AMLOMED 5 / AMLOMED 10

Amlodipine 5 mg/10 mg Tablets

DESCRIPTION

Tablet

AMLOMED 5: White to off white circular uncoated tablets.

AMLOMED 10: White to off white circular uncoated tablets with a breakline on one side and plain on the other side.

COMPOSITION

Each Uncoated Tablet Contains:
AMLOMED 5: Amlodipine Besylate USP equivalent to Amlodipine 5 mg
AMLOMED 10: Amlodipine Besylate USP equivalent to Amlodipine 10 mg

MODE OF ACTION

Amlodipine is a dihydropyridine calcium-ion influx inhibitor that inhibits the transmembrane influx of calcium ions into cardiac and vascular smooth muscle tissues. It's antihypertensive action is as a result of it's direct relaxant effect on vascular smooth muscle. It is used in the management of hypertension and stable angina in adults, binds to both dihydropyridine and nondihydropyridine binding sites. The contractile process of cardiac muscle and vascular smooth muscle are dependent upon the movement of extra cellular calcium ions into these cells through specific ion channels, inhibits calcium ion influx across cell membranes selectively with a great effect on vascular smooth muscle cells than on cardiac muscle cells. Serum calcium concentration is not affected by it's kinetic interaction with calcium channel receptor is characterized by a gradual rate of association and dissociation with the receptor binding site, resulting in gradual onset of action.

Amlodipine is a peripheral arterial vasodilator that acts directly on vascular smooth muscle causing reduction of blood pressure. The precise mechanisms of action in relieving the angina have not been fully delineated.

SUMMARY OF PHARMACODYNAMICS AND PHARMACOKINETICS

Amlodipine is well absorbed following oral administration with peak blood concentrations occurring after 6 to 12 hours, The bioavailability has been estimated between 64 to 90% and it is not altered by the presence of food. 93% of the drug is bound to plasma proteins. It has a prolonged terminal elimination half life of 35 to 50 hours and steady-state of plasma concentrations are achieved after 7 to 8 days of administration.

Amlodipine is extensively metabolized in the liver, 60% of the metabolites are excreted in urine together with 10% of unchanged drug.

Elderly patients have decreased clearance of with a resulting increase in AUC of approximately 40-60% and a lower initial dose may be required.

INDICATIONS

Amlodipine is indicated for the first line treatment of hypertension and can be used as the solo agent to control blood pressure in the majority of patients. Patients not adequately controlled on a single antihypertensive agent may benefit from the addition of amlodipine, which has been used in combination with a thiazide diuretic, alpha blockers, beta adrenoceptor blocking agent, or an angiotensin-converting enzyme inhibitor. Amlodipine is indicated for the first line treatment of myocardial ischemia, whether due to fixed obstruction (stable angina) and/or vasospasm/vasoconstriction (Prinzmetal's or variant angina) of coronary vasculature. Amlodipine may be used where the clinical presentation suggests a possible vasospastic/vasoconstrictive component but where vasospasm/vasoconstriction has not been confirmed. Amlodipine may be used alone, as monotherapy, or in combination with other antianginal drugs in patients with angina that is refractory to nitrates and/or adequate doses of beta blockers.

ADVERSE REACTION/SIDE EFFECTS

Amlodipine is well-tolerated. The most common adverse effects of are associated with its vasodilatory action and often diminished on continued therapy. They include dizziness, flushing, headache, hypotension, peripheral edema, tachycardia and palpitations. Nausea and other gastro-intestinal disturbances, increased micturition frequency, lethargy, eye pain and mental depression have also occurred. A paradoxical increase in ischaemic chest pain may occur at the start of treatment and in a few patients excessive fall in blood pressure has led to cerebral or myocardial ischaemia or transient blindness.

There have been reports of rashes, fever and abnormalities in liver function due to hypersensitivity reactions.

Hepatitis, jaundice and hepatic enzyme elevations have also been reported very infrequently (mostly consistent with cholestasis). As with other calcium channel blockers the following adverse events have been rarely reported and cannot be distinguished from the natural history of the underlying disease: myocardial infarction, arrhythmia (including ventricular tachycardia and atrial fibrillation) and chest pain.

PRECAUTIONS/WARNINGS

Amlodipine should be administered with caution to patients with low cardiac reserve.

Patients with heart failure:

Patients with cardiac failure should be treated with caution. In a long-term study including patients suffering from severe heart failure (NYHA grade III and IV) the reported incidence of pulmonary oedema was higher in the amlodipine treated group than in the placebo group, but this was not indicating an aggravation of the heart failure.

Use in patients with impaired hepatic function:

The half-life of amlodipine is prolonged in patients with impaired liver function; dosage recommendations have not been established. Amlodipine should therefore be administered with caution in these patients.

Use in elderly patients:

In the elderly, increase of the dosage should take place with care.

Use in children:

Amlodipine should not be given to children due to insufficient clinical experience.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose - galactose malabsorption should not take this medicine.

DRUG INTERACTIONS

Amlodipine has been safely administered with thiazide diuretics, alpha blockers. beta blockers,angiotensin-converting enzyme inhibitors, long-acting nitrates,sublingual glyceryl trinitrate, non-steroidal anti-inflammatory drugs, antibiotics, and oral hypoglycaemic drugs.

In vitro data from studies with human plasma, indicate that amlodipine has no effect on protein binding of digoxin, phenytoin, warfarin or indomethacin.

Special Studies: Effect of other agents on amlodipine.

Cimetidine: Co-administration of Amlodipine with cimetidine did not alter the pharmacokinetics of Amlodipine.

Grapefruit Juice. Co-administration of 240 mL of grapefruit juice with a single oral dose of Amlodipine 10 mg in 20 healthy volunteers had no significant effect on the pharmacokinetics of Amlodipine.

Sildenafil: When Amlodipine and sildenafil were used in combination, each agent independently exerted its own blood pressure lowering effect.

Special Studies. Effect of amlodipine on other agents.

Atorvastatin. Co-administration of multiple 10mg doses of Amlodipine with 80 mg of atorvastatin resulted in no significant change in the steady state pharmacokinetic parameters of atorvastatin.

Digoxin: Co-administration of Amlodipine with digoxin did not change serum digoxin levels or digoxin renal clearance in normal volunteers.

Warfarin: In healthy male volunteers, the co-administration of Amlodipine does not significantly alter the effect of warfarin on prothrombin response time. Co- administration of Amlodipine with warfarin did not change the warfarin prothrombin response time.

Cyclosporin: Pharmacokinetic studies with cyclosporin have demonstrated that Amlodipine does not significantly alter the pharmacokinetics of cyclosporin.

Drug/Laboratory test Interactions. None known.

USE IN PREGNANCY
There are no adequate and well - controlled studies in pregnant women. Amlodipine should be used during pregnancy only by judging the potential benefits against the potential risk to the fetus.

Nursing Mothers: It is not known whether is excreted in human milk. In the absence of this information, it is recommended that nursing be discontinued while Amlodipine is administered.

CONTRAINDICATIONS
Amlodipine is contra-indicated in patients with hypersensitivity to amlodipine, dihydropyridine derivatives or to any of the excipients.

RECOMMENDED DOSAGE AND ADMINISTRATION

Method of administration
Tablet for oral administration.

In adults: For both hypertension and angina the usual initial dose is 5 mg Amlodipine once daily which may be increased to a maximum dose of 10 mg depending on the individual patient's response.

No dose adjustment of Arnlodipine is required upon concomitant administration of thiazide diuretics, beta blockers, and angiotensin-converting enzyme inhibitors.

Use in children: Not recommended.

Use in the elderly: Amlodipine. used at similar doses in elderly or younger patients, is equally well tolerated. Therefore normal dosage regimens are recommended.

Patients with hepatic impairment: See section Special warnings and precautions for use.

Patients with renal impairment. Changes in amlodipine plasma concentrations are not correlated with degree of renal impairment, therefore the normal dosage is recommended. Amlodipine is not dialysable.

OVERDOSAGE, SYMPTOMS AND TREATMENT
Available data suggest that gross overdosage could result in excessive peripheral vasodilatation and possibly reflex tachycardia. Marked and probably prolonged systemic hypotension up to and including shock with fatal outcome have been reported.

Administration of activated charcoal to healthy volunteers immediately or up to two hours after ingestion of amlodipine has been shown to significantly decrease amlodipine absorption. Gastric lavage may be worthwhile in some cases.Clinically significant hypotension duo to amlodipine overdosage calls for active cardiovascular support including frequent monitoring of cardiac and respiratory function, elevation of extremities, and attention to circulating fluid volume and urine output A vasoconstrictor may be helpful in restoring vascular tone and blood pressure provided that there is no contraindication to its use. Intravenous calcium gluconate may be beneficial in reversing the effects of calcium channel blockade. Since amlodipine is highly protein. bound, dialysis is not likely to be of benefit.

PRESENTATION
Amlomed tablets are available in 5 mg & 10 mg strengths,

Each blister contains 10 nos. of uncoated tablets. Available in 30's, 100's and 500's pack.

STORAGE CONDITION
Store below 30°C. Protect from light and moisture.

SHELF LIFE
Tablets must be used within 36 months from the date of manufacture.

MANUFACTURED BY:
Sai Mirra Innopharm Pvt. Ltd.
PLOT NO. 288, 298 & 299, SIDCO Estate,
Ambattur, 600 098 Chennai, INDIA.

PRODUCT REGISTRATION HOLDER:
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