

# Sensimet<sup>®</sup>

Rosiglitazone and Metformin HCl BP

## Composition:

**Sensimet<sup>®</sup> 1:** Each film coated tablet contains Rosiglitazone 1 mg as Rosiglitazone maleate INN and Metformin Hydrochloride BP 500 mg.

**Sensimet<sup>®</sup> 2:** Each film coated tablet contains Rosiglitazone 2 mg as Rosiglitazone maleate INN and Metformin Hydrochloride BP 500 mg.

## Pharmacology:

Combination of two antidiabetic agents with different mechanisms of action to improve glycemic control in patients with type 2 diabetes: Rosiglitazone maleate, a member of the thiazolidinedione class, and Metformin hydrochloride, a member of the biguanide class. Thiazolidinediones are insulin sensitizing agents that act primarily by enhancing peripheral glucose utilization, whereas biguanides act primarily by decreasing endogenous hepatic glucose production.

Rosiglitazone is a highly selective and potent agonist for the peroxisome proliferator-activated receptor-gamma (PPAR $\gamma$ ). Activation of PPAR $\gamma$  nuclear receptors regulates the transcription of insulin-responsive genes involved in the control of glucose production, transport, and utilization. In addition, PPAR $\gamma$ -responsive genes also participate in the regulation of fatty acid metabolism.

The pharmacologic mechanism of action of Metformin is different from other classes of oral antihyperglycemic agents. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and increases peripheral glucose uptake and utilization. Unlike sulfonylureas, With Metformin therapy, insulin secretion remains unchanged while fasting insulin levels and day-long plasma insulin response may actually decrease.

## Indication and usage:

**Sensimet<sup>®</sup>** is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus who are already treated with combination Rosiglitazone and Metformin or who are not adequately controlled on Metformin alone.

## Dosage and administration:

The selection of the dose of **Sensimet<sup>®</sup>** should be based on the patient's current doses of Rosiglitazone and/or Metformin. The safety and efficacy of **Sensimet<sup>®</sup>** as initial therapy for patients with type 2 diabetes mellitus have not been established.

The following recommendations regarding the use of **Sensimet<sup>®</sup>** in patients inadequately controlled on Rosiglitazone and Metformin monotherapies are based on clinical practice experience with Rosiglitazone and Metformin combination therapy.

- The dosage of antidiabetic therapy with **Sensimet**<sup>®</sup> should be individualized on the basis of effectiveness and tolerability while not exceeding the maximum recommended daily dose of 8 mg/2,000 mg.
- **Sensimet**<sup>®</sup> should be given in divided doses with meals, with gradual dose escalation. This reduces GI side effects (largely due to Metformin) and permits determination of the minimum effective dose for the individual patient.
- Sufficient time should be given to assess adequacy of therapeutic response. Fasting plasma glucose (FPG) should be used to determine the therapeutic response to **Sensimet**<sup>®</sup>. After an increase in Metformin dosage, dose titration is recommended if patients are not adequately controlled after 1 to 2 weeks. After an increase in Rosiglitazone dosage, dose titration is recommended if patients are not adequately controlled after 8 to 12 weeks.

For patients inadequately controlled on Metformin monotherapy: The usual starting dose of **Sensimet**<sup>®</sup> is 4 mg Rosiglitazone (total daily dose) plus the dose of Metformin already being taken.

For patients inadequately controlled on Rosiglitazone monotherapy: The usual starting dose of **Sensimet**<sup>®</sup> is 1,000 mg Metformin (total daily dose) plus the dose of Rosiglitazone already being taken.

Starting Dose of **Sensimet**<sup>®</sup>

PRIOR THERAPY	Usual <b>Sensimet</b> <sup>®</sup> Starting Dose	
	Tablet strength	No. of Tablets
Metformin HCl  1,000 mg/day 2,000 mg/day	2 mg/500 mg 2 mg/1,000 mg	1 tablet twice a day 1 tablet twice a day
Rosiglitazone  4 mg/day 8 mg/day	2 mg/500 mg 4 mg/500 mg	1 tablet twice a day 1 tablet twice a day

**Contraindication:** Combination of Rosiglitazone and Metformin tablets are contraindicated in patients with:

- Renal disease or renal dysfunction which may also result from conditions such as cardiovascular collapse (shock), acute myocardial infarction, and septicemia
- Congestive heart failure requiring pharmacologic treatment.
- Known hypersensitivity to Rosiglitazone maleate or Metformin hydrochloride.
- Acute or chronic metabolic acidosis, including diabetic ketoacidosis, with or without coma. Diabetic ketoacidosis should be treated with insulin.

Combination of Rosiglitazone and Metformin should be temporarily discontinued in patients undergoing radiologic studies involving intravascular administration of iodinated contrast materials, because use of such products may result in acute alteration of renal function.

**Adverse reactions:**

The incidence and types of adverse events reported in clinical trials of Rosiglitazone as monotherapy are upper respiratory tract infection, headache, back pain, hyperglycemia, fatigue, sinusitis, diarrhea, and hypoglycemia. Adverse reactions reported in greater than 5% of the Metformin patients, and that were more common in Metformin- than placebo-treated patients are diarrhea, nausea, vomiting, flatulence, asthenia, indigestion, abdominal discomfort, headache.

**Precaution:**

When a patient stabilized on any diabetic regimen is exposed to stress such as fever, trauma, infection, or surgery, a temporary loss of glycemic control may occur. At such times, it may be necessary to withhold combination of Rosiglitazone and Metformin and temporarily administer insulin. Combination of Rosiglitazone and Metformin may be reinstated after the acute episode is resolved. Combination of Rosiglitazone and Metformin should be used with caution in patients with edema.

**Drug Interactions:**

If an inhibitor or an inducer of CYP2C8 (such as gemfibrozil or rifampin) is started or stopped during treatment with Rosiglitazone, changes in diabetes treatment may be needed based upon clinical response.

Although drug interactions with cationic drugs (e.g., amiloride, digoxin, morphine, procainamide, quinidine, quinine, ranitidine, triamterene, trimethoprim, and vancomycin) remain theoretical (except for cimetidine), careful patient monitoring and dose adjustment of combination of Rosiglitazone and Metformin and/or the interfering drug is recommended in patients who are taking cationic medications that are excreted via the proximal renal tubular secretory system.

When drugs that produce hyperglycemia which may lead to loss of glycemic control are administered to a patient receiving combination of Rosiglitazone and Metformin, the patient should be closely observed to maintain adequate glycemic control.

**Use in pregnancy and lactation:**

Pregnancy Category C: Because current information strongly suggests that abnormal blood glucose levels during pregnancy are associated with a higher incidence of congenital anomalies as well as increased neonatal morbidity and mortality, most experts recommend that insulin monotherapy be used during pregnancy to maintain blood glucose levels as close to normal as possible. Combination of Rosiglitazone and Metformin should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus. There are no adequate and well-controlled studies in pregnant women with combination of Rosiglitazone and Metformin or its individual components.

It is not known whether Rosiglitazone and/or Metformin are excreted in human milk. Because many drugs are excreted in human milk, combination of Rosiglitazone and Metformin should not be administered to a nursing woman.

**Pediatric Use:**

Safety and effectiveness of combination of Rosiglitazone and Metformin in pediatric patients have not been established.

**Geriatric Use:**

Because aging is associated with reduced renal function, combination of Rosiglitazone 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. Generally, elderly patients should not be titrated to the maximum dose of combination of Rosiglitazone and Metformin.

**Warnings:**

Lactic acidosis is a rare, but serious, metabolic complication that can occur due to Metformin accumulation during treatment with combination of Rosiglitazone and Metformin. The risk of lactic acidosis increases with the degree of renal dysfunction and the patient's age. The risk of lactic acidosis may, therefore, be significantly decreased by regular monitoring of renal function in patients taking combination of Rosiglitazone and Metformin and by use of the minimum effective dose of combination of Rosiglitazone and Metformin.

In particular, treatment of the elderly should be accompanied by careful monitoring of renal function. Treatment with combination of Rosiglitazone and Metformin should not be initiated in patients  $\geq 80$  years of age unless measurement of creatinine clearance demonstrates that renal function is not reduced, as these patients are more susceptible to developing lactic acidosis. In addition, combination of Rosiglitazone and Metformin should be promptly withheld in the presence of any condition associated with hypoxemia, dehydration, or sepsis. Because impaired hepatic function may significantly limit the ability to clear lactate, combination of Rosiglitazone and Metformin should generally be avoided in patients with clinical or laboratory evidence of hepatic disease.

**Storage:**

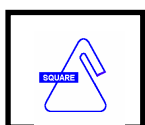
Store in a cool and dry place. Protect from light and moisture.

**How supplied:**

**Sensimet<sup>®</sup> 1:** Each box contains 3x10 Tablets in blister pack

**Sensimet<sup>®</sup> 2:** Each box contains 3x10 Tablets in blister pack

**Manufactured by:**



**SQUARE**  
*PHARMACEUTICALS LTD.*  
*BANGLADESH*

® Register