Abridged Prescribing Information

Sitagliptin and Metformin Hydrochloride Tablets BP 50 mg/500 mg and 50 mg/1000 mg
Cetapin® -S

PRESCRIBING INFORMATION WARNING: LACTIC ACIDOSIS

- **Postmarketing cases of metformin-associated lactic acidosis have resulted in death, hypothermia, hypotension, and resistant bradyarrhythmias. Symptoms included malaise, myalgias, respiratory distress, somnolence, and abdominal pain. Laboratory abnormalities included elevated blood lactate levels, anion gap acidosis, increased lactate/pyruvate ratio; and metformin plasma levels generally >5 mcg/mL.**
- **Risk factors include renal impairment, concomitant use of certain drugs, age ≥65 years old, radiological studies with contrast, surgery and other procedures, hypoxic states, excessive alcohol intake, and hepatic impairment.**
- **Steps to reduce the risk of and manage metformin-associated lactic acidosis in these high-risk groups are provided in the Full Prescribing Information.**
- **If lactic acidosis is suspected, discontinue Sitagliptin + Metformin and institute general supportive measures in a hospital setting. Prompt hemodialysis is recommended.**

Composition: Sitagliptin and Metformin Hydrochloride Tablets BP 50 mg/500 mg; Sitagliptin and Metformin Hydrochloride Tablets BP 50 mg/1000 mg.

Indication: It is indicated as an adjunct to improve glycemic control in patients with type- 2 diabetes mellitus. As triple combination therapy with a peroxisome proliferator-activated receptor gamma (PPARy) agonist (i.e a thiazolidinedione) as an adjunct to diet and exercise in patients inadequately controlled on their maximal tolerated dose of metformin and a PPARy agonist and as add-on to insulin (i.e., triple combination therapy) as an adjunct to diet and exercise to improve glycemic control in patients when stable dose of insulin and metformin alone do not provide adequate glycemic control.

Dosage and Administration: It should be given twice daily with meals to reduce the gastrointestinal adverse reactions associated with metformin**.** The dose should be individualized and should not exceed the maximum recommended daily dose of 100 mg Sitagliptin. For adults with normal renal function (GFR ≥ 90 mL/min) and not adequately controlled on metformin alone, the usual starting dose should provide Sitagliptin dosed as 50 mg twice daily (100 mg total daily dose) plus the dose of metformin already being taken. Similarly for patients inadequately controlled on dual combination therapy with the maximal tolerated dose of metformin and a sulphonylurea and in patients with Insulin and the maximal tolerated dose of metformin. No dose adjustment is needed for patients with mild renal impairment (glomerular filtration rate [GFR] ≥ 60 mL/min). The maximum daily dose of metformin should preferably be divided into 2-3 daily doses in increased risk of renal impairment and elderly. This drug product should not be used in patients with hepatic impairment.

Safety related information

Contraindications: It is contraindicated in patients with hypersensitivity to the active substances or to any of the excipients listed any type of acute metabolic acidosis (such as lactic acidosis, diabetic ketoacidosis), diabetic pre-coma; severe renal failure (GFR< 30 mL/min), acute conditions with the potential to alter renal function, acute or chronic disease which may cause tissue hypoxia, hepatic impairment, acute alcohol intoxication, alcoholism; breast-feeding.

Special Warnings and Precautions for Use: It should not be used in patients with type 1 diabetes and for the treatment of diabetic ketoacidosis. If pancreatitis is suspected, product should be discontinued; if acute pancreatitis is confirmed, it should not be restarted. Caution should be exercised in patients with a history of pancreatitis. Metformin accumulation occurs at acute worsening of renal function and increases the risk of lactic acidosis therefore, patient should stop taking metformin and seek immediate medical attention. Should be temporarily discontinued in patients with GFR < 30 mL/min and during conditions with the potential to alter renal function. Patients may be a risk of hypoglycemia. Product should be discontinued, in case of hypersensitivity reaction, bullous pemphigoid, during surgery under general, spinal or epidural anesthesia and prior to or at the time of the imaging procedure. If acidosis of either form occurs in clinical status of patients with previously controlled type 2 diabetes, treatment must be stopped immediately, and other appropriate corrective measures initiated. This product contains less than 1 mmol sodium (23 mg) per tablet, essentially 'sodium-free'. The safety and effectiveness of Sitagliptin and Metformin have not been established in pediatric patients. Should be cautious while Dose selection for an elderly patient, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy and the higher risk of lactic acidosis. Sitagliptin and Metformin is

contraindicated in severe renal impairment, patients with GFR below 30 mL/min. Use of metformin in patients with hepatic impairment has been associated with some cases of lactic acidosis. Sitagliptin and Metformin is not recommended in patients with hepatic impairment.

Pregnancy and Lactation: The drug should not be used during pregnancy and who are breastfeeding.

Adverse reactions: Common adverse reactions include hyperglycemia, nausea, flatulence, vomiting, Uncommon: somnolence, diarrhea, constipation, upper abdominal pain. Not known: arthralgia

For full prescribing information please contact: Sanofi India Ltd., Sanofi House, CTS No. 117-B, L&T Business Park, Saki Vihar Road, Powai, Mumbai – 400072

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Source: Prescribing information of Sitagliptin and Metformin Tablets manufactured by MSN Laboratories Private Limited, dated May 2022 (accessed on 11th May 2023)