

# Premil®

(Repaglinide Tablet )

## Description

The active ingredient of Premil is Repaglinide. Repaglinide belongs to a new class of oral antidiabetic drug called meglitinide which stimulates insulin release from  $\beta$  cells of pancreas.

## Indications

Premil is indicated as an adjunct to diet and exercise to lower the blood glucose level in patients with type 2 diabetes mellitus (NIDDM) whose hyperglycaemia cannot be controlled satisfactorily by diet and exercise alone. It is also indicated for use in combination with Metformin to lower blood glucose in patients whose hyperglycaemia cannot be controlled by exercise, diet, and either Repaglinide or Metformin alone. Repaglinide binds to specific receptors in the  $\beta$  cell membrane leading to the closure of ATP dependent  $K^+$  channels and the depolarisation of  $\beta$  cell membrane. This in turn, leads to  $Ca^{++}$  influx, increased intracellular  $Ca^{++}$  and the stimulation of insulin secretion.

## Dosage and Administration

Premil has to be taken just before or up to 30 minutes before the meal. Premil can be taken two, three or four times a day, depending on how many meals are taken. If a meal is missed, Premil should also be avoided. If an extra meal is taken, an extra dose of Premil should be taken with that meal. If a dose of Premil is missed, it should not be taken between meals. Rather the usual dose should be taken before the next meal.

The dose ranges from 0.5 to 4 mg before each meal. The starting dose of Repaglinide in patients with  $HbA_{1c} < 8\%$  is 0.5 mg before each meal. In patients with  $HbA_{1c} > 8\%$  the starting dose is 1 or 2 mg before each meal. The dose may be increased gradually up to 4 mg before each meal.

## Contraindications

Premil is contraindicated in patients with diabetic ketoacidosis, with or without coma, in patients with type I diabetes and in patients with known hypersensitivity to any of the components of the product.

## **Precautions**

Premil should also be used with caution in renal and hepatic insufficiency.

## **Drug Interactions**

The dose of Premil may need to be adjusted, if taken with other medications. The possible interactions of Repaglinide with other drugs are : i) Inhibitors of the cytochrome P450 enzyme system (azole antifungals and macrolides) may lead to lower Repaglinide clearance and longer half life. ii) Inducers of the cytochrome P450 enzyme system (Rifampin, Phenobarbital, Carbamazepine, Troglitazone, etc.) may accelerate Repaglinide metabolism and shorten its effect. iii) Cimetidine has no significant effect on Repaglinide absorption or clearance. iv) Repaglinide has no significant effect on Digoxin, Theophyllin, or Warfarin. v) Highly protein bound drugs (e.g., NSAIDs) may increase the plasma level of unbound Repaglinide and potentiate its glucose lowering effect. Thus, co-administration of these drugs with Repaglinide may increase the risk of hypoglycaemia. vi) The risk of hypoglycaemia may also be increased when hypoglycaemic agents are co-administered with certain drugs such as salicylates, sulphonamides, Chloramphenicol, coumarins, Probenecid, monoamine oxidase (MAO) inhibitors, and  $\beta$  adrenergic blockers.

## **Side Effects**

Hypoglycaemia is possible with all blood glucose lowering drugs. If there are symptoms of low blood glucose (for example, headache, dizziness, tiredness, nervousness or shakiness, rapid heartbeat, or nausea), blood glucose should be tested right away. If it is low (less than 70 mg/dl on a home glucose meter), a simple carbohydrate food (for example, orange juice, quick dissolving sugar, candies, or glucose tablets) should be taken. If the symptoms do not go away, doctor should be informed.

Some of the other common symptoms reported by patients taking Repaglinide include cold and flu-like symptoms, diarrhoea, joint ache, and back pain.

There is some evidence that oral anti-diabetic drugs may increase the risk of heart problems. But experts are not sure what the real risk is, if any, from taking oral anti-diabetic drugs.

## **Use in Special Populations**

*Pregnancy and lactation* : In pregnancy, safety of Repaglinide has not been established. Hence, Premil should be used during pregnancy only if it is clearly needed. It is not known whether Repaglinide is excreted in human milk. Because many drugs are excreted in human milk and because of potential for serious adverse reactions in nursing infants from Repaglinide, a decision should be made whether to discontinue nursing or the drug, taking into account the importance of the drug to the mother.

## **Commercial Packs**

Premil® 0.5 Tablet : Box containing 30 tablets in 3 x 10's blister strips. Each tablet contains Repaglinide USP 0.5 mg.

Premil® 1 Tablet : Box containing 30 tablets in 3 x 10's blister strips. Each tablet contains Repaglinide USP 1 mg.

Premil® 2 Tablet : Box containing 30 tablets in 3 x 10's blister strips. Each tablet contains Repaglinide USP 2 mg.