SMIFT 50mg/500mg 50mg/1000mg Tablets

سمفٹ ۵۰ملی گرام/۵۰۰ملی گرام، ۵۰ملی گرام/۱۰۰۰ملی گرام گولیاں

[SITAGLIPTIN / METFORMIN HCl]

DESCRIPTION:
SMIFT (Sitagliptin/Metformin HCl) contains two oral antihyperglycemic agents used in the management of type 2 diabetes: Sitagliptin/Metformin HCl. Sitagliptin is an orally-active, potent, and highly selective inhibitor of the dipeptidyl peptidase 4 (DPP-4) enzymes. Metformin HCl is a biguanide with antihyperglycemic effects, lowering both basal and postprandial plasma glucose.
QUALITATIVE & QUANTITATIVE COMPOSITION:
SMIFT (Sitagliptin/Metformin HCl) is available for oral administration as:
1) SMIFT Tablets 50mg/500mg
Each film coated tablet contains:
Sitagliptin as Sitagliptin Phosphate Monohydrate USP 50mg
Metformin HCl USP.....500mg
(Product Specs.: Sigma)
2) SMIFT Tablets 50mg/1000mg
Each film coated tablet contains:
Sitagliptin as Sitagliptin Phosphate Monohydrate USP 50mg
Metformin HCl USP...1000mg
(Product Specs.: Sigma)
CLINICAL PHARMACOLOGY:
MECHANISM OF ACTION:
SITAGLIPTIN:
Sitagliptin exert its actions by slowing the inactivation of incretin hormones, including glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP). The incretins are part of an endogenous system involved in the physiologic regulation of glucose homeostasis. By increasing and prolonging active incretin levels, Sitagliptin increases insulin release and decreases glucagon levels in the circulation in a glucose-dependent manner.
METFORMIN HCL:
Metformin HCl exerts its effect by;
- Decreases hepatic glucose production.
- Decreases intestinal absorption of glucose.
- Improves insulin sensitivity by increasing peripheral glucose uptake and utilization.

It does not stimulate insulin secretion and therefore does not produce hypoglycemia.
PHARMACOKINETICS:
Absorption:
Sitagliptin:
The absolute bioavailability is approximately 87% after oral administration. Co-administration of a high-fat meal with sitagliptin had no effect on the pharmacokinetics of sitagliptin.
Metformin HCl:
The absolute bioavailability of a single dose 500mg dose is about 50% to 60% given under fasting condition. Food decreases the extent and slightly delays the absorption of Metformin HCl.
Distribution:
Sitagliptin:
The mean volume of distribution following intravenous dose is approximately 198L. About 38% of Sitagliptin reversibly bound to plasma proteins.
Metformin HCl:
Metformin is negligibly bound to plasma proteins. Metformin partitions into erythrocytes. At usual clinical doses of Metformin HCl tablets, steady-state plasma concentrations are reached within 24-48 hours. The mean volume of distribution ranged between 63 – 276 L.
Metabolism:
Sitagliptin:
Eliminated unchanged in urine (approximately 79%), and metabolism is a minor pathway.
Metformin HCl:
Excreted unchanged in the urine and does not undergo hepatic metabolism.
Excretion:
Sitagliptin:
Elimination occurs primarily via renal route and involves active tubular secretion. The $t_{1/2}$ following a 100-mg oral dose of sitagliptin was approximately 12.4 hours.
Metformin HCl:
Renal clearance is approximately 3.5 times greater than creatinine clearance, which indicates that tubular secretion is the major route of metformin elimination. Approximately 90% of the absorbed drug is eliminated via the renal route within the first 24 hours, with a plasma elimination $t_{1/2}$ of approximately 6.2 hours. In blood, the elimination $t_{1/2}$ is approximately 17.6 hours.
Special Populations:
Renal Insufficiency:
The plasma AUC of Sitagliptin increases approximately 2-fold in patients with moderate renal insufficiency and an approximately 4-fold in patients with severe renal insufficiency and in patients with ESRD on hemodialysis. In patients with decreased renal function (based on creatinine clearance), the plasma and blood half-life of Metformin HCl is prolonged and the renal clearance is decreased.
Elderly:
SMIFT therapy is not recommended to initiate in geriatric patient ≧80 years without monitoring renal function.
THERAPEUTIC INDICATIONS:
SMIFT (Sitagliptin/Metformin HCl) is indicated as an adjunct to diet and exercise in patients with type 2 diabetes mellitus:
- When diet and exercise alone do not provide adequate glycemic control.
- When glycemic control is not achieved on Metformin HCl or Sitagliptin alone or in patients already being treated with the combination of Sitagliptin and Metformin HCl.
- In triple combination with a sulphonylurea, when glycemic control is not achieved on maximal tolerated dose of Metformin HCl and a sulphonylurea.
- In triple combination with a peroxisome proliferator-activated receptor gamma (PPAR γ) agonist (thiazolidinedione) when glycemic control is not achieved on their maximal tolerated dose of Metformin HCl and a PPAR γ agonist.
- In triple combination with an insulin, when glycemic control is not achieved on maximal tolerated dose of Metformin HCl and an insulin

DOSAGE AND ADMINISTRATION:
The dosage of **SMIFT** should be individualized on the basis of patient's current regimen, effectiveness and tolerability while not exceeding the maximum recommended daily dose of 100mg Sitagliptin and 2000 mg metformin.
It should be given twice daily with meals, with gradual dose escalation, to reduce the gastrointestinal (GI) side effects associated with Metformin HCl.

INDICATION	STARTING DOSE	MAXIMUM DOSE
When diet and exercise alone do not provide adequate glycemic control	**SMIFT** 50mg/500mg Tablet twice daily	**SMIFT** 50mg/1000mg Tablet twice daily
When glycemic control is not achieved on Sitagliptin monotherapy		
When glycemic control is not achieved on Metformin HCl monotherapy	*Sitagliptin 50mg twice daily plus Metformin HCl dose already being taken	
Patient switching from Sitagliptin co-administered with Metformin HCl	**SMIFT** may be initiated at the dose of Sitagliptin and Metformin HCl already being taken	
In triple combination with an insulin secretagogue (e.g., sulfonylurea), thiazolidinedione or insulin.	Sitagliptin 50mg twice daily Plus Metformin HCl dose already being taken	

* Patients taking metformin HCl 850mg twice daily, the recommended starting dose of **SMIFT** is 50mg/1000mg Tablet twice daily.
Co-administration of **SMIFT** with an insulin secretagogue or insulin may require lower doses of the insulin secretagogue or insulin to reduce the risk of hypoglycemia.

CONTRAINDICATIONS:
SMIFT is contraindicated in:
- Patients with known hypersensitivity to Sitagliptin, Metformin HCl or any other component of the product.
- Patients with type 1 diabetes.
- Renal dysfunction or any disease decreases serum creatinine.
- Acute or chronic metabolic acidosis, including ketoacidosis, with or without coma.
- Hepatic impairment due to risk of lactic acidosis.
- Children below 18 years of age.

PRECAUTIONS:

WARNING: LACTIC ACIDOSIS: Lactic acidosis is a rare, but serious complication that can occur due to metformin accumulation. The risk increases with conditions such as sepsis, dehydration, excess alcohol intake, hepatic insufficiency, renal impairment, and acute congestive heart failure. The onset is often subtle, accompanied only by nonspecific symptoms such as malaise, myalgias, respiratory distress, somnolence, and nonspecific abdominal distress. Laboratory abnormalities include low pH, increased anion gap and elevated blood lactate. If acidosis is suspected, **SMIFT** should be discontinued and the patient is hospitalized immediately

Monitoring of Renal Function:
If renal dysfunction is anticipated, particularly in elderly patients, renal function should be assessed more frequently and discontinue **SMIFT** if is evidence of renal impairment is present.
Pancreatitis:
If pancreatitis is suspected after initiation of sitagliptin, sitagliptin should be discontinued.
Iodinated Contrast Agent:
The intravascular administration of iodinated contrast agents in radiological studies can lead to renal failure.
SMIFT should be discontinued prior to, or at the time of the test and not reinstituted until 48 hours afterwards, and only after renal function found to be normal.
Surgery:
SMIFT must be discontinued at the time of surgery. Therapy may be restarted no earlier than 48 hours following surgery.
Pregnancy & Nursing Mother:
SMIFT is contraindicated in pregnancy and during nursing.
DRUG INTERACTIONS:
Digoxin:
Sitagliptin has a small effect on plasma digoxin concentrations. Patients at risk of digoxin toxicity should be monitored closely.
Furosemide:
Furosemide increased Metformin HCl plasma and blood concentration without any significant change in Metformin HCl renal clearance.
Nifedipine:
Nifedipine enhances the absorption of Metformin HCl. Metformin HCl had minimal effects on nifedipine.
Cationic Drugs:
Careful patient monitoring and dose adjustment of **SMIFT** and/or cationic drugs e.g., amiloride, digoxin, morphine, procainamide, quinidine, quinine, ranitidine, triamterene, trimethoprim, or vancomycin that are excreted via the proximal renal tubular secretory system is recommended.
Other:
Thiazides & other diuretics, corticosteroids, phenothiazines, thyroid drugs, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, calcium channel blocking drugs and isoniazid produce hyperglycaemia. Patient should be closely observed to maintain adequate glycemic control.
ADVERSE REACTIONS:
Very common: hypoglycemia
Common: nausea, headache, diarrhea, constipation, vomiting & peripheral edema.
OVERDOSAGE:
In the event of an overdose initiate supportive therapy. Prolonged hemodialysis may be considered if clinically appropriate.

INSTRUCTIONS:
-Store below 30˚C.
-Protect from light & moisture.
-Keep out of reach of children.
To be sold on prescription of a registered medical practitioner only.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
ہدایت: دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
روشنی اور نمی سے **بچائیں**۔ بچوں کی پہنچ سے دور رکھیں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔

HOW SUPPLIED:
SMIFT Tablets 50mg/500mg are available in packs of 10's, 14's & 30's.
SMIFT Tablets 50m/1000mg are available in packs of 10's & 14's.

SIGMA PHARMA
Manfactured By:
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