AMLODIPINE

SITIvax

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10 mg Tablet
Calcium Channel Blocker

FORMULATION:
Each tablet contains: Amlodipine (as Besilate) BP ..... 10 mg

PRODUCT DESCRIPTION: White, circular, flat, scored, un-coated tablets.
INDICATION: It is used in the management of hypertension and prophylaxis of angina pectors.
PHARMACOKINETICS: Amlodipine is well absorbed after oral doses with peak blood concentrations occurring after 6 to 12 hours. The bioavailability varies but is usually about 60% - 65% Amlodipine is reported to be about 97.5% bound to plasma proteins, it has a prolonged terminal elimination half-life of 35 to 50 hours and steady-state plasma concentrations are not achieved until after 7 to 8 days of use. Amlodipine is extensively metabolized in the liver metabolites are mostly excreted in urine together with less than 10% of a dose as unchanged drug. Amlodipine is not removed by dialysis.
PHARMACODYNAMICS: Hemodynamics: Following administration of therapeutic doses to patients with hypertension, amlodipine produces vasodilation resulting in a reduction of supine and standing blood pressures. These decreases in blood pressure are not accompanied by a significant change in heart rate or plasma catecholamine levels with chronic dosing. Although the acute intravenous administration of amlodipine decreases arterial blood pressure and increases heart rate in hemodynamic studies of patients with chronic stable angina, chronic oral administration of amlodipine in clinical trials did not lead to clinically significant changes in heart rate or blood pressures in normotensive patients with angina.
With chronic once daily oral administration, antihypertensive effectiveness is maintained for at least 24 hours. Plasma concentrations correlate with effect in both young and elderly patients. The magnitude of reduction in blood pressure with amlodipine is also correlated with the height of pretreatment elevation; thus, individuals with moderate hypertension (diastolic pressure 105–114 mmHg) had about a 50% greater response than patients with mild hypertension (diastolic pressure 90–104 mmHg). Normotensive subjects experienced no clinically significant change in blood pressures (+1/–2 mmHg).
In hypertensive patients with normal renal function, therapeutic doses of amlodipine resulted in a decrease in renal vascular resistance and an increase in glomerular filtration rate and effective renal plasma flow without change in filtration fraction or proteinuria. As with other calcium channel blockers, hemodynamic measurements of cardiac function at rest and during exercise (or pacing) in patients with normal ventricular function treated with AMLODIPINE have generally demonstrated a small increase in cardiac index without significant influence on dP/dt or on left ventricular end diastolic pressure or volume. In hemodynamic studies, amlodipine has not been associated with a negative inotropic effect when administered in the therapeutic dose range to intact animals and man, even when co-administered with beta-blockers to man. Similar findings, however, have been observed in normal or well-compensated patients with heart failure with agents possessing significant negative inotropic effects.
Electrophysiologic Effects: Amlodipine does not change sinoatrial nodal function or atrioventricular conduction in intact animals or man. In patients with chronic stable angina, intravenous administration of 10 mg did not significantly alter A-H and H-V conduction and sinus node recovery time after pacing. Similar results were obtained in patients receiving amlodipine and concomitant beta-blockers. In clinical studies in which amlodipine was administered in combination with beta-blockers to patients with either hypertension or angina, no adverse effects on electrocardiographic parameters were observed. In clinical trials with angina patients alone, amlodipine therapy did not alter electrocardiographic intervals or produce higher degrees of AV blocks.
ADULT DOSAGE AND ADMINISTRATION: In hypertension the usual initial dose is 5 mg once daily increased, if necessary, to 10 mg once daily. Similar doses are given in the treatment of stable angina and prinzmetal angina. Lower initial doses may be used in elderly patients and those with hepatic impairment. Or as prescribed by the physician.
CONTRAINDICATIONS: Amlodipine is contraindicated in patients with known sensitivity to amlodipine.
WARNINGS AND PRECAUTIONS: Hypotension Symptomatic hypotension is possible, particularly in patients with severe aortic stenosis. Because of the gradual onset of action, acute hypotension is unlikely. Increased Angina or Myocardial Infarction Worsening angina and acute myocardial infarction can develop after starting or increasing the dose of amlodipine, particularly in patients with severe obstructive coronary artery disease. Patients with Hepatic Failure Because amlodipine is extensively metabolized by the liver and the plasma elimination half-life (t 1/2) is 56 hours in patients with impaired hepatic function, titrate slowly when administering amlodpine to patients with severe hepatic impairment.
USE IN PREGNANCY AND LACTATION: Safety of Amlodipine besilate in human pregnancy or lactation has not been established, Amlodipine besilate does not demonstrate toxicity in animal reproductive studies other than to delay parturition and a prolong labor in rats at a dose level 50 times the maximum recommended dose in humans. Accordingly, use in pregnancy is only recommended when there is no safer alternative and when the disease itself carries greater risk for the mother and fetus.
DRUG INTERACTIONS: Amlodipine besilate has been safety administered with thiazide diuretics, blockers, beta blockers, angiotensin-converting enzyme inhibitors, long-acting nitrates, sublingual nitroglycerin, NSAID, antibiotics and oral hypoglycemic drugs. Studies have indicated that the co-administration of amlodipine besilate with digoxin did not change serum digoxin levels or digoxin renal cl arance in normal volunteers, and that co-administration of cimetidine did not alter the pharmacokinetics af amlodipine. In vitro data from studies with human indicate that amlodipine besilate has no effect of protein- binding of the drugs tested digoxin, phenytoin, warfarin or indomethacin). In healthy male volunteers, the co-administration of amlodipine does not significantly alter the effect of warfarin on prothombin response time. Pharmacokinetic studies with cyclosporine have demonstrated that amlodipine does not significantly alter the pharmacokinetics of cyclosporine.
ADVERSE EFFECTS: The most common adverse effects of Amlodipine besilate are associated with its vasodilator action and often diminish on continued therapy; they include dizziness, flushing, headache, hypotension, peripheral oedema, tachycardia, and palpitations Nausea and other gastrointestinal disturbances, increased micturition frequency lethargy, eye pain, visual disturbances, 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 ischemia or transient blindness, There have been reports of rashes (inducing erythema multiforme), fever, and abnormalities in liver function, including cholestasis to hypersensitivity reactions. Gingival hyperplasia, myalgia, tremor, and impotence have been reported. Some tablets- formulated for once- daily use are covered in a membrane which is not digested and may cause gastrointestinal obstruction, bezoars may rarely occur. Over dosage may be associated with bradycardia and hypotension,; hyperglycaemia, metabolic acidosis, and coma may also occur. Amlodipine besilate has been reported to be teratogenic in animals.

The following events occurred in <1% but >0.1% of patients in controlled clinical trials or under conditions of open trials or marketing experience where a causal relationship is uncertain; they are listed to alert the physician to a possible relationship:

Cardiovascular: arrhythmia (including ventricular tachycardia and atrial fibrillation), bradycardia, chest pain, peripheral ischemia, syncope, tachycardia, vasculitis.

Central and Peripheral Nervous System: hypoesthesia, neuropathy peripheral, paresthesia, tremor, vertigo.

Gastrointestinal: anorexia, constipation, dysphagia, diarrhea, flatulence, pancreatitis, vomiting, gingival hyperplasia.

General: allergic reaction, asthenia,1 back pain, hot flushes, malaise, pain, rigors, weight gain, weight decrease.

Musculoskeletal System: arthralgia, arthrosis, muscle cramps,1 myalgia.

Psychiatric: sexual dysfunction (male1 and female), insomnia, nervousness, depression, abnormal dreams, anxiety, depersonalization.

Respiratory System: dyspnea, 1 epistaxis.

Skin and Appendages: angioedema, erythema multiforme, pruritus,1 rash,1 rash erythematous, rash maculopapular.

Special Senses: abnormal vision, conjunctivitis, diplopia, eye pain, tinnitus.

Urinary System: micturition frequency, micturition disorder, nocturia.

Autonomic Nervous System: dry mouth, sweating increased.

Metabolic and Nutritional: hyperglycemia, thirst.

Hemopoietic: leukopenia, purpura, thrombocytopenia.

These events occurred in less than 1% in placebo-controlled trials, but the incidence of these side effects was between 1% and 2% in all multiple dose studies

REPORTING OF SUSPECTED ADVERSE REACTIONS: To allow continued monitoring of benefit/risk balance product the medicinal product, reporting of adverse reaction is necessary. Healthcare professionals are encouraged to report any suspected adverse reactions directly to the importer/ distributor and/or report To FDA: www.fda.gov.ph. Patients are advised to seek immediate medical attention at first signs of adverse reactions.

OVERDOSE AND TREATMENT: Activated charcoal may be given orally to adults or children who present within 1 hour ingesting a potentially toxic overdose of Amlodipine besitate, alternatively, gastric lavage may be considered in adults. Supportive and Symptomatic care should be given. Hypotension may respond to placing the patient in the supine position with the feet raised and the administration of plasma expanders, although cardiac overload should be avoided. If hypotension is not corrected, calcium gluconate or calcium chloride should be given intravenously glucagon may also be used. If hypotension persists, intravenous administration of a Sympathomimetic such as isoprenaline, dopamine, or noradrenaline may also be necessary. Bradycardia may be treated with atropine, isoprenaline, or cardiac pacing. Dialysis is not useful as Amlodipine bestate is highly protein bound. Plasmapheresis may be beneficial.

PRECAUTIONS: Amlodipine Besilate should be used with caution in patients with hypotension, in patients whose cardiac reserve is poor, and in those with heart failure since deterioration of heart failure has been noted, Amlodipine besilate should not be used in cardiogenic shock, in patients who have suffered a myocardial infarction in the previous 2 to 4 weeks, or in acute unstable angina. Amlodipine besilate should not be used to treat an angina attack in chronic stable angina, in patients with severe aortic stenosis Amlodipine besilate may increase the risk of developing Heart failure. Sudden withdrawal of amiodipinebesilate might be associated with an exacerbation of angina. The dose may need to be reduced inpatients with hepatic impairment. Amlodipine besilate should be discontinued in patients who experience ischaemic pain following its administration.

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

STORAGE CONDITION: Store at temperatures not exceeding 30°C.

AVAILABILITY: Alu/Alu Foil Strip x 10's (Box of 100's)

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