To be used by registered medical practitioner or laboratory only.

PRIMODIL

TABLETS

(Amlodipine Besilate Tablets)

COMPOSITION

Each uncoated tablet contains:

Amlodipine Besilate BP equivalent to Amlodipine 10mg

PRODUCT DESCRIPTION

Primodil 10 tablets

White, circular, flat, beveled edge, uncoated tablet with "medley" emblem debossed on one side & break line on other side

PHARMACOLOGY

Pharmacodynamics

Amlodipine is a dihydropyridine calcium antagonist (calcium ion antagonist or slow-channel blocker) that inhibits the transmembrane influx of calcium ions into vascular smooth muscle and cardiac muscle. The contractile processes of cardiac muscle and vascular smooth muscle are dependent upon the movement of extracellular calcium ions into these cells through specific ion channels. Amlodipine inhibits calcium ion influx across cell membranes selectively, with a greater effect on vascular smooth muscle cells than on cardiac muscle cells. Amlodipine is a peripheral arterial vasodilators that acts directly on vascular smooth muscle to cause a reduction in peripheral vascular resistance and reduction in blood pressure. It has favourable effects on renal haemodynamics & does not affect insulin levels.

Exertional Angina: In patients with exertional angina, Amlodipine reduces the total peripheral resistance (after – load) against which the heart works and reduces the rate pressure product, and thus myocardial oxygen demand, at any given level of exercise.

Vasospastic Angina: Amlodipine has been demonstrated to block constriction and restore blood flow in coronary arteries and arterioles in response to calcium, potassium epinephrine, serotonin, and thromboxane A_2 analog in experimental animal models and in human coronary vessels in vitro. This inhibition of coronary spasm is responsible for the effectiveness of Amlodipine in vasospastic (Prinzmetal's or variant) angina.

Pharmacokinetics

After oral administration of therapeutic doses of amlodipine besilate, absorption produces peak plasma concentrations between 6 and 12 hours. Absolute bioavailability has been estimated to be between 64 and 90%. The bioavailability of amlodipine besilate is not altered by the presence of food.

Amlodipine besilate is extensively (about 90%) converted to inactive metabolites via hepatic metabolism with 10% of the parent compound and 60% of the metabolites excreted in the urine. *Ex vivo* studies have shown that approximately 93% of the circulating drug is bound to plasma proteins in hypertensive patients. Elimination from the plasma is biphasic with a terminal elimination half-life of about 30-50 hours. Steady-state plasma levels of amlodipine besilate are reached after 7-8 days of consecutive daily dosing.

The pharmacokinetics of amlodipine besilate are not significantly influenced by renal impairment. Patients with renal failure may therefore receive the usual initial dose.

Elderly patients and patients with hepatic insufficiency have decreased clearance of amlodipine with a resulting increase in AUC of approximately 40-60%, and a lower initial dose may be required. A similar increase in AUC was observed in patients with moderate to severe heart failure.

INDICATION

PRIMODIL is indicated for the first line management of Hypertension, Stable angina, Variant/Prinzmetal's angina.

PRIMODIL may be used alone or in combination with other antihypertensive and/or antianginal drugs for effective management.

RECOMMENDED DOSAGE

Oral: Adults: For hypertension and angina pectoris 5mg once daily. Dosage may be increased maximum to 10mg once daily. For patients with hepatic dysfunction, initially, 2.5mg once daily.

MODE OF ADMINISTRATION

Oral

CONTRAINDICATIONS

Amlodipine is contraindicated in patients with a known sensitivity to hydropyridines, amlodipine, or any other inert ingredients.

PRECAUTIONS

General: Caution with any other peripheral vasodilator, should be exercised when administering Primodil, particularly in patients with severe aortic stenosis.

Use in patients with Congestive Heart Failure: In general, calcium channel blockers should be used with caution in patients with heart failure.

Patients with Hepatic Failure: Since Primodil is extensively metabolized by the liver and the plasma elimination half life (t ½) is 56 hours in patients with impaired hepatic function, caution should be exercised when administering Primodil to patients with severe hepatic impairment.

INTERACTION WITH OTHER MEDICAMENTS

Primodil potentiates the effects of thiazides and ACE inhibitors. No interaction with digoxin, cimetidine and warfarin has been reported.

PREGNANCY AND LACTATION

No evidence of teratogenicity or other embryo/fetal toxicity was found when pregnant rats or rabbits were treated orally with up to 10 mg/kg amlodipine (respectively 8 times and 23 times [based on patient weight of 50 kg] the maximum recommended human dose of 10 mg on a mg/m^2 basis) during their respective periods of major organogenesis. However, litter size was significantly decreased (by about 50%) and the number of intrauterine deaths was significantly increased (about 5-fold) in rats administered 10 mg/kg amlodipine for 14 days before mating and throughout mating and gestation. Amlodipine has been shown to prolong both the gestation period and the duration of labor in rats at this dose. There are no adequate and well-controlled studies in pregnant women. Amlodipine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

ADVERSE EFFECTS

The common side effects of PRIMODIL are ankle edema, headache, dizziness, somnolence, fatigue, nausea, flushing and palpitation. Their occurrence is dose-related and found more frequently in elderly. Pruritis, rash, dyspnoea, weakness, dyspepsia, muscle cramps, frequency of micturition/nocturia, cough impotence, asthma, epistaxis, nervousness and conjunctivitis occur less commonly.

OVERDOSE AND TREATMENT

Overdosage might be expected to cause excessive peripheral vasodilation with marked hypotention & possibly a reflex tachycardia. In humans, experience with intentional overdosage of Primodil is limited. If massive overdose should occur, active cardiac & respiratory monitoring should be instituted. Frequent blood pressure measurements are essential. Should hypotention occur, cardiovascular support including elevation of the extremities and the judicious administration of fluids should be initiated.If hypotention remains unresponsive to these conservative measures, administration of vasopressors (such as phenylephrine) should be considered with attention to circulating volume and urine output. Intravenous calcium gluconate may help to reverse the effects of calcium entry blockade. As Primodil is highly protein bound, hemodialysis is not likely to be of benefit.

STORAGE

Store at a temperature not exceeding 30°C, in a dry place.

SHELF-LIFE

36 months from the date of manufacture.

PRESENTATION

Primodil tablets 10 mg: Blister pack of 10 tablets. Box containing 10 blisters of 10 tablets each

DATE OF REVISION : 14 December 2023

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Manufactured by :

MEDLEY PHARMACEUTICALS LTD.

Plot 18 &19, Zari Causeway Road, Kachigam, Daman, IN-396210. INDIA

Regd. Office : Medley House, D2, MIDC Area, Andheri (East), Mumbai - 400 093, INDIA.

Product Registration Holder :

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Primodil

TABLETS

(AMLODIPINE BESILATE TABLETS)

SAME SIZE DESIGN, SIZE: 210 x 137 MM