.

Combination Product

Food does not affect the extent and rate of absorption of Vildagliptin from the combination product Galvecta Plus. The Cmax and AUC of the metformin hydrochloride component from the combination product are decreased by 26% and 7% respectively when given with food. The absorption of metformin hydrochloride was also delayed as reflected by the Tmax (2.0 to 4.0 hrs) when given with food. These changes in Cmax and AUC are consistent but lower than those observed when metformin hydrochloride when given alone under fed conditions. The effects of food on the pharmacokinetics of both the vildagliptin component and metformin hydrochloride component of Galvecta Plus are similar to the pharmacokinetics of vildagliptin and metformin hydrochloride when given alone with food.

Distribution

Vildagliptin

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 L, suggesting extravascular distribution.

Metformin Hydrochloride

The apparent volume of distribution (V/F) of metformin hydrochloride following single oral doses of 850 are about 654 ± 358 L. Metformin hydrochloride is negligibly bound to plasma proteins. Metformin hydrochloride partitions into erythrocytes, most likely as a function of time. At usual clinical doses and dosing schedules of metformin hydrochloride, steady state plasma concentrations of metformin hydrochloride are reached within 24 to 48 hours and are generally < 1 microgram/mL.

Metabolism

Vildagliptin

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). 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.

Metformin Hydrochloride

Metformin is excreted unchanged in the urine and does not undergo hepatic metabolism. In patients with significantly decreased renal function, the plasma half-life of metformin is prolonged and renal clearance is decreased.

Elimination

Vildagliptin

Following oral administration of [14C]-vildagliptin, approximately 85% of the dose is excreted into the urine and 15% of the dose is recovered in the faeces. Renal excretion of the unchanged vildagliptin accounts for 23% of the dose after oral administration. After an intravenous administration to healthy subjects, the total plasma and renal clearances of vildagliptin are 41 L/hour and 13 L/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 dose.

Metformin Hydrochloride

Metformin hydrochloride is excreted unchanged in the urine and does not undergo hepatic metabolism (no metabolites have been identified in humans) or biliary excretion. Renal clearance is approximately 3.5 times greater than creatinine clearance, which indicates that tubular secretion is the major route of elimination. Following oral administration, approximately 90% of the absorbed drug is eliminated via the renal route within the first 24 hours, with a plasma elimination half-life of approximately 6.2 hours. In blood, the elimination half-life is approximately 17.6 hours, suggesting that the erythrocyte mass may be a compartment of distribution.

INDICATIONS

GALVECTA PLUS (Vildagliptin, Metformin Hydrochloride) is indicated for the treatment of patients with Type II diabetes mellitus.

- GALVECTA PLUS (Vildagliptin, Metformin Hydrochloride) is indicated as an adjunct to diet and exercise to improve glycaemic control in patients whose diabetes is not adequately controlled on metformin hydrochloride alone or who are already treated with the combination of vildagliptin and metformin hydrochloride, as separate formulations. Treatment should not be initiated with this fixed-dose combination.

- GALVECTA PLUS (Vildagliptin, Metformin Hydrochloride) is indicated in combination with a sulfonylurea (i.e. triple combination therapy) as an adjunct to diet and exercise in patients inadequately controlled with metformin and a sulfonylurea.

- GALVECTA PLUS (Vildagliptin, Metformin Hydrochloride) is indicated as add-on to insulin as an adjunct to diet and exercise to improve glycemic control in patients when stable dose of insulin and metformin do not provide adequate glycemic control.

DOSAGE AND ADMINISTRATION

The dose of anti-hyperglycaemic therapy with Galvecta Plus should be individualised on the basis of the patient's current regimen, effectiveness and tolerability while not exceeding the maximum recommended daily dose of 100 mg vildagliptin. Based on the patient's current dose of metformin, Galvecta Plus maybe initiated at either the 50mg/500mg or 50mg/850mg or 50 mg/1000mg tablet strength twice daily, one tablet in the morning and the other in the evening. The recommended daily dose is 100mg vildagliptin plus 2000mg metformin hydrochloride.

For patients inadequately controlled at their maximal tolerated dose of metformin monotherapy:

The starting dose of Galvecta Plus should provide vildagliptin as 50 mg twice daily (100 mg total daily dose) plus the dose of metformin already being taken.

For patients switching from co-administration of vildagliptin and metformin as separate tablets:

Galvecta Plus should be initiated at the dose of vildagliptin and metformin already being taken.

For patients inadequately controlled on dual combination with metformin and a sulphonylurea:

The doses of Galvecta Plus should provide vildagliptin as 50 mg twice daily (100 mg total daily dose) and a dose of metformin similar to the dose already being taken. When Galvecta Plus is used in combination with a sulphonylurea, a lower dose of the sulphonylurea may be considered to reduce the risk of hypoglycaemia.

For patients inadequately controlled on dual combination therapy with insulin and the maximal tolerated dose of metformin:

The dose of Galvecta Plus 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.

Dosing considerations in special populations

Elderly (≥ 65 years)
As metformin is excreted via the kidney, and elderly patients have a tendency to decreased renal function, elderly patients taking Vildagliptin, Metformin Hydrochloride should have their renal function monitored regularly.

Renal impairment
Galvecta Plus must not be used in patients with creatinine clearance < 60 ml/min.

Hepatic impairment
Galvecta Plus 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).

Administration Requirements
Galvecta Plus (Vildagliptin, Metformin Hydrochloride) should be taken orally. Taking Vildagliptin/ Metformin Hydrochloride with or just after food helps reduce gastrointestinal symptoms associated with metformin.

CONTRAINDICATIONS

Galvecta Plus should not be administered to breast-feeding women.

Hypersensitivity

Vildagliptin/ Metformin Hydrochloride is contraindicated in patients with known hypersensitivity to vildagliptin or metformin hydrochloride

Renal Disease
Vildagliptin/ Metformin Hydrochloride is contraindicated in patients with renal disease or renal dysfunction defined as creatinine clearance < 60 ml/min or in acute conditions with the potential to alter renal function such as severe dehydration, severe infection, shock or intravascular administration of iodinated contrast agents.

Diseases causing tissue hypoxia
Vildagliptin/ Metformin Hydrochloride is contraindicated in patients with acute or chronic disease which may cause tissue hypoxia such as congestive heart failure, respiratory failure, recent myocardial infarction, shock (due to potential risk of acidosis with its metformin component).

Ketoacidosis / Diabetic pre-coma
Vildagliptin/ Metformin Hydrochloride combination is contraindicated in patients with acute or chronic metabolic acidosis, including diabetic ketoacidosis, with or without coma due to its metformin component. Diabetic ketoacidosis should be treated with insulin.

Hepatic Insufficiency and alcoholism
GALVECTA PLUS is contraindicated in Hepatic insufficiency, acute alcohol intoxication and alcoholism

WARNINGS AND PRECAUTIONS

Joint pain, severe and persistent, has been reported with dipeptidyl peptidase-4 (DPP-4) inhibitors with onset occurring from 1 day to years after initiation; may require discontinuation, and symptoms may reoccur when rechallenged with same drug or with another DPP-4 inhibitor.

General
Galvecta Plus is not a substitute for insulin in insulin-requiring patients. Vildagliptin/ Metformin Hydrochloride should not be used in patients with Type I diabetes or for the treatment of diabetic ketoacidosis.

Renal Impairment
Galvecta Plus should not be used in patients with renal failure or renal dysfunction with creatinine clearance < 60 ml/min. (see CONTRAINDICATIONS) Metformin hydrochloride is known to be substantially excreted by the kidney and the risk of metformin hydrochloride accumulation and lactic acidosis increases with the degree of renal function impairment. Renal function should be monitored at start of therapy and periodically thereafter.

Hepatic Impairment and Alcoholism
Galvecta Plus is not recommended in patients with clinical or laboratory evidence of hepatic impairment, including patients with a pre-treatment ALT or AST >3 times the upper limit of normal due to its vildagliptin component.
Since impaired hepatic function has been associated with some cases of lactic acidosis (a risk associated with metformin hydrochloride), Vildagliptin/ Metformin Hydrochloride should not be used in patients with clinical or laboratory evidence of hepatic disease as well as in acute alcohol intoxication and alcoholism. (See CONTRAINDICATIONS)

Liver Enzyme Monitoring
Rare cases of hepatic dysfunction (including hepatitis) have been reported with vildagliptin. 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 Vildagliptin/ Metformin Hydrochloride. LFTs should be monitored during Vildagliptin/ Metformin Hydrochloride treatment at three-month intervals during the first year and periodically thereafter. If an increase in AST or ALT of 3 X upper limit of normal or greater is observed at start of treatment, therapy should not be initiated and if observed during therapy, withdrawal of therapy with Vildagliptin/ Metformin Hydrochloride is recommended. Patients who develop jaundice or other signs suggestive of liver dysfunction should discontinue Vildagliptin/ Metformin Hydrochloride. Following withdrawal of treatment with Vildagliptin/ Metformin Hydrochloride and LFT normalization, Vildagliptin/ Metformin Hydrochloride should not be reinitiated.

Lactic Acidosis
Lactic acidosis is a very rare but serious metabolic complication that can occur due to metformin accumulation. Reported cases of lactic acidosis in patients on metformin have occurred primarily in diabetic patients with significant renal failure. The incidence of lactic acidosis can and should be reduced by also assessing other associated risk factors, such as poorly controlled diabetes, ketosis, prolonged fasting, excessive alcohol intake,

hepatic insufficiency and any conditions associated with hypoxia (see CONTRAINDICATIONS). If metabolic acidosis is suspected in any patient, drug product should be discontinued and the patient hospitalized immediately.

Skin disorders
Monitoring should be required for skin disorders, such as blistering or ulceration in routine care of diabetic patients prescribed vildagliptin containing products. There have been post-marketing reports of bullous and exfoliative skin lesions.

Acute pancreatitis
Use of vildagliptin containing products has been associated with a risk of developing acute pancreatitis. Patients should be informed of the risks. If pancreatitis is suspected, vildagliptin should be discontinued; if acute pancreatitis is confirmed, vildagliptin should not be restarted. Caution should be exercised in patients with a history of acute pancreatitis.

Hypoglycemia
Sulphonylureas are known to cause hypoglycemia. Patients receiving vildagliptin containing products in combination with a sulphonylurea may be at risk for hypoglycemia. Therefore, a lower dose of sulphonylurea may be considered to reduce the risk of hypoglycemia.

Administration of Intravascular Iodinated Contrast Materials
Galvecta Plus should be temporarily discontinued in patients undergoing radiologic tests involving intravascular administration of iodinated contrast materials, because such products may result in acute alteration of renal function and increase the risk of lactic acidosis due to possible metformin accumulation. In patients undergoing such tests , Vildagliptin/ Metformin Hydrochloride should be temporarily discontinued at the time of or prior to the procedure, withheld for 48 hours subsequent to the procedure and reinstituted only after renal function has been re-evaluated and found to be normal.

Hypoxic States
Cardiovascular collapse (shock), acute congestive heart failure, acute myocardial infarction and other conditions characterized by hypoxemia have been associated with severe lactic acidosis in patients taking metformin containing products such as Galvecta Plus. Pre-renal azotemia commonly occurs in these patients. Vildagliptin/Metformin is not recommended for such patients. (See CONTRAINDICATIONS)

Surgical Procedures
Due to its metformin component, use of Galvecta Plus should be temporarily suspended for any surgical procedure (except minor procedures not associated with restricted intake of food and fluids) and should not be restarted until the patient's oral intake has resumed and renal function has been evaluated as normal. Galvecta Plus should be discontinued 48 hours before elective surgery with general anesthesia and should not usually be resumed earlier than 48 hours afterwards.

Vitamin B12 Levels
The metformin component of Galvecta Plus has been associated with a decrease in serum vitamin B12. Such decrease is very rarely associated with anemia or any clinical effects and appears to be rapidly reversible with discontinuation of metformin hydrochloride and/or vitamin B12 supplementation. Measurement of hematological parameters on at least an annual basis is advised for patients receiving Vildagliptin/ Metformin Hydrochloride. Certain individuals (e.g., those with inadequate vitamin B12 or calcium intake or absorption) appear to be predisposed to developing subnormal vitamin B12 levels. In these patients, routine serum vitamin B12 measurements at minimally two-to-three-year intervals may be useful.

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 are prone to dizziness should avoid driving vehicles or using machines.

ADVERSE REACTIONS:

Adverse reactions reported in patients who received Vildagliptin and metformin in **clinical studies** as dual therapy or as triple add-on therapies are listed below:

Vildagliptin with metformin
Metabolism and nutrition disorders
Common Hypoglycaemia
Nervous system disorders
Common Tremor , Headache, Dizziness
Uncommon Fatigue
Gastrointestinal disorders
Common Nausea

Vildagliptin with metformin and sulfonylurea
Metabolism and nutritional disorders
Common Hypoglycaemia
Nervous system disorders
Common Dizziness, tremor
Skin and subcutaneous tissue disorders
Common Hyperhidrosis
General disorders and administration site conditions
Common Asthenia

Vildagliptin with insulin (with/without) metformin
Metabolism and nutrition disorders
Common Decreased blood glucose
Nervous system disorders
Common Headache, chills
Gastrointestinal disorders
Common Nausea, gastro-oesophageal reflux disease
Uncommon Diarrhoea, flatulence

Post-marketing adverse reactions reported with the combination product Vildagliptin/metformin are listed below:

Vildagliptin with metformin
Gastrointestinal disorders
Not known Pancreatitis
Hepatobiliary disorders
Not known Hepatitis (reversible), abnormal liver function tests
Musculoskeletal disorders
Unknown Myalgia
Skin and sub-cutaneous tissue disorders
Not known Urticaria, bullous or exfoliative skin lesions

Adverse reactions reported with monotherapy of Vildagliptin or metformin alone in **clinical studies** and with **post-marketing*** reporting are given below:

Monotherapy with Vildagliptin
Infections and infestations
Very rare Upper respiratory tract infection, Nasopharyngitis
Metabolism and nutrition disorders
Uncommon Hypoglycemia
Nervous system disorders
Common Dizziness
Uncommon Headache
Vascular disorders
Uncommon Oedema peripheral
Gastrointestinal disorders
Uncommon Constipation
*Frequency unknown** Pancreatitis
Musculoskeletal and connective tissue disorders
Uncommon Arthralgia
*Frequency unknown** Myalgia
Hepatobiliary disorders
*Frequency unknown** Hepatitis
Skin and subcutaneous tissue disorders
*Not Known** Urticaria, Bullous or exfoliative skin lesions

Monotherapy with Metformin
Metabolism and nutrition disorders
Very rare Lactic acidosis, Vitamin B12 absorption decreased
Nervous system disorders
Common Taste disturbance
Gastrointestinal disorders
Very common Gastrointestinal disorders such as nausea, vomiting, diarrhea, abdominal pain and loss of appetite.
Hepatobiliary disorders
Very rare Isolated reports of liver function tests abnormalities or hepatitis resolving upon metformin discontinuation.
Skin and subcutaneous tissue disorders
Very rare Skin reactions such as erythema, pruritus, and urticaria

DRUG INTERACTIONS

Vildagliptin

ACE-inhibitors
There may be an increased risk of angioedema in patients concomitantly taking ACE-inhibitors.

Metformin Hydrochloride

Interactions for which concomitant use is not recommended

Alcohol
Acute alcohol intoxication is associated with an increased risk of lactic acidosis, particularly in case of fasting, malnutrition or hepatic insufficiency. Avoid consumption of alcohol and alcohol-containing medicinal products with metformin containing products.

Iodinated contrast agents
Intravascular administration of iodinated contrast agents may lead to renal failure, resulting in metformin accumulation and an increased risk of lactic acidosis.
In patients with CrCl > 60 ml/min, metformin containing products must be discontinued prior to, or at the time of the test and not be reinstituted until at least 48 hours afterwards, and only after renal function has been re-evaluated and has not deteriorated further .In patients with moderate renal impairment (CrCl between 45 and 60 ml/min), metformin containing products must be discontinued 48 hours before administration of iodinated contrast media and not be reinstituted until at least 48 hours afterwards and only after renal function has been re-evaluated and has not deteriorated further.

Cationic drugs
Cationic drugs (e.g., amiloride, digoxin, morphine, procainamide, quinidine, quinine, ranitidine, cimetidine, triamterene, trimethoprim, or vancomycin) that are eliminated by renal tubular secretion theoretically have the potential for interaction with metformin by competing for common renal tubular transport systems delaying the absorption of metformin and may increase the risk of lactic acidosis. Therefore, close monitoring of glycaemic control, dose adjustment and changes in diabetic treatment should be considered when cationic drug that are eliminated by renal tubular secretion are co-administered with metformin containing drug products.

Combinations requiring precautions for use

Diuretics, especially loop diuretics
They may increase the risk of lactic acidosis due to their potential to decrease renal function.

Vildagliptin / Metformin combination

Reduction of hypoglycemic effect

As with other oral anti diabetic drugs, the hypoglycemic effect of vildagliptin and metformin may be reduced by certain drugs, including thiazides, corticosteroids, thyroid products and sympathomimetics. Strict monitoring of glycemic control and dose adjustment of hypoglycemic medications may be necessary in patients using these drugs.

USE IN SPECIAL POPULATIONS
Pregnancy
Galvecta Plus should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus. However, there are no adequate and well-controlled studies in pregnant women, and animal studies are not always predictive of the human response. 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

Nursing mothers
No studies have been conducted with the combined components of Galvecta Plus. Metformin is excreted into human breast milk. It is not known whether vildagliptin is excreted in human milk or not. Due to both the potential risk of neonate hypoglycaemia related to metformin and the lack of human data with vildagliptin, Galvecta Plus should not be administered to breast-feeding women.

Hepatic Impairment

Vildagliptin
The use of vildagliptin is not recommended in patients with hepatic impairment including patients with a pre-treatment ALT or AST > 3 times the upper limit of normal. (See DOSAGE AND ADMINISTRATION) and CONTRAINDICATIONS.

Metformin hydrochloride
No pharmacokinetic studies of metformin hydrochloride have been conducted in subjects with hepatic insufficiency.

Renal Impairment
The combination product of vildagliptin and metformin should not be used in patients with creatinine clearance < 60 ml/min

OVER DOSAGE

Vildagliptin
Information regarding overdose with vildagliptin is limited.

Symptoms
Information on the likely symptoms of overdose with vildagliptin was taken from a rising dose tolerability study in healthy subjects given vildagliptin for 10 days. At 400 mg, there were three cases of muscle pain, and individual cases of mild and transient paraesthesia, fever, oedema and a transient increase in lipase levels. At 600 mg, one subject experienced oedema of the feet and hands, and increases in creatine phosphokinase (CPK), AST, C-reactive protein (CRP) and myoglobin levels. Three other subjects experienced oedema of the feet, with paraesthesia in two cases. All symptoms and laboratory abnormalities resolved without treatment after discontinuation of the study medicinal product.

Management
In the event of an overdose, supportive management is recommended. Vildagliptin cannot be removed by haemodialysis. However, the major hydrolysis metabolite (LAY 151) can be removed by haemodialysis to a limited extent (3% over a 3-4 hour haemodialysis session starting 4 hours post dose).

Metformin
The minimum toxic dose is not well established. ADULT: In adults, ingestions of 5 g or less are generally well tolerated. Severe toxicity developed after ingestions of 25 or more of metformin. PEDIATRIC: Ingestions of up to 1700 mg of metformin were well tolerated in healthy children.

Symptoms
A large overdose of metformin may lead to lactic acidosis, which is a medical emergency and must be treated in hospital. Hypoglycemia has not been seen with metformin doses of up to 85 g.

Management
The most effective method of removing metformin and lactate is haemodialysis. Supportive management is recommended.

PRESENTATION
Galvecta Plus (50/500) : Pack of 14 Tablets
Galvecta Plus (50/850) : Pack of 14 Tablets
Galvecta Plus (50/1000) :Pack of 14 Tablets

INSTRUCTIONS
Use as advised by the physician.
Keep all medicines out of the reach of children.
To be sold on the prescription of a registered medical practitioner only.
Protect from light, heat and moisture.
Store below 30°C.
For suspected adverse drug reaction, report at reports@pharmevo.biz

For more information on our products
call PharmAssist helpline 0800-82222
Monday to Friday 9:00 am to 6:00 pm
or email us at : pharmassist@pharmevo.biz

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ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔
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