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SITA®
(Sitagliptin) **Tablet**

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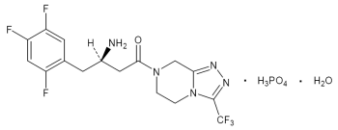
COMPOSITION:
Sita Tablet 50mg:
Each film coated tablet contains:
Sitagliptin phosphate monohydrate equivalent to
Sitagliptin ..... 50 mg.

Product Specs.: CCL Pharmaceuticals

Sita Tablet 100mg:
Each film coated tablet contains:
Sitagliptin phosphate monohydrate equivalent to
Sitagliptin ..... 100 mg.

Product Specs.: CCL Pharmaceuticals

DESCRIPTION:
SITA Tablets contain sitagliptin phosphate, an orally-active inhibitor of the dipeptidyl peptidase-4 (DPP-4) enzyme. Sitagliptin phosphate monohydrate is described chemically as 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazine phosphate (1:1) monohydrate. The empirical formula is $C_{16}H_{15}F_6N_5O \cdot H_3PO_4 \cdot H_2O$ and the molecular weight is 523.32. The structural formula is:



CLINICAL PHARMACOLOGY:
Mechanism of action:
Sitagliptin is a DPP-4 inhibitor, which is believed to exert its actions in patients with type 2 diabetes by slowing the inactivation of incretin hormones. Concentrations of the active intact hormones are increased by **SITA**. By increasing and prolonging active incretin levels, **SITA** increases insulin release and decreases glucagon levels in the circulation in a glucose-dependent manner. Sitagliptin demonstrates selectivity for DPP-4 and does not inhibit DPP-8 or DPP-9 activity in vitro at concentrations approximating those from therapeutic doses.
Pharmacokinetics:
Absorption: The absolute bioavailability of sitagliptin is approximately 87%. Because coadministration of a high-fat meal with **SITA** had no effect on the pharmacokinetics, **SITA** may be administered with or without food.
Distribution: The mean volume of distribution at steady state following a single 100 mg intravenous dose of sitagliptin to healthy subjects is approximately 198 liters. The fraction of sitagliptin reversibly bound to plasma proteins is low (38%).
Metabolism: Approximately 79% of sitagliptin is excreted unchanged in the urine with metabolism being a minor pathway of elimination.
Elimination: Elimination of sitagliptin occurs primarily via renal excretion. Sitagliptin is eliminated in feces (13%) or urine (87%). The apparent terminal $t_{1/2}$ following a 100 mg oral dose of sitagliptin was approximately 12.4 hours and renal clearance was approximately 350 mL/min.
Pharmacokinetics in special populations:
Renal Impairment: Plasma AUC levels of sitagliptin were increased approximately 2-fold and 4-fold in patients with moderate renal insufficiency and in patients with severe renal insufficiency, including patients with ESRD on hemodialysis, respectively. Sitagliptin is modestly removed by hemodialysis. 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 dialysis.
Hepatic insufficiency: In patients with moderate hepatic insufficiency (Child-Pugh score 7 to 9), mean AUC and Cmax of sitagliptin increased approximately 21% and 13%, respectively and No dosage adjustment for **SITA** is necessary for patients with mild or moderate hepatic insufficiency.There is no clinical experience in patients with severe hepatic insufficiency (Child-Pugh score >9).
Body mass index (bmi): No dosage adjustment is necessary based on BMI.
Gender: No dosage adjustment is necessary based on gender.
Geriatric: When the effects of age on renal function are taken into account, age alone did not have a clinically meaningful impact on the pharmacokinetics of sitagliptin based on a population pharmacokinetic analysis.
Pediatric: Studies characterizing the pharmacokinetics of sitagliptin in pediatric patients have not been performed.
Race: No dosage adjustment is necessary based on race.

IN VIVO ASSESSMENT OF DRUG INTERACTIONS:
Effects of sitagliptin on other drugs: Sitagliptin did not meaningfully alter the pharmacokinetics of metformin, glyburide, simvastatin, rosiglitazone, warfarin, or oral contraceptives, providing in vivo evidence of a low propensity for causing drug interactions with substrates of CYP3A4, CYP2C8, CYP2C9, and organic cationic transporter (OCT).
Effects of other drugs on sitagliptin: sitagliptin is not susceptible to clinically meaningful interactions by coadministered medications like metformin and cyclsporine.

INDICATIONS AND USAGE:
Monotherapy and combination therapy: **SITA** is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Important limitations of use: **SITA** should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.
Sitagliptin has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using **SITA**.

DOSAGE NAD ADMINISTRATION:
Recommended dosing:
The recommended dose of **SITA** is 100 mg once daily. **SITA** can be taken with or without food.

DOSE MODIFICATION RECOMMENDATIONS:
Patients with renal insufficiency:
- For patients with mild renal insufficiency (creatinine clearance [CrCl] greater than or equal to 50 mL/min, no dosage adjustment for **SITA** is required.
- For patients with moderate renal insufficiency (CrCl greater than or equal to 30 to less than 50 mL/min, the dose of **SITA** is 50 mg once daily.
- For patients with severe renal insufficiency (CrCl less than 30 mL/min, approximately or with end-stage renal disease (ESRD) requiring hemodialysis or peritoneal dialysis, the dose of **SITA** is 25 mg once daily. **SITA** may be administered without regard to the timing of dialysis.
- Because there is a need for dosage adjustment based upon renal function, assessment of renal function is recommended prior to initiation of **SITA** and periodically thereafter. Creatinine clearance can be estimated from serum creatinine using the Cockcroft-Gault formula.

Concomitant use with an insulin secretagogue (e.g., sulfonylurea) or with insulin: When **SITA** is used in combination with an insulin secretagogue (e.g., sulfonylurea) or with insulin, a lower dose of the insulin secretagogue or insulin may be required to reduce the risk of hypoglycemia.

CONTRAINDICATIONS:
History of a serious hypersensitivity reaction to sitagliptin, such as anaphylaxis or angioedema.

WARNINGS AND PRECAUTIONS:
Pancreatitis: After initiation of **SITA**, patients should be observed carefully for signs and symptoms of pancreatitis. If pancreatitis is suspected, **SITA** should promptly be discontinued and appropriate management should be initiated. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using **SITA**.
Heart failure: An association between dipeptidyl peptidase-4 (DPP-4) inhibitor treatment and heart failure has been observed in trials for two other members of the DPP-4 inhibitor class. Consider the risks and benefits of Sitagliptin prior to initiating treatment in patients at risk for heart failure, such as those with a prior history of heart failure and a history of renal impairment, and observe these patients for signs and symptoms of heart failure during therapy. Advise patients of the characteristic symptoms of heart failure and to immediately report such symptoms. If heart failure develops, evaluate and manage according to current standards of care and consider discontinuation.
Renal impairment: Assessment of renal function is recommended prior to initiating **SITA** and periodically thereafter. There has been post marketing reports of worsening renal function, including acute renal failure, sometimes requiring dialysis. A return to baseline levels of renal insufficiency has been observed with supportive treatment and discontinuation of potentially causative agents.

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Consideration can be given to cautiously reinitiating **SITA** if another etiology is deemed likely to have precipitated the acute worsening of renal function.
Use with medications known to cause hypoglycemia: When **SITA** was used in combination with a sulfonylurea or with insulin, medications known to cause hypoglycemia, the incidence of hypoglycemia was increased. Therefore, a lower dose of sulfonylurea or insulin may be required to reduce the risk of hypoglycemia.
Hypersensitivity reactions: If a hypersensitivity reaction is suspected, discontinue **SITA**, assess for other potential causes for the event, and institute alternative treatment for diabetes.
Angioedema has also been reported with other DPP-4 inhibitors. Use caution in a patient with a history of angioedema with another DPP-4 inhibitor because it is unknown whether such patients will be predisposed to angioedema with **SITA**.
Severe and disabling arthralgia: Patients experienced relief of symptoms upon discontinuation of the medication. Consider DPP-4 inhibitors as a possible cause for severe joint pain and discontinue drug if appropriate
Bullous pemphigoid: Bullous pemphigoid requiring hospitalization have been reported with DPP-4 inhibitor use. If bullous pemphigoid is suspected, **SITA** should be discontinued and referral to a dermatologist should be considered for diagnosis and appropriate treatment.
Macrovascular outcomes: There have been no conclusive evidence of macrovascular risk reduction with sitagliptin or any other anti-diabetic drug.

DRUG INTERACTIONS:
Digoxin: Patients receiving digoxin should be monitored appropriately. No dosage adjustment of digoxin or **SITA** is recommended.

USE IN SPECIFIC POPULATIONS:
Pregnancy Category B:
Pregnancy:
This drug should be used during pregnancy only if clearly needed
Nursing mothers:
Sitagliptin is secreted in the milk of lactating rats at a milk to plasma ratio of 4:1. It is not known whether sitagliptin is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when **SITA** is administered to a nursing woman.
Pediatric use:
Safety and effectiveness of **SITA** in pediatric patients under 18 years of age have not been established.
Geriatric use:
This drug is known to be substantially excreted by the kidney. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection in the elderly, and it may be useful to assess renal function in these patients prior to initiating dosing and periodically thereafter

ADVERSE REACTIONS:
The incidences of selected gastrointestinal adverse experiences in patients treated with sitagliptin were: abdominal pain, nausea, vomiting and diarrhea.
Add-on combination with a sulfonylurea: More common side effect is hypoglycemia.
Add-on combination with metformin and a ppary agonist: Common side effects are headache, diarrhoea, nausea, hypoglycaemia,vomiting,upper respiratory tract infection , nausea , cough , fungal skin infection , peripheral oedema , and vomiting .
Initial combination therapy with metformin: diarrhoea; metformin, dyspepsia, flatulence, vomiting,headache.
Initial combination therapy with a ppary agonist: Asymptomatic decreased blood glucose. Symptomatic hypoglycaemia

OVERDOSAGE:
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 as dictated by the patient's clinical status. Sitagliptin is modestly dialyzable. Prolonged hemodialysis may be considered if clinically appropriate. It is not known if sitagliptin is dialyzable by peritoneal dialysis.

INSTRUCTIONS:
- Store below 30°C.
- Protect from heat, sunlight & moisture.
- Keep out of the reach of children.
- To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:

***SITA* Tablet 50 mg**	:	Pack of 1 x 14 tablets.
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ہدایات:
۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف ڈاکٹر کے نسخہ پر فروخت کریں۔

FOR FURTHER INFORMATIONS PLEASE CONTACT:

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