

Sensulin[®]

Rosiglitazone

Composition:

Sensulin[®] 2 : Each film coated tablet contains Rosiglitazone 2 mg as Rosiglitazone maleate INN.

Sensulin[®] 4 : Each film coated tablet contains Rosiglitazone 4 mg as Rosiglitazone maleate INN.

Pharmacology:

Rosiglitazone, a member of the thiazolidinedione class of antidiabetic agents, improves glycemic control by improving insulin sensitivity. Rosiglitazone is a highly selective and potent agonist for the peroxisome proliferator-activated receptor-gamma (PPAR- γ). In humans, PPAR receptors are found in key target tissues for insulin action such as adipose tissue, skeletal muscle, and liver. Activation of PPAR- γ nuclear receptors regulates the transcription of insulin-responsive genes involved in the control of glucose production, transport, and utilization. In addition, PPAR- γ -responsive genes also participate in the regulation of fatty acid metabolism. Pharmacological studies in animal models indicate that Rosiglitazone improves sensitivity to insulin in muscle and adipose tissue and inhibits hepatic gluconeogenesis. Rosiglitazone maleate is not chemically or functionally related to the sulfonylureas, the biguanides, or the alpha-glucosidase inhibitors.

Indication and Usage:

Sensulin[®] (Rosiglitazone) is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.

Sensulin[®] is indicated-

- as monotherapy.
- for use in combination with a sulfonylurea, metformin, or insulin when diet, exercise, and a single agent do not result in adequate glycemic control.
- also for use in combination with a sulfonylurea plus metformin when diet, exercise, and both agents do not result in adequate glycemic control.

Dosage and Administration:

The management of antidiabetic therapy should be individualized. **Sensulin[®]** (Rosiglitazone) may be administered either at a starting dose of 4 mg as a single daily dose or divided and administered in the morning and evening. For patients who respond inadequately following 8 to 12 weeks of treatment, as determined by reduction in FPG, the dose may be increased to 8 mg daily as monotherapy or in combination with metformin, sulfonylurea, or sulfonylurea plus metformin. **Sensulin[®]** may be taken with or without food.

Monotherapy: The usual starting dose of Rosiglitazone is 4 mg administered either as a single dose once daily or in divided doses twice daily. In clinical trials, the 4 mg twice daily regimen resulted in the greatest reduction in FPG and HbA_{1c}.

Combination therapy: When Rosiglitazone is added to existing therapy, the current dose(s) of the agent(s) can be continued upon initiation of Rosiglitazone therapy.

Sulfonylurea: When used in combination with sulfonylurea, the usual starting dose of Rosiglitazone is 4 mg administered as either a single dose once daily or in divided doses twice daily. If patients report hypoglycemia, the dose of the sulfonylurea should be decreased.

Metformin: The usual starting dose of Rosiglitazone in combination with metformin is 4 mg administered as either a single dose once daily or in divided doses twice daily. It is unlikely that the dose of metformin will require adjustment due to hypoglycemia during combination therapy with Rosiglitazone.

Insulin: For patients stabilized on insulin, the insulin dose should be continued upon initiation of therapy with Rosiglitazone. Rosiglitazone should be dosed at 4 mg daily. Doses of Rosiglitazone greater than 4 mg daily in combination with insulin are not currently indicated. It is recommended that the insulin dose be decreased by 10% to 25% if the patient reports hypoglycemia or if FPG concentrations decrease to less than 100 mg/dL. Further adjustments should be individualized based on glucose-lowering response.

Sulfonylurea plus metformin: The usual starting dose of Rosiglitazone in combination with a sulfonylurea plus metformin is 4 mg administered as either a single dose once daily or in divided doses twice daily. If patients report hypoglycemia, the dose of the sulfonylurea should be decreased.

Maximum Recommended Dose: The dose of Rosiglitazone should not exceed 8 mg daily, as a single dose or divided twice daily. The 8 mg daily dose has been shown to be safe and effective in clinical studies as monotherapy and in combination with metformin, sulfonylurea, or sulfonylurea plus metformin. Doses of Rosiglitazone greater than 4 mg daily in combination with insulin are not currently indicated. No dosage adjustments are required for the elderly. No dosage adjustment is necessary when Rosiglitazone is used as monotherapy in patients with renal impairment.

Contraindication:

Rosiglitazone is contraindicated in patients with known hypersensitivity to this product or any of its components.

Adverse Reaction:

The incidence and types of adverse events reported in clinical trials of Rosiglitazone as monotherapy are similar to that of placebo. Overall, the types of adverse experiences reported when Rosiglitazone was used in combination with a sulfonylurea or metformin were similar to those during monotherapy with Rosiglitazone. Events of anemia and edema tended to be reported more frequently at higher doses, and were generally mild to moderate in severity and usually did not require discontinuation of treatment with Rosiglitazone.

Precaution:

Due to its mechanism of action, Rosiglitazone is active only in the presence of endogenous insulin. Therefore, Rosiglitazone should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. Rosiglitazone, like other thiazolidinediones, alone or in combination with other antidiabetic agents, can cause fluid retention, which may exacerbate or lead to heart failure. Patients should be observed for signs and symptoms of heart failure. In combination with insulin, thiazolidinediones may also increase the risk of other cardiovascular adverse events. Rosiglitazone should be discontinued if any deterioration in cardiac status occurs. Rosiglitazone should be used with caution in patients with edema. Liver enzymes should be checked prior to the initiation of therapy with Rosiglitazone in all patients and periodically thereafter per the clinical judgement of the healthcare professional. Therapy with Rosiglitazone should not be initiated in patients with increased baseline liver enzyme levels (ALT >2.5X upper limit of normal).

Drug Interaction:

In vitro drug metabolism studies suggest that Rosiglitazone does not inhibit any of the major P450 enzymes at clinically relevant concentrations. A decrease in the dose of Rosiglitazone may be needed when gemfibrozil is introduced. Dosage adjustment is also required when administered with rifampin. Rosiglitazone was shown to have no clinically relevant effect on the pharmacokinetics of nifedipine and oral contraceptives.

Use in Pregnancy & Lactation:

There are no adequate and well-controlled studies in pregnant women. Rosiglitazone should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus. Drug-related material was detected in milk from lactating rats. It is not known whether Rosiglitazone is excreted in human milk. Because many drugs are excreted in human milk, Rosiglitazone should not be administered to a nursing woman.

Use in Children:

The safety and effectiveness of Rosiglitazone in pediatric patients have not been established.

Storage:

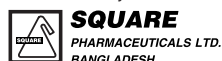
Protect from light and moisture. Store in a cool and dry place.

How Supplied:

Sensulin[®] 2 : Each box contains 3 x 10's in blister strip pack.

Sensulin[®] 4 : Each box contains 3 x 10's in blister strip pack.

Manufactured by:



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