Sitomet®

Sitagliptin and Metformin Hydrochloride

Description

Sitomet® is a combination of two anti-hyperglycemic agents-Sitagliptin Phosphate Monohydrate and Metformin Hydrochloride with complementary mechanisms of action to improve glycemic control in patients with type 2 diabetes.

Sitagliptin is a dipeptidyl peptidase-4 (DPP-4) inhibitor, which exerts its action by slowing the inactivation of incretin hormones. Incretin hormones, including glucagon-like peptide-1(GLP-1) and glucose-dependent insulinotropic polypeptide (GIP), are released by the intestine throughout the day and levels are increased in response to a meal. These hormones are rapidly inactivated by the enzyme, DPP-4. The incretins are part of an endogenous system involved in the physiologic regulation of glucose homeostasis. When blood glucose concentrations are normal or elevated, GLP-1 and GIP increase insulin synthesis and release from pancreatic beta cells by intracellular signaling pathways involving cyclic AMP. GLP-1 also lowers glucagon secretion from pancreatic alpha cells, leading to reduced hepatic glucose production.

Metformin Hydrochloride is a member of biguanide class. The pharmacologic mechanism of action of Metformin is different from other classes of oral anti-hyperglycemic agents. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and increases peripheral glucose uptake and utilization.

Indications

Sitomet® is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both Sitagliptin and Metformin is appropriate.

Sitomet® is indicated as part of triple combination therapy with sulfonylurea as an adjunct to diet and exercise in patients with type 2 diabetes mellitus inadequately controlled with any two of the three agents: Metformin, Sitagliptin or a Sulfonylurea.

Dosage and administration

Dose of this combination should be individualized on the basis of the patient's current regimen, effectiveness and tolerability while not exceeding the maximum recommended daily dose of 100 mg Sitagliptin and 2000 mg Metformin.

Sitagliptin and Metformin combination should generally be given twice daily with meals, with gradual dose escalation, to reduce the gastrointestinal (GI) side effects due to Metformin.

Patients not currently treated with Metformin: The recommended starting dose is 50 mg Sitagliptin/500 mg Metformin Hydrochloride twice daily, with gradual dose escalation recommended to reduce gastrointestinal side effects associated with Metformin.

***Patients already treated with Metformin*:** They should provide Sitagliptin dosed as 50 mg twice daily (100 mg total daily dose) and the dose of Metformin already being taken. For patients taking Metformin 850 mg twice daily, the recommended starting dose of this combination is 50 mg Sitagliptin/1000 mg Metformin Hydrochloride twice daily.

***Patients treated with an insulin secretagogue or insulin*:** Co-administration of the combination with an insulin secretagogue (e.g., sulfonylurea) or insulin may require lower doses of the insulin secretagogue or insulin to reduce the risk of hypoglycemia.

***Patients switching from co-administration of Sitagliptin and Metformin*: Sitomet®** may be initiated at the dose of Sitagliptin and Metformin already being taken.

***Patients inadequately controlled on dual combination therapy*:** Combination therapy with any two of the following three anti-hyperglycemic agents: Sitagliptin, Metformin or a Sulfonylurea, the usual starting dose of **Sitomet®** should provide Sitagliptin dosed as 50 mg twice daily (100 mg total daily dose). In determining the starting dose of Metformin component, the patient's level of glycemic control and current dose (if any) of Metformin should be considered.

Use in pregnancy & lactation
The safety of the combination (Sitagliptin & Metformin) in pregnant women is not known. The combination of Sitagliptin & Metformin should be used during pregnancy only if clearly needed.

It is not known whether Sitagliptin is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when this combination is administered to a nursing woman.

Geriatric use
Because Sitagliptin and Metformin are substantially excreted by the kidney, and because aging can be associated with reduced renal function, combination of Sitagliptin and Metformin should be used with caution as age increases. Care should be taken in dose selection and should be based on careful and regular monitoring of renal function.

Pediatric use
Safety and effectiveness of Sitagliptin and Metformin in pediatric patients under 18 years of age have not been established.

Precautions
The combination of Sitagliptin and Metformin should not be used in patients with hepatic disease. Before initiating the combination and at least annually thereafter, renal function must be assessed and should be verified as normal. The combination may be needed to discontinue and temporarily insulin may be used during periods of stress and decreased intake of fluids and food as may be occurred with fever, trauma, infection or surgery.

Side effects
Side effects like upper respiratory tract infection, nasopharyngitis, and headache can occur. Hypoglycemia occurs in patients treated with the combination of Sitagliptin and Sulfonylurea, with or without Metformin.

The common side effects of Metformin are diarrhea, nausea/vomiting, flatulence, abdominal discomfort, indigestion, asthenia and headache.

Contraindications

Sitagliptin and Metformin combination is contraindicated in patients with renal disease or renal dysfunction, e.g, as suggested by serum creatinine levels 1.5 mg/dL (males), 1.4 mg/dL (females); acute or chronic metabolic acidosis, including diabetic ketoacidosis, with or without coma; history of a serious hypersensitivity reaction to the combination or Sitagliptin, such as anaphylaxis or angioedema.

Drug interactions
Cationic drugs (e.g., amiloride, digoxin, morphine, procainamide, quinidine, quinine, ranitidine, 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. Co-administration of Digoxin and Sitagliptin may slightly increase the mean peak drug concentration of Digoxin. But no dosage adjustment of Digoxin or Sitagliptin is recommended.

Pharmaceutical precautions
Store in a cool and dry place. Protect from light. Keep away from the reach of children.

Presentation :
Sitomet® 50/500 tablet: Each coated tablet contains Sitagliptin 50 mg as Phosphate Monohydrate INN and Metformin Hydrochloride BP 500 mg.

Sitomet® 50/1000 tablet: Each coated tablet contains Sitagliptin 50 mg as Phosphate Monohydrate INN and Metformin Hydrochloride BP 1000 mg.

Package quantities
Sitomet® 50/500 tablet: Each carton contains 30 tablets in blister pack.

Sitomet® 50/1000 tablet: Each carton contains 10 tablets in blister pack.

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