

Amlodipine Besilate

Amcal

5 mg Tablet

10 mg Tablet

Calcium Channel Blocker

FORMULATION

Each tablet contains:

Amlodipine (as besilate) 5 mg

Amlodipine (as besilate) 10 mg

CLINICAL PHARMACOLOGY

Amlodipine is a calcium influx inhibitor (slow channel blocker or calcium ion antagonist).

Amlodipine inhibits the transmembrane influx of calcium ions into the cardiac muscle and smooth muscle, for which selectivity of action is ten times higher. The mechanism of antihypertensive action of Amlodipine is due to a direct relaxant effect on vascular smooth muscle. Amlodipine reduces the total ischaemic burden by the following actions:

1. Amlodipine dilates the peripheral arterioles and thus reduces the total peripheral resistance (afterload) against which the heart works. Since there is no associated reflex tachycardia, this reduces myocardial energy consumption and oxygen requirements and probably accounts for the effectiveness of Amlodipine in myocardial ischaemia.
2. The mechanism of action of Amlodipine probably involves dilation of the main coronary arteries and coronary arterioles, both in normal and ischaemic regions. This dilation increases myocardial oxygen delivery in patients with coronary artery spasm (Prinzmetal's or variant angina).

PHARMACOKINETICS

Amlodipine is well absorbed following oral administration with peak blood concentration occurring after 6 to 12 hours. The bioavailability is about 60 to 66%. It has prolonged terminal elimination half-life of 35 to 50 hours and steady state plasma concentrations are not achieved until metabolized in the liver, metabolites are mostly excreted in urine with less than 10% of a dose as unchanged drug. Amlodipine is reported to be about 97.5% bound to plasma proteins.

THERAPEUTIC INDICATIONS

Amlodipine is used in the management of hypertension and angina pectoris.

DOSE AND ADMINISTRATION

For both hypertension and angina, the usual initial dose is 5 mg once daily, increased, if necessary, to 10 mg once daily depending on the individual patient's response. Amlodipine may be taken before or after meal since absorption remains the same in either case. No dose adjustment of Amlodipine is required with concomitant administration of thiazide diuretics, beta-blockers and angiotensin converting enzyme inhibitors. Due to slow onset of action, acute hypotension is not a feature of Amlodipine administration. Amlodipine has not been associated with any adverse metabolic effects or changes in plasma lipids, and is suitable for use in patients with asthma, diabetes and gout. Or as prescribed by the physician.

CONTRAINDICATION

Amlodipine is contraindicated in patients with known hypersensitivity to dihydropyridines.

PRECAUTIONS

Use in Renal Failure: Amlodipine may be used in such patients at normal doses. Changes in amlodipine plasma concentrations are not correlated with degree of renal impairment. Amlodipine is not dialyzable.

Use in Patients with Impaired Hepatic Function: As with all calcium antagonists, amlodipine half-life is prolonged in patients with impaired liver function and dosage recommendations have not been established. Amlodipine should therefore be administered with caution in these patients.

Use in pregnancy and lactation: Safety of amlodipine in human pregnancy or lactation has not been established. However, Amlodipine postpones premature labor and is used as a tocolytic agent. 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 the child.

ADVERSE EFFECTS

Summary of the safety profile

The most commonly reported adverse reactions during treatment are somnolence, dizziness, headache, palpitations, flushing, abdominal pain, nausea, ankle swelling, oedema and fatigue.

Tabulated list of adverse reactions

The following adverse reactions have been observed and reported during treatment with amlodipine with the following frequencies: Very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1,000$ to $\leq 1/100$); rare ($\geq 1/10,000$ to $\leq 1/1,000$); very rare ($\leq 1/10,000$).

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

System organ class	Frequency	Adverse reactions
Blood and lymphatic system disorders	Very rare	Leukocytopenia, thrombocytopenia
Immune system disorders	Very rare	Allergic reactions
Metabolism and nutrition disorders	Very rare	Hyperglycaemia
Psychiatric disorders	Uncommon	Insomnia, mood changes (including anxiety), depression
	Rare	Confusion
Nervous system disorders	Common	Somnolence, dizziness, headache (especially at the beginning of the treatment)
	Uncommon	Tremor, dysgeusia, syncope, hypoesthesia, paresthesia
	Very rare	Hypertonia, peripheral neuropathy

Eye disorders	Uncommon	Visual disturbance (including diplopia)
Ear and labyrinth disorders	Uncommon	Tinnitus
Cardiac disorders	Common	Palpitations
	Very rare	Myocardial infarction, arrhythmia (including bradycardia, ventricular tachycardia and atrial fibrillation)
Vascular disorders	Common	Flushing
	Uncommon	Hypotension
	Very rare	Vasculitis
Respiratory, thoracic and mediastinal disorders	Uncommon	Dyspnoea, rhinitis
	Very rare	Cough
Gastrointestinal disorders	Common	Abdominal pain, nausea
	Uncommon	Vomiting, dyspepsia, altered bowel habits (including diarrhoea and constipation), dry mouth
	Very rare	Pancreatitis, gastritis, gingival hyperplasia
Hepatobiliary disorders	Very rare	Hepatitis, jaundice, hepatic enzymes increased*
Skin and subcutaneous tissue disorders	Uncommon	Alopecia, purpura, skin discolouration, hyperhidrosis, pruritus, rash, exanthema
	Very rare	Angioedema, erythema multiforme, urticaria, exfoliative dermatitis, Stevens-Johnson syndrome, Quincke oedema, photosensitivity
Musculoskeletal and connective tissue disorders	Common	Ankle swelling
	Uncommon	Arthralgia, myalgia, muscle cramps, back pain
Renal and urinary disorders	Uncommon	Micturition disorder, nocturia, increased urinary frequency
Reproductive system and breast disorders	Uncommon	Impotence, gynecomastia
General disorders and administration site conditions	Common	Oedema, fatigue
	Uncommon	Chest pain, asthenia, pain, malaise
Investigations	Uncommon	Weight increase, weight decrease

*mostly consistent with cholestasis
 Exceptional cases of extrapyramidal syndrome have been reported.

INTERACTIONS

Amlodipine may enhance the antihypertensive effects of other antihypertensive drugs such as beta-blockers although the combination is well tolerated. Enhanced antihypertensive effects may also be seen with concomitant use of drugs such as aldesleukin and antipsychotic that cause hypotension.

Amlodipine has been safely administered with thiazide diuretics, angiotensin converting enzyme inhibitors, long acting nitrates, sublingual nitroglycerine, non-steroidal anti-inflammatory drugs, antibiotics and oral hypoglycaemic drugs. When such drug combinations were used, Amlodipine was usually tolerated and did not result in any negative interactions.

Special studies have indicated that co-administration of Amlodipine with digoxin did not change serum digoxin levels or digoxin renal clearance in normal volunteers and that co-administration of cimetidine did not alter the pharmacokinetics of Amlodipine.

In vitro data from studies with human plasma indicate that Amlodipine has no effect on protein binding of the drugs tested (digoxin, phenytoin, warfarin, or indomethacin).

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

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

AVAILABILITY

Amlodipine besilate 5 mg tablet - blister pack x14's (box of 70's)

Amlodipine besilate 10 mg tablet -blister pack x 10's (box of 30's, 50's & 100's)

Manufactured by:

Panion & BF Biotech Inc.

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 Taoyuan County 234, Taiwan, R.O.C.

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