Cilostazol

Clazol

50 mg Tablet
100 mg Tablet
ANTI-PLATELET

FORMULATION
Each tablet contains:
Cilostazol……..…… 50 mg
Cilostazol…… 100 mg

CHEMISTRY
Cilostazol is 6-[4-(1-Cyclohexyl-1Htetrazol-5-yl) butoxy]-3,4-dihydrocarbostyril.

CLINICAL PHARMACOLOGY
The mechanism of the effects of Cilostazol on the symptoms of intermittent claudication is not fully understood. Cilostazol and several of its metabolites are cyclic AMP (cAMP) phosphodiesterase III inhibitors (PDE III inhibitors), inhibiting phosphodiesterase activity and suppressing cAMP degradation with a resultant increase in cAMP in platelets and blood vessels, leading to inhibition of platelet aggregation and vasodilation.
Cilostazol reversibly inhibits platelet aggregation induced by a variety of stimuli, including thrombin, A.P. collagen, arachidonic acid, epinephrine and shear stress.
Cilostazol affects both vascular body and cardiovascular function. It produces non-homogenous dilation of vascular beds, with greater dilation in femoral body than in vertebral, carotid or superior mesenteric arteries. Renal arteries were not responsive to the effects of Cilostazol.

PHARMACOKINETICS
Cilostazol is absorbed following oral administration and absorption is increased if taken with a high fat meal. Cilostazol is extensively metabolized in the liver to both active and inactive metabolites, which are predominantly excreted in the urine (74%) with the remainder in the faeces (20%). The active metabolites have apparent elimination half-lives of 11 to 13 hours. Cilostazol is 95 to 98% protein bound.

INDICATIONS
Cilostazol is a phosphodiesterase inhibitor with antiplatelet and vasodilating activity. It is used in the management of peripheral vascular disease. It is also indicated for the reduction of symptoms of intermittent claudication, as indicated by an increased walking distance.

CONTRAINDICATIONS
Cilostazol and several of its metabolites are inhibitors of phosphodiesterase III. Several drugs with this pharmacologic effect have caused decreased survival compared to placebo in patients with class III-IV congestive heart failure. It is contraindicated in patients with congestive heart failure of any severity.
Cilostazol is contraindicated in patients with haemostatic disorders or active pathologic bleeding peptic ulcer and intracranial bleeding. It also inhibits platelet aggregation in a reversible manner. Cilostazol is also contraindicated in patients with known or suspected hypersensitivity to any of its components.

ADVERSE EFFECTS
Adverse effects of Cilostazol include headache, dizziness, palpitations and diarrhea. Cardiovascular toxicity has been reported in animal studies of Cilostazol and prolonged oral use of other phosphodiesterase inhibitors (such as amrinone) for treatment of heart failure has been associated with increased mortality. The use of Cilostazol in patients with any degree of heart failure is therefore contraindicated.

PRECAUTIONS AND WARNINGS
Cilostazol is contraindicated in patients with congestive heart failure. In patients without congestive heart failure, the long-term effects of PDE III (including CILOSTAZOL) are unknown. Patients in the 3-6 month placebo-controlled trials of Cilostazol were relatively stable (no recent myocardial infarction or stokes, no rest pain or other signs of rapidly progressing disease) and only 19 patients died (0.7% in the placebo group and 0.8% in the group on Cilostazol). The calculated relative risk of death 1.2 has a wide 95% confidence limit (0.5-3.1). There are no data as to longer-term risk or risk in patients with more severe underlying heart disease.
Hematologic adverse reactions: Rare cases have been reported of thrombocytopenia or leukopenia progressing to agranulocytosis when Cilostazol was not immediately discontinued. The agranulocytosis, however, was reversible on discontinuation of Cilostazol.

DRUG INTERACTIONS
Cilostazol is extensively metabolized to active and inactive metabolites by cytochrome P450 isoenzymes, mainly CYP3A4 and to a lesser extent CYP2C19. Therefore concomitant administration of other drugs that inhibit or are metabolized by these hepatic enzymes may result in changes in plasma concentrations of either drug and, possibly, adverse effects. Grapefruit juice may also inhibit the metabolism of Cilostazol and concomitant administration should be avoided.
Caution should be exercised when Cilostazol is co administered with inhibitors of C.P.A. such as ketoconazole and erythromycin or inhibitors of CYP2C19 such as omeprazole. Pharmacokinetic studies have demonstrated that omeprazole and erythromycin significantly increased the systemic exposure of Cilostazol and/or its major metabolites. Population pharmacokinetic studies showed higher concentrations of Cilostazol among patients concurrently treated with ditiazem, an inhibitor of C.P.A.Cilostazol does not, however, appear to cause increased blood levels of drugs metabolized by CYP3A4, as it had no effect on lovastatin, a drug with metabolism very sensitive to C.P.A. inhibition.

DOSAGE AND ADMINISTRATION
The dose of Cilostazol for the reduction of symptoms of intermittent claudication is 100 mg orally twice daily, at least 30 minutes before or 2 hours after food. Response to treatment may occur in 2 to 4 weeks, but up to 12 weeks may be required. Or as prescribed by the physician.
A dose of 50mg twice daily should be considered during co administration of such inhibitors of CYP3A4 as ketoconazole, itraconazole, erythromycin and diltiazem and during co administration of such inhibitors of CYP2C19 as omeprazole.

OVERDOSAGE, SYMPTOMS & ANTIDOTE
Information on acute overdosage with Cilostazol in humans is limited. The signs and symptoms of an acute overdose can be anticipated to be those of excessive pharmacologic effect: severe headache, diarrhea, hypotension, tachycardia, and possibly cardiac arrhythmias. The patient should be carefully observed and given supportive treatment. Since Cilostazol is highly protein-bound, it is unlikely that it can be efficiently removed by hemodialysis or peritoneal dialysis. The oral LD50 of Cilostazol is >5.0 g/kg in mice and rats and >2.0 g/kg in dogs.

CAUTION
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

STORE AT TEMPERATURES NOT EXCEEDING 30°C.
PROTECT FROM LIGHT

AVAILABILITY
CILOSTAZOL (CLAZOL) 50 mg Tablet X 50 tablets/box in strip foil
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Manufactured by : Macleods Pharmaceuticals Limited.
Plot No. 25-27, Survey No. 366, Premier Industrial Estate
Kachigam, Daman 396210 (U.T.), India
Imported by : **OEP PHILIPPINES, INC.**
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