Amlo™

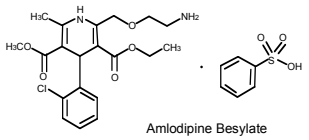
[Amlodipine besylate Tablets]

5mg, 10mg Tablets

DESCRIPTION

AMLO (Amlodipine besylate) is a calcium ion influx inhibitor of the dihydropyridine group (slow channel blocker or calcium ion antagonist) and inhibits the transmembrane influx of calcium ions into cardiac and vascular smooth muscle.

Chemically, amlodipine besylate is 3-Ethyl 5-methyl (±) 2-[(2-aminoethoxy)methyl]-4-(o-chlorophenyl)-1,4 dihydro-6-methyl-3,5-pyridinedicarboxylate, monobenzenesulfonate. Its molecular formula is $C_{20}H_{25}ClN_2O_5.C_6H_6O_3S$ and the structural formula is:



Amlodipine Besylate

QUALITATIVE & QUANTITATIVE COMPOSITION

AMLO (Amlodipine besylate) is available for oral administration as:

1. AMLO Tablets 5mg
   Each tablet contains:
   Amlodipine.....5mg
   (as amlodipine besylate USP)
2. AMLO Tablets 10mg
   Each tablet contains:
   Amlodipine.....10mg
   (as amlodipine besylate USP)

CLINICAL PHARMACOLOGY

Mechanism of Action

The mechanism of the antihypertensive action of amlodipine is due to a direct relaxant effect on vascular smooth muscle. The precise mechanism by which amlodipine relieves angina has not been fully determined but amlodipine reduces total ischemic burden by the following two actions:

1. Amlodipine dilates peripheral arterioles and thus, reduces the total peripheral resistance (afterload) against which the heart works. Since the heart rate remains stable, this unloading of the heart reduces myocardial energy consumption and oxygen requirements.
2. Amlodipine blocks constriction of coronary arteries and coronary arterioles and restores blood flow, both in normal and ischemic regions. This dilatation increases myocardial oxygen delivery in patients with coronary artery spasm (Prinzmetal's or variant angina).

Pharmacokinetics

Absorption:

After oral administration amlodipine is well absorbed with peak blood levels between 6-12 hours post dose. The absolute bioavailability has been estimated to be between 64% and 80%. The bioavailability of amlodipine is not altered by food.

Distribution:

The volume of distribution is approximately 21 L/kg and approximately 97.5% of circulating amlodipine is bound to plasma proteins.

Metabolism:

Amlodipine is extensively metabolised (90%) by the liver to inactive metabolites.

Elimination:

The terminal plasma elimination half life is about 35-50 hours and is consistent with once daily dosing. Steady state plasma levels of amlodipine are reached after 7-8 days of consecutive daily dosing. 60% of the metabolites are excreted in urine along with 10% of parent compound. The elimination of plasma is biphasic.

Special Populations

Children:

In children 6 to 12 years and in adolescents 13-17 years of age the typical oral clearance (CL/F) was 22.5 and 27.4 L/hr respectively in males and 16.4 and 21.3 L/hr respectively in females. Data in children below 6 years of age is limited.

Elderly:

Amlodipine clearance tends to be decreased with resulting increases in AUC and elimination half-life in elderly.

Hepatic Impairment:

Patients with hepatic impairment have decreased clearance of amlodipine which results in a longer half-life and an increase in AUC (approximately 40%-60%).

THERAPEUTIC INDICATIONS

AMLO (Amlodipine besylate) is indicated for:

1. The treatment of hypertension.
2. The treatment and prophylaxis of chronic stable angina pectoris.
3. The treatment of confirmed or suspected vasopastic angina (Prinzmetal's or Variant Angina).

AMLO (Amlodipine besylate) may be used alone or in combination with other antianginal or antihypertensive agents.

DOSAGE & ADMINISTRATION

Adults

For Hypertension and Angina:

The usual initial dose of AMLO (Amlodipine besylate) is 5mg once daily. It may be increased to a maximum dose of 10mg depending on the individual patient's response.

It may be used as monotherapy or in combination with other anti-anginal medicinal products in patients with angina that is refractory to nitrates and/or to adequate doses of beta blockers.

Dose Adjustment:

No dose adjustment of AMLO (Amlodipine besylate) is required upon concomitant administration of thiazide diuretics, beta blockers and angiotensin-converting enzyme inhibitors.

Children and adolescents with hypertension from 6 years to 17 years of age:

The recommended antihypertensive oral dose in pediatric patients ages 6-17 years is 2.5 mg once daily as a starting dose, up-titrated to 5 mg once daily if blood pressure goal is not achieved after 4 weeks. Doses in excess of 5 mg daily have not been studied in pediatric patients.

Elderly Patients:

Amlodipine is well tolerated when used in elderly or younger patients at similar doses. Normal dosage regimens are recommended in the elderly, but up-titration should be done with care.

Renal Impairment:

As the changes in amlodipine plasma concentrations are not correlated with degree of renal impairment, therefore normal dosage is recommended.

Hepatic Impairment:

Amlodipine should be initiated at the lowest dose and titrated slowly in patients with severe hepatic impairment. Dose selection should be done with caution and should start at the lower end of the dosing range as dosage recommendations have not been established in patients with mild to moderate hepatic impairment.

ADVERSE REACTIONS

The following adverse reactions have been observed during the treatment with amlodipine:

Common:

Somnolence, dizziness, headache, palpitations, flushing, abdominal pain, nausea, ankle swelling, edema and fatigue.

Uncommon:

Insomnia, mood changes (including anxiety), depression, tremor, dysgeusia, syncope, hypoesthesia, paresthesia, visual disturbance (including diplopia), tinnitus, hypotension, dyspnoea, rhinitis, vomiting, dyspepsia, altered bowel habits (including diarrhea and constipation), dry mouth, alopecia, purpura, skin discolouration, hyperhydrosis, pruritus, rash, exanthema, arthralgia, myalgia, muscle cramps, back pain, micturition disorder, nocturia, increased urinary frequency, chest pain, asthenia, pain, malaise, impotence, gynecomastia, weight increase and weight decrease.

Rare:

Confusion.

CONTRAINDICATIONS

Amlodipine is contraindicated in patients with:

- hypersensitivity to dihydropyridine derivatives, amlodipine or any of the component of this product.
- severe hypotension.
- shock (including cardiogenic shock).
- obstruction of the outflow tract of the left ventricle (e.g. high grade aortic stenosis).
- hemodynamically unstable heart failure after acute myocardial infarction.

PRECAUTIONS

Genaral:

The safety and efficacy of amlodipine in hypertensive crisis has not been established.

Patients with Cardiac Failure:
Amlodipine should be used with caution in patients with congestive heart failure, as they may increase the risk of future cardiovascular events & mortality.

Use in Patients with Impaired Hepatic Function:
Amlodipine should be initiated at the lower end of the dosing range and caution should be used, both on initial treatment and when increasing the dose. Slow dose titration and careful monitoring may be required in patients with severe hepatic impairment.

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.

Hypotension:
Careful monitoring of blood pressure is recommended, especially in patients with a history of cerebrovascular insufficiency and those taking medications known to lower blood pressure.

Elderly:
Increase in dosage should take place with care in elderly patients.

Drug Interactions

Cytochrome P450 System:
Dihydropyridine calcium channel blockers undergo biotransformation by the cytochrome P450 system, mainly via CYP3A4 isoenzyme. Co-administration of amlodipine with other drugs which follow the same route of biotransformation may result in altered bioavailability of amlodipine or these drugs.
Dosages of similarly metabolized drugs, particularly those of low therapeutic ratio and especially in patients with renal and/or hepatic impairment, may require adjustment when starting or stopping concomitantly administered amlodipine to maintain optimum therapeutic blood levels.

Beta-blockers:
When beta-adrenergic receptor blocking drugs are administered concomitantly with amlodipine, patients should be carefully monitored since blood pressure lowering effect of beta-blockers may be augmented by amlodipine's reduction in peripheral vascular resistance.

Grapefruit Juice
Published data indicates that through inhibition of the cytochrome P450 system, grapefruit juice can increase plasma levels and augment pharmacodynamic effects of some dihydropyridine calcium channel blockers.

Pregnancy
There are no adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy only if the potential benefit justifies the risk to the fetus.

Nursing Mother
It is not known whether amlodipine is excreted in human milk. Therefore, it is recommended that nursing should be discontinued while amlodipine is administered. If the potential benefits to the mother justify the potential risk to the nursing infants.

OVERDOSAGE
Symptoms:
Excessive peripheral vasodilatation and possibly reflex tachycardia could be the result of overdosage.

Treatment:
Active cardiovascular support 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. Gastric lavage may also be beneficial.

STORAGE
Store below 30°C.
Protect from sunlight and moisture.
The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED
AMLO (Amlodipine besylate) Tablets 5mg are available in blister pack of 20's.
AMLO (Amlodipine besylate) Tablets 10mg are available in blister pack of 20's.

Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

Please read the contents carefully before use.
This package insert is continually updated from time to time.

Manufactured by:

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