

Glyros®

Glimepiride USP and Rosiglitazone maleate INN

COMPOSITION

Glyros® 1 tablet: Each film coated tablet contains Glimepiride USP 1 mg and Rosiglitazone 4 mg as Rosiglitazone maleate INN.

Glyros® 2 tablet: Each film coated tablet contains Glimepiride USP 2 mg and Rosiglitazone 4 mg as Rosiglitazone maleate INN.

PHARMACOLOGY

Glyros® combines 2 antidiabetic agents with complementary mechanisms of action to improve glycemic control in patients with type 2 diabetes: Glimepiride, a member of the sulfonylurea class, and Rosiglitazone maleate, a member of the thiazolidinedione class.

The primary mechanism of action of Glimepiride in lowering blood glucose appears to be dependent on stimulating the release of insulin from functioning pancreatic beta cells. In addition, extrapancreatic effects may also play a role in the activity of sulfonylureas such as Glimepiride. Administration of Glimepiride can lead to increased sensitivity of peripheral tissues to insulin.

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

INDICATION AND USAGE

Glyros® (Combination of Glimepiride and Rosiglitazone) is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes who are already treated with a combination of Rosiglitazone and sulfonylurea as separate tablet or who are not adequately controlled on a sulfonylurea alone or for those patients who have initially responded to Rosiglitazone alone and require additional glycemic control.

DOSAGE AND ADMINISTRATION

Glyros® should be given once daily with the first meal of the day. The dosage of antidiabetic therapy with **Glyros®** should be individualized on the basis of effectiveness and tolerability. No exact dosage relationship exists between **Glyros®** and other antidiabetic agents.

For patients inadequately controlled on sulfonylurea monotherapy or who have initially responded to Rosiglitazone alone and require additional glycemic control, the usual starting dose of **Glyros®** is 1 mg/4 mg or 2 mg/4 mg once daily.

When switching from combination therapy of Glimepiride and Rosiglitazone as separate tablets, the usual starting dose of **Glyros®** is the dose of Glimepiride and Rosiglitazone already being taken. The maximum recommended daily dose of **Glyros®** is 4 mg of Glimepiride and 8 mg of Rosiglitazone.

For patients previously treated with sulfonylurea monotherapy switched to **Glyros®**, it may take 2 weeks to see a reduction in blood glucose and 2 to 3 months to see the full effect of the Rosiglitazone component. If additional glycemic control is needed, the dose of the Glimepiride component may be increased. As with other sulfonylurea-containing antidiabetic agents, no transition period is necessary when transferring patients to **Glyros®**.

For patients previously treated with thiazolidinedione monotherapy switched to **Glyros®**, dose titration is recommended if patients are not adequately controlled after 1 to 2 weeks.

PRECAUTIONS

Hypoglycemia: **Glyros®** is a combination tablet containing Glimepiride and Rosiglitazone. All sulfonylurea drugs are capable of producing severe hypoglycemia. Proper patient selection, dosage, and instructions are important to avoid hypoglycemic episodes. Debilitated or malnourished patients and those with adrenal, pituitary, renal, or hepatic insufficiency are particularly susceptible to the hypoglycemic action of glucose lowering drugs. **Loss of Control of Blood Glucose:**

When a patient stabilized on any antidiabetic 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 Glimepiride and Rosiglitazone and temporarily administer insulin. **Edema:** Combination of Glimepiride and Rosiglitazone should be used with caution in patients with edema.

Since thiazolidinediones, including Rosiglitazone can cause fluid retention, which can exacerbate or lead to congestive heart failure, Combination of Glimepiride and Rosiglitazone should be used with caution in patients at risk for heart failure. **Weight Gain:** Dose-related weight gain was seen with Rosiglitazone alone and in combination with other hypoglycemic agents. The mechanism of weight gain is unclear but probably involves a combination of fluid retention and fat accumulation. **Hepatic Effects:** Liver enzymes should be checked prior to the initiation of therapy with combination of Glimepiride and Rosiglitazone in all patients and periodically thereafter per the clinical judgment of the healthcare professional.

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Therapy with combination of Glimepiride and Rosiglitazone should not be initiated in patients with increased baseline liver enzyme levels (ALT >2.5X upper limit of normal). If ALT levels remain >3X the upper limit of normal, therapy with combination of Glimepiride and Rosiglitazone should be discontinued. If any patient develops symptoms suggesting hepatic dysfunction, which may include unexplained nausea, vomiting, abdominal pain, fatigue, and anorexia, and/or dark urine, liver enzymes should be checked.

CONTRAINDICATIONS

Combination of Glimepiride and Rosiglitazone is contraindicated in patients with:

- Known hypersensitivity to Glimepiride or Rosiglitazone or any of the components of combination of Glimepiride or Rosiglitazone.
- Diabetic ketoacidosis, with or without coma. This condition should be treated with insulin.

Use in Pregnancy:

Pregnancy: Pregnancy Category C. Combination of Glimepiride and Rosiglitazone should not be used during pregnancy. Most experts recommend that insulin monotherapy be used during pregnancy to maintain blood glucose levels as close to normal as possible. **Nursing mothers:** No studies have been conducted with combination of Glimepiride or Rosiglitazone. It is not known whether Glimepiride and/or Rosiglitazone are excreted in human milk. Because many drugs are excreted in human milk, combination of Glimepiride or Rosiglitazone should not be administered to a nursing woman.

Use in Pediatric patients:

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

Use in Geriatric patients:

Glimepiride: The drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Rosiglitazone: Age does not significantly affect the pharmacokinetics of Rosiglitazone. Therefore, no dosage adjustments are required for the elderly.

ADVERSE EFFECTS

Glimepiride: Hypoglycemia, dizziness, asthenia, headache, nausea, allergic skin reactions, e.g., pruritus, erythema, urticaria, and morbilliform or maculopapular eruptions. **Rosiglitazone:** The most common adverse experiences with Rosiglitazone are upper respiratory tract infection, injury, and headache. Events of anemia and edema tended to be reported more frequently at higher doses, angioedema and urticaria have been reported rarely.

DRUG INTERACTION

Glimepiride: The hypoglycemic action of sulfonylureas may be potentiated by certain drugs, including NSAIDs and other drugs that are highly protein bound, such as salicylates, sulfonamides, chlormphenicol, coumarins, probenecid, MAO inhibitors, beta adrenergic blocking agents, and clarithromycin. Certain drugs tend to produce hyperglycemia and may lead to loss of control. These drugs include thiazides, and other diuretics, corticosteroids, phenothiazines, thyroid products, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, and isoniazide. A potential interaction between oral miconazole and oral hypoglycemic drugs leading to severe hypoglycemia has been reported. **Rosiglitazone:** Rosiglitazone was shown to have no clinically relevant effect on the pharmacokinetics of nifedipine and oral contraceptives (ethinyl estradiol and norethindrone). A decrease in the dose of Rosiglitazone may be needed when gemfibrozil is introduced. Rosiglitazone did not alter the steady-state pharmacokinetics of digoxin in healthy volunteers. Rosiglitazone had no clinically relevant effect on the steady-state pharmacokinetics of warfarin.

STORAGE

Store in a cool and dry place, protected from light. Keep out of reach of children.

HOW SUPPLIED

Glyros® 1 tablet: Each box contains 3 x 10's tablet in blister pack.

Glyros® 2 tablet: Each box contains 3 x 10's tablet in blister pack

Manufactured by :



SQUARE
PHARMACEUTICALS LTD.
BANGLADESH

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