Esglip

Sitagliptin Tablets USP

Esglip 50mg
Esglip 100mg

For the use only of a Registered Medical Practitioner or Hospital or a Laboratory.

ESGLIP – 50
COMPOSITION:
Each film coated tablet contains:
Sitagliptin Phosphate USP (as Monohydrate) eq. to Sitagliptin 50mg
Colour:
Yellow Oxide of Iron & Red Oxide of Iron
ESGLIP – 100
COMPOSITION:
Each film coated tablet contains:
Sitagliptin Phosphate USP (as Monohydrate) eq. to Sitagliptin 100mg
Colour:
Yellow Oxide of Iron & Red Oxide of Iron
PHARMACOLOGICAL CLASSIFICATION:
Anti-diabetic
INDICATIONS:
Monotherapy
Sitagliptin is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.
Combination Therapy
Sitagliptin is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin or Sulfonylurea or a PPARyagonist when the single agent alone, with diet and exercise, does not provide adequate glycemic control.
DOSE, METHOD OF ADMINISTRATION AND USAGE:
The recommended dose of Sitagliptin is 100mg once daily as monotherapy or as combination therapy with metformin or a PPARy agonist. Sitagliptin can be taken with or without food.
PATIENTS WITH RENAL INSUFFICIENCY
For patients with renal insufficiency (creatinine clearance [CrCl] ≥ 50 mL/min, approximately corresponding to serum creatinine levels of ≤ 1.7 mg/dL in men ≤ 1.5 mg/dL in women), no dosage adjustment for Sitagliptin is required.
For patients with moderate renal insufficiency (CrCl ≥ 30 to <50 mL/min, approximately corresponding to serum creatinine levels of > 1.7 to ≤ 3.0 mg/dL in men and >1.5 to ≤ 2.5 mg/dL in women), the dose of Sitagliptin is 50mg once daily.
For patients with severe renal insufficiency (CrCl<30 mL/min, approximately corresponding serum creatinine levels of >3.0 mg/dL in men and >2.5 mg/dL in women) or with end-stage renal disease (ERSD) requiring hemodialysis or peritoneal dialysis, the dose of Sitagliptin is 25 mg daily. Sitagliptin may be administered without regard to the timing of hemodialysis. Because there is a need for dosage adjustment based upon renal function, assessment of renal function is recommended prior to initiation of Sitagliptin and periodically thereafter. If a dose of Sitagliptin is missed, it should be taken as soon as the patient remembers. A double dose of Sitagliptin should not be taken on the same day.
Patients with hepatic insufficiency
No dosage adjustment is necessary for patients with mild to moderate hepatic insufficiency. Sitagliptin has not been studied in patients with severe hepatic insufficiency.
Elderly
No dosage adjustment is necessary for elderly patients.
Pediatric Population:
There are no data available on the use of Sitagliptin in patient younger than 18 years of age. There, use of Sitagliptin in the pediatric patients is not recommended.
USE IN SPECIAL POPULATIONS
PREGNANCY
Sitagliptin was not teratogenic in rats at oral doses up to 250 mg/kg or in rabbits given up to 125mg/kg during organogenesis (up to 32 and 22 times, respectively, the human exposure based on the recommended daily adult human dose of 100 mg/day). In rats, a slight increase in the incidence of fetal rib malformations (absent, hypoplastic and wavy ribs) was observed at oral doses of 1000mg/kg/day (approximately 100 times the human exposure based on the recommended daily adult human dose of 100 mg/day)/ Slight decreases in mean prewaning body weights of both sexes and post weaning body weight gains of males were observed in the offspring of rats given oral dose of 1000mg/kg/day. However, animal reproduction studies are not always predictive of the human response.
There are no adequate and well-controlled studies in pregnant women; therefore, the safety of Sitagliptin in pregnant women is not known. Sitagliptin, like oral antihyperglycemic agents, is not recommended for use in pregnancy.
NURSING MOTHERS
Sitagliptin is secreted in the milk of lactating rats. It is not known whether Sitagliptin is secreted in human milk. Therefore, Sitagliptin should not be used by a woman who is nursing.
PEDIATRIC USE
Safety and effectiveness of Sitagliptin in patients under 18 years have not been established.
USE IN THE ELDERLY
In clinical studies, the safety and effectiveness of Sitagliptin in the elderly (>65 years) were comparable to those seen in younger patients (<65 years). No dosage adjustment is required based on age. Elderly patients are more likely to have renal insufficiency; as with other patients, dosage adjustment may be required in presence of significant renal insufficiency (see DOSE, METHOD OF ADMINISTRATION AND USAGE, patients with renal insufficiency).
CONTRAINDICATIONS
Sitagliptin is contraindicated in patients who are hypersensitive to any components of this product. (See warnings and precaution, Hypersensitivity Reactions and Undesirable Effects, Postmarketing experience,)
WARNINGS AND PRECAUTIONS
Sitagliptin should not be used in patients with type 1 diabetes of for the treatment of diabetes ketoacidosis.
Pancreatitis: In postmarketing experience there have been reports of acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis (see UNDESIRABLE EFFECTS, postmarketing Experience), in patients taking sitagliptin. Because these reports are made voluntarily from a population of uncertain size, it is generally not possible to reliably estimate their frequency of establish a causal relationship to drug exposure. Patients should be informed of the characteristic symptom of acute pancreatitis: persistent severe abdominal pain. Resolution of pancreatitis has been observed after discontinuation of sitagliptin. If pancreatitis is suspected, Sitagliptin and other potentially suspect medicinal products should be discontinued. Use in patients with renal insufficiency: Sitagliptin is renally excreted. To achieve plasma concentrations of Sitagliptin similar to those in patients with normal renal function, lower dosages are recommended in patients with moderate and severe renal insufficiency, as well as in ESRD patients requiring hemodialysis or peritoneal dialysis. (See DOSE, METHOD OF ADMINISTRATION AND USAGE, patients with renal insufficiency.)
Hypoglycemia in combination with a Sulfonylurea or with insulin: In clinical trials of Sitagliptin as monotherapy and as part of combination therapy with patient agents not known to cause hypoglycemia (i.e. metformin or PPARy. Agonist (thiazolidinedione)), rates of hypoglycemia reported with Sitagliptin were similar to rates in patients taking placebo. As is typical with other antihyperglycemic agents when Sitagliptin was used in combination with a sulfonylurea or with insulin, medications known to cause hypoglycemia, the incidence of sulfonylurea or insulin – induced hypoglycemia was increased over that of placebo (see UNDESIRABLE EFFECTS). Therefore, to reduce the risk of sulfonylurea –or insulin – induced hypoglycemia, a lower dose of sulfonylurea or insulin may be considered (See DOSE, **METHOD OF ADMINISTRATION AND USAGE).**
Hypersensitivity reactions: There have been postmarketing reports of serious hypersensitivity reactions in patients treated with Sitagliptin. These reactions include anaphylaxis, angioedema, and exfoliative skin conditions including Stevens – Johnson syndrome. Because these reactions are reported voluntarily from a population of uncertain size, it is generally not possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Onset of these reactions occurred within the first 3 months after initiation of treatment with Sitagliptin, with some reports occurring after the first dose. If a hypersensitivity reaction is suspected, discontinue Sitagliptin, assess for other potential causes for the event, and institute alternative treatment for diabetes. (See CONTRA INDICATIONS AND UNDESIRABLE EFFECTS, postmarketing experience.)
DRUG INTERACTIONS
In drug interaction studies, Sitagliptin did not have clinically meaningful effects on the pharmacokinetics of the following metformin, rosiglitazone, glyburide, simvastatin, warfarin, and contraceptives. Based on this data, Sitagliptin does not inhibit CYP isozymes CYP3A4, 2C8, OR 2C9. Based on in vitro data Sitagliptin is also not expected to inhibit CYP2D6, 1A2, 2C19 or 2b6 to induce CYP3A4.
Co-administration of multiple twice- daily doses of metformin with Sitagliptin did not meaningfully alter the pharmacokinetics of Sitagliptin in patients with type 2 diabetes. Population pharmacokinetic analyses have been conducted in patients with type 2 diabetes.
Concomitant medications did not have a clinically meaningful effect on the pharmacokinetics of sitagliptin. Medications assessed were those that are commonly administered to patients with type 2 diabetes including cholesterol-lowering agents (e.g., Statins, fibrates, Ezetimibe), anti-platelet agents (i.e. Clopidogrel) Anti hypertensive (e.g. ACE inhibitors, angiotensin receptor blockers, beta-blockers, calcium channel blockers, hydrochlorthiazide), analgesics and nonsteroidal anti-inflammatory agents (e.g., naproxen, diclofenac, celocoxib), anti- depressants (e.g., bupropion, fluoxetine, sertraline), antihistamines (e.g., cetirizine), proton-pump inhibitors (e.g., omeprazole, lansoprazole), and medications for erectile dysfunction (e.g., sildenafil). There was a slight increase in the area under the curve (AUC, 11%) and mean drug concentration (Cmax, 18%) of digoxin with the co-administration of sitagliptin. These increases are not considered to be clinically meaningful. Patients receiving digoxin should be monitored appropriately. No dosage adjustment of digoxin or sitagliptin is recommended. The AUC and Cmax of sitagliptin were increased approximately 29% and 68% respectively, in subjects with co- administration of a single 100-mg oral dose of sitagliptin and a single 600-mg oral dose cyclosporine, a potent probe inhibitor of p- glycoprotein. The observed changes in sitagliptin pharmacokinetics are not considered to be clinically meaningful. No dosage adjustment for Sitagliptin is recommended when co-administered with cyclosporine or other pglyco-protein inhibitors (e.g. ketoconazole).
UNDESIRABLE EFFECTS
Sitagliptin was generally well tolerated in controlled clinical studies as both monotherapy (one study of 18 and one of 24week duration and add-on combination therapy with metformin or pioglitazone (both of 24-week duration), there were 1082 patients treated with Sitagliptin 100 mg once daily and 778 patients given placebo. (Two of these studies also included 456 patients treated with Sitagliptin 200mg daily, two times the recommended daily dose.) There were no drug – related adverse reactions reported that occurred with an incidence of > 1% in patients receiving Sitagliptin 100 mg. overall, the safety profile of the 200 mg daily dose was similar to that of the 100mg daily dose. In a prespecified pooled analysis of the above studies, the overall incidence of adverse experiences of hypoglycemia in patients treated with Sitagliptin 100mg was similar to placebo (1.2% vs 0.9%). The incidences of selected gastrointestinal adverse experiences in patients treated with Sitagliptin or placebo were: abdominal pain (Sitagliptin, 2.3% placebo, 2.1%), nausea (1.4%, 0.6%). Vomiting (0.8%, 0.9%), and diarrhea (3.0%, 2.3%). In all studies, adverse reactions of hypoglycemia were based on all reports of symptomatic hypoglycemia; a concurrent glucose measurement was not required. Add-on combination with sulfonylurea: In a 24-week placebo-controlled study of Sitagliptin 100mg in combination with glimepiride or with glimipiride and metformin (Sitagliptin, N=222, placebo N=219), the drug- related adverse reaction reported in>1% of patients treated with Sitagliptin and more commonly than in patients treated with placebo was hypoglycemia Sitagliptin, 9.5%; placebo, 0.9%).

Add –on combination with metformin and a PPARy Agonist: In a placebo controlled study of Sitagliptin 100mg in combination with metformin and rosiglitazone (Sitagliptin, N=170; placebo, N=92), the drug- related adverse reactions reported through the primary time point at week 18 in>1% of patients treated with Sitagliptin and more commonly than in patients treated with placebo were: headache (Sitagliptin, 2.4% placebo, 0.0%), diarrhea (1.8%, 1.1%) nausea (1.2%, 1.1%), hypoglycemia (1.2%, 0.0%) and vomiting (1.2%, 0.0%). Through week 54, the drug- related adverse reactions reported in>15of patients treated with sitagliptin and more commonly than in patients treated with placebo were: headache (2.4%, 0.0%), hypoglycemia (2.4%, 0.0%), upper respiratory tract infection (1.8%, 0.0%), nausea (1.2%, 1.1%), cough (1.2%cough (1.2%, 0.0%), fungal skin infection (1.2%, 0.0%), peripheral edema (1.2%, 0.0%) and vomiting (1.2%, 0.0%).
Initial combination therapy with metformin: In a 24 – week placebo-controlled factorial study of initial therapy with sitagliptin 100mg in combination with metformin 1000mg or 2000mg per day (administered as sitagliptin 50 mg/metformin 500mg or 1000mg twice daily), the drug related adverse reactions reported in>1% of patients treated with sitagliptin plus metformin (N=372) and more commonly than in patients treated with metformin alone (N=364) were: diarrhea (sitagliptin plus metformin, 3.5%; metformin,3.3% dyspepsia (1.3%;1.1%), flatulence (1.35;0.5%), vomiting (1.1%; 0.3%), and headache (1.3%; 1.1%). The incidence of hypoglycemia was 1.1% in patients given sitagliptin in combination with metformin and 0.5% in patients given metformin alone.
Initial combination therapy with a PPARy Agonist: In a 24-week study of initial therapy with Sitagliptin at 100mg/day in combination with pioglitazone at 30mg/day, the only drug related adverse reaction reported in >1% of the patients treated with Sitagliptin with pioglitazone (N=261) and more commonly than in patients treated with pioglitazone alone (N=259) was (asymptomatic) decreased blood glucose (Sitagliptin with pioglitazone, 1.1%; pioglitazone, 0.0%). The incidence of (symptomatic) hypoglycemia was 0.4% in patients given Sitagliptin in combination with pioglitazone and 0.8% in patients given pioglitazone.
Add-on combination with insulin: In a 24 week placebo-controlled study of Sitagliptin 100mg in combination with insulin (with or without metformin), the drug-related adverse reactions reported in>1% of patients treated with Sitagliptin (N=322) and more commonly than in patient treated with placebo (N=319) were: hypoglycemia (Sitagliptin, 9.6% placebo, 5.3%), influenze (1.2%, 0.3%), and headache (1.2%, 0.0%)
Pancreatitis: In a pooled analysis of 19 double-blind clinical trials that included data from 10,246 patients randomized to receive sitagliptin 100mg/day (N=5429) or corresponding (active or placebo) control (N=4817), the incidence of acute pancreatitis was 0.1 per 100 patient years in each group (4 patients with an event in 4708 patient years for sitagliptin and 4 patients with an event in 3942 patient years for control). (See WARNINGS AND PRECAUTIONS, Pancreatitis).
No clinically meaningful changes in vital signs or in ECG (including in QTC interval) were observed in patients treated with Sitagliptin
Postmarketing experience: additional adverse reactions have been identified during postmarketing use of Sitagliptin as monotherapy and/or in combination with other antihyperglycemic agents. Because of these reactions are reported voluntarily from a population of uncertain size, it is generally not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.
Hypersensitivity reactions including anaphylaxis, angioedema, rash, Urticaria, cutaneous vasculitis and exfoliative skin conditions, including Steven- Jonson syndrome (see CONTRA-INDICATIONS AND WARNINGS AND PRECAUTIONS, HYPE-RSENSITIVITY REACTIONS); acute pancreatits, including fatal and non-fatal hemorrhagic and necrotizing pancreatits (see WARNINGS AND PRECAUTIONS, Pancreatits); worsening renal function, including acute renal failure (sometimes requiring dialysis); upper respiratory tract infections; nasopharyngitis; constipation; vomiting; headache arthralgia; back pain.
OVERDOSE
During controlled clinical trials in healthy subjects, single doses of up to 800mg Sitagliptin were generally well tolerated. Minimal increase in QTc, not considered to clinically relevant were observed in one study at a dose 800 mg Sitagliptin. There is not experience with doses above 800mg in clinical studies. In phase 1 multiple-dose studies, there were no dose related clinical adverse reactions observed with Sitagliptin with dose up to 600mg per day for periods up to 10 days and 400mg per day for period of upto 28days.
In the event of an overdose, it is reasonable to employ the usual supportive measures, e.g., remove unabsorbed material from the gastrointestinal tract, employ clinical monitoring (including obtaining an electrocardiogram), and institute supportive therapy if required.
Sitagliptin is modestly dialyzable. In clinical studies, approximately 13.5% of the dose was removed over a 3- to 4 hour hemodialysis session. Prolonged hemodialysis may be considered if clinically appropriate. It is not known if sitagliptin is dialyzable by peritoneal dialysis.
Storage Conditions:
Store in a dry place, at a temperature not exceeding 30°C.
Keep all medicines out of reach of children.
Shelf life is 2 years:
The preparation should not be used after the expiry date.
Distribution Condition:
With Prescription
Presentation:
ESGLIP-50 : Alu/Alu Blister of 1x10 & 3x10 tablets
ESGLIP-100 : Alu/Alu Blister of 1x10 & 3x10 tablets

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Ref : EGP50-100/LL/12/20
Date of issue: March 2020