Amlodipine besilate

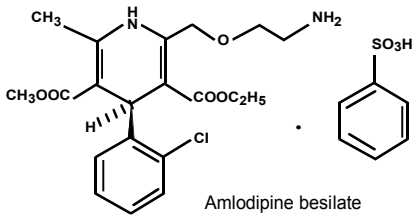
Lopicard®

5mg, 10mg Tablet
Calcium Channel Blocker

DESCRIPTION

Amlodipine (Lopicard®) 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 besilate is 3-Ethyl-5-methyl(±)-2-[(2-aminoethoxy)methyl]-4-(2-chlorophenyl)-1,4-dihydro-6-methyl-3,5-pyridinedicarboxylate, monobenzenesulphonate. Its molecular formula is $C_{20}H_{25}ClN_2O_5 \cdot C_6H_6O_3S$ and the structural formula is:



Amlodipine besilate

FORMULATION

Amlodipine (Lopicard®) is available for oral administration as:

1. Amlodipine (Lopicard®) Tablets 5mg
   Each tablet contains:
   Amlodipine…5mg
   (as amlodipine besilate)

2. Amlodipine (Lopicard®)Tablets 10mg
   Each tablet contains:
   Amlodipine…10mg
   (as amlodipine besilate)

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 against which the heart works. Since the heart rate remains stable, this unloading of the heart reduces myocardial energy consumption and oxygen requirements.
2. The mechanism of action of amlodipine also probably involves dilatation of the main coronary arteries and coronary arterioles, both in normal and ischemic regions. This dilatation increases myocardial oxygen delivery in patients with coronary artery spasm.

Pharmacokinetics

Absorption

Oral administration of therapeutic doses of amlodipine produces peak plasma concentrations between 6 and 12 hours. Absolute bioavailability has been estimated to be between 64% and 80%. The bioavailability of amlodipine when administered alone is not altered by the presence of food.

Distribution

Approximately 97.5% of the circulating amlodipine drug is bound to plasma proteins in hypertensive patients. The volume of distribution is approximately 21L/kg. Steady-state plasma levels of amlodipine are reached after 7 to 8 days of consecutive daily dosing.

Metabolism

Amlodipine is extensively (90%) converted to inactive metabolites via hepatic metabolism.

Excretion

Elimination from the plasma is biphasic with a terminal elimination half-life of about 35-50 hours. 10% of the parent amlodipine compound and 60% of the metabolites of amlodipine are excreted in the urine.

Special Populations

Geriatric Patients:

In elderly hypertensive patients there was a decrease in clearance of amlodipine from plasma as compared to young volunteers with a resulting increase in the AUC of about 60%.

Hepatic Insufficiency:

Following single oral administration of 5mg of amlodipine, patients with chronic mild-moderate hepatic insufficiency showed about 40% increase in AUC of amlodipine as compared to normal volunteers.

THERAPEUTIC INDICATIONS

Amlodipine (Lopicard®) is used for the management of hypertension and angina pectoris.

DOSAGE AND ADMINISTRATION

For both hypertension and angina the usual initial dose of Amlodipine (Lopicard®) is 5mg once daily which may be increased to a maximum dose of 10mg depending on the individual patient's response. No dose adjustment of Amlodipine (Lopicard®) is required upon concomitant administration of thiazide diuretics, beta blockers and angiotensin-converting enzyme inhibitors.

Geriatric Patients:

The recommended initial dose of Amlodipine (Lopicard®) in patients over 65 years of age is 5mg once daily. If required, increasing the dose should be done gradually and with caution.

Hepatically Insufficient Patients:

Dosage requirements have not been established in patients with impaired hepatic function. Therefore, the dosage should be carefully and gradually adjusted depending on the patient's tolerance and response. A lower starting dose of 2.5mg once daily should be considered.

ADVERSE REACTIONS

Amlodipine therapy is generally well tolerated at doses of up to 10mg/day. Most of the reported reactions are of mild to moderate severity and are related to the drug's vasodilator effect on the periphery. Headache and edema are reported most frequently. Dizziness, flushing, and palpitations also occur and appear to be dose-related. Other adverse reactions that have been reported and do not appear to be dose-related include fatigue, nausea/vomiting, abdominal pain and drowsiness.

CONTRAINDICATIONS

1. Amlodipine is contraindicated in patients with known sensitivity to dihydropyridines, amlodipine or any other components.
2. Amlodipine should not be used in cardiogenic shock, clinically significant aortic stenosis, unstable angina (excluding Prinzmetal's angina).
3. Amlodipine is contraindicated in patients with severe hypotension (less than 90mmHg systolic).
4. Amlodipine is contraindicated in pregnancy and lactation.
5. Amlodipine is not recommended for use in children.

PRECAUTIONS

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

Hepatic function: When amlodipine is used in hepatically impaired patients, the dosage should be carefully and gradually adjusted depending on the patient's tolerance and response.

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.

Peripheral Edema: Care should be taken to differentiate this peripheral edema from the effects of increasing left ventricular dysfunction.

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.

Interaction with 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.

STORAGE CONDITIONS

Store at temperatures not exceeding 30°C.
Protect from sunlight and moisture.
The expiration date refers to the product correctly stored at the required conditions.

AVAILABILITY

Amlodipine (Lopicard®) 5mg tablets are available in blister packs of 20's.

Amlodipine (Lopicard®) 10mg tablets are available in blister packs of 20's.

CAUTION

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

Keep out of reach of children.

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

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