xxxxxxxx-5343

AMLODIPINE BESILATE

5 mg Tablet
CALCIUM CHANNEL BLOCKER

FORMULATION
Each tablet contains:
Amlodipine Besilate equivalent to
Amlodipine .....5 mg

CLINICAL PHARMACOLOGY
Amlodipine acts as a calcium ion channel antagonist in peripheral, vascular and coronary smooth muscle cells, thus producing marked vasodilation in peripheral and coronary vascular beds. The reduction in peripheral blood pressure produced by Amlodipine is a result of peripheral arterial vasodilation resulting in a reduction of peripheral vascular resistance. In patients with mild to moderate essential hypertension, Amlodipine has a sustained and gradual onset of antihypertensive effect. Amlodipine, in once daily dosage regimen of 2.5 to 10mg has been shown to produce reductions in mean systolic and diastolic pressure of about 10 to 18% in hypertensive patients. Moreover, in such patients, Amlodipine also increased renal blood flow as well as glomerular filtration rate, and reduced renovascular resistance. Urine volume and urinary sodium excretion were unchanged suggesting that Amlodipine has no long-term effect on sodium homeostasis. Plasma renin activity as well as aldosterone and catecholamine levels were not significantly affected. Amlodipine reduces myocardial oxygen demand, increases myocardial oxygen supply and improves exercise capacity in patients with symptomatic myocardial ischaemia. In patients with stable angina pectoris, Amlodipine, through reduction in peripheral vascular resistance, reduces afterload as well as the rate-pressure product, thereby reducing myocardial oxygen demand. Amlodipine also inhibits coronary spasm and restores coronary blood flow in patients of vasospastic (Prinzmetal's) angina.
Amlodipine has no significant effects on the sinoatrial or atrioventricular node. In clinical studies where Amlodipine was administered concomitantly with beta-blockers to patients with either hypertension or angina, no adverse effects on electrocardiographic parameters were observed.
Animal studies have demonstrated a cardioprotective effect for Amlodipine in both in-vivo and in-vitro models of ischaemic reperfusion; reductions in tissue calcium content and increase in shortening fraction have been noted after reperfusion. After oral administration of therapeutic doses, Amlodipine is slowly and almost completely absorbed; peak plasma concentration is attained within 6 to 12 hours with absolute bioavailability between 64 and 90%. The bioavailability of Amlodipine is not altered by the presence of food. Amlodipine has relatively long elimination half-life of 35 to 45 hours, which permits once-daily oral doses, to inactive metabolites with most metabolites excreted in the urine. Amlodipine is more than 95% bound to plasma proteins.

DRUG INTERACTIONS
Amlodipine has been safely administered with thiazide diuretics, beta-adrenoceptor blocking drugs, angiotensin-converting enzyme inhibitors, long-acting nitrate, sublingual glyceryl trinitrate, non-steroidal anti-inflammatory drugs, antibiotics, and oral hypoglycaemic agents.
Co-administration of Amlodipine with digoxin did not change serum digoxin levels or digoxin renal clearance in normal volunteers. Co-administration of cimetidine did not alter the pharmacokinetics of Amlodipine.
In healthy volunteers, co-administration of Amlodipine did not significantly alter the effect of warfarin on prothrombin time. The introduction of Amlodipine is not likely to result in the need for modification of an established warfarin agents.

INDICATION
For the treatment of hypertension and prophylaxis of angina.

DOSAGE AND ADMINISTRATION
Adults : For both hypertension and angina, the recommended initial dose is 5mg. Amlodipine taken orally once daily which may be increased to a maximum dose of 10mg depending on the individual patient's response. Small, fragile or elderly patients & patients with hepatic insufficiency may be started on Amlodipine 2.5mg once daily and this dose may be used when adding Amlodipine to other antihypertensive or antianginal therapy.
Amlodipine can be administered with or without food.
Use in elderly : Although elderly patients may have higher plasma concentrations of Amlodipine than younger patients, the terminal elimination half-lives in both are similar. Amlodipine is similarly well-tolerated in elderly or younger patients. Therefore, the normal dosage of Amlodipine is recommended for elderly people.
Use in patients with renal impairment : Amlodipine is extensively metabolised to inactive metabolites with 10% of excreted drug in the urine. Changes in amlodipine plasma concentrations are not correlated with the degree of renal impairment; therefore, the normal dosage is recommended in patients with renal impairment. Amlodipine is not dialysable.
Use in patients with impaired hepatic function : The half-life of Amlodipine is prolonged in patients with impaired liver function. Amlodipine should therefore be administered with caution in such patients.

CONTRAINDICATIONS
Amlodipine is contraindicated in patients with a known hypersensitivity to dihydropyridines (e.g. nifedipine, nicardipine, isradipine).

USE IN PREGNANCY, LACTATION AND CHILDREN
There is no clinical experience with Amlodipine in pregnancy or lactation. Amlodipine should not be administered during pregnancy or lactation or to women of child-bearing potential unless effective contraception is ensured. Since there is no clinical experience, use of Amlodipine is not currently recommended for children and adolescents of less than 18 years of age.

ADVERSE EFFECTS
Amlodipine is generally well tolerated. The most commonly observed side effects are headache, oedema, fatigue, flushing and dizziness. Less common side effects include nausea, abdominal pain, somnolence and palpitations. Rare side effects include muscle cramps, frequency of micturition or nocturia, coughing, breathlessness, epistaxis, impotence, nervousness and conjunctivitis. No clinically significant pattern of laboratory test abnormalities related to Amlodipine has been observed.
Amlodipine has not been associated with any adverse effects or changes in plasma lipids. Amlodipine has been used safely in patients with well compensated congestive heart failure, peripheral vascular disease, chronic obstructive pulmonary disease, abnormal lipid profiles and diabetes mellitus.

WARNING/PRECAUTION
The half-life of amlodipine is prolonged in patients with impaired liver function; Amlodipine should be administered with caution in patients receiving either peripheral vasodilators (especially in patients with severe aortic stenosis) or in patients with severe heart failure.

OVERDOSAGE
There is no well documented experience with Amlodipine overdosage. Since absorption of Amlodipine is slow, gastric lavage should be performed. Available data suggests that the gross overdosage could result in excessive peripheral vasodilation with subsequent marked and probably prolonged hypotension, which calls for active cardiovascular support including monitoring of cardiac and respiratory function, elevation of extremities, attention to circulating fluid volume and urine output. Intravenous calcium gluconate may help to reverse the effects of calcium entry blockade. A vasoconstrictor agent may be helpful in restoring vascular tone and blood pressure provided there is no contraindication to its use. Since Amlodipine is highly protein bound, dialysis is unlikely to be of benefit.

STORAGE CONDITION
Store at a temperatures not exceeding 25^{o}C. Protect from light and moisture.

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

AVAILABILITY
Amlodipine Besilate 5 mg Tablet - PVC/Alu Blister, 10 Tablets per strip : Box of 100's

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Manufactured by :
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Imported and Distributed by :
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