

Amlodipine: MOA, Uses, Dosage, Side Effects

Amlodipine is a dihydropyridine calcium-channel blocker. It is a peripheral and coronary vasodilator, but, unlike the calcium-channel blockers verapamil or diltiazem, has little or no cardiac conduction and negative inotropic activity is rarely seen at therapeutic doses.

Class

- **Calcium Channel Blocker (CCB)**
- **Subclass** : Dihydropyridine CCB

Mechanism of Action

Amlodipine selectively inhibits **L-type calcium channels** in **vascular smooth muscle and myocardial cells** , reducing calcium influx:

- ? **Intracellular calcium** ? ? **activation of myosin light chain kinase (MLCK)** ? ? **myosin phosphorylation** ? **vascular smooth muscle relaxation**
- ? **Peripheral vascular resistance** ? ? **afterload & blood pressure**
- ? **Coronary artery dilation** ? ? **myocardial oxygen supply**

Unlike **verapamil** and **diltiazem** , amlodipine has **minimal effects on cardiac conduction** and **contractility** at therapeutic doses.

Pharmacological Effects

- **Vasodilation** (peripheral and coronary arteries)
- ? **Afterload** ? beneficial in angina
- ? **Coronary blood flow** ? relief of coronary vasospasm
- **Reflex tachycardia** may occur, especially at initiation

Clinical Uses

- **Hypertension (HTN)**
- **Chronic Stable Angina**
- **Prinzmetal (Variant) Angina**
- **Coronary Artery Disease (CAD)**
- **Diabetic Nephropathy**
- **Left Ventricular Hypertrophy (LVH)**
- **Raynaud Phenomenon**
- **Silent Myocardial Ischemia**

Pharmacokinetics

Parameter	Description
Absorption	Oral bioavailability: 64–90%
Onset	24–96 hours
Peak Plasma	6–12 hours
Duration of Action	~ 24 hours
Steady State	Reached in 7–8 days
Protein Binding	93–98%
Volume of Distribution	~ 21 L/kg
Metabolism	Hepatic (CYP3A4) to inactive pyridine analogs
Half-life	30–50 hours
Excretion	Renal (10% unchanged; 60% metabolites)

Dosing & Administration

For Hypertension

- **Adults** : 5 mg once daily (max: 10 mg/day)
- **Elderly/Debilited** : Start at 2.5 mg/day
- **Children ≥6 yrs** : 2.5–5 mg/day (max: 5 mg)
- **Children <6 yrs** : 0.05–0.2 mg/kg/day (max: 0.3–0.6 mg/kg, up to 20 mg)

For Angina & CAD

- **Adults** : 5–10 mg once daily
- **Elderly/Debilited** : 5 mg once daily

Hepatic Impairment

- Start with **2.5 mg** for hypertension or **5 mg** for angina
- Titrate based on response

Combination Therapies

- **Amlodipine + Atorvastatin** : HTN + hyperlipidemia
- **Amlodipine + ACE inhibitors/ARBs** : e.g., benazepril, perindopril, olmesartan
- **Amlodipine + Aliskiren** : direct renin inhibitor combo

Adverse Effects

Most effects are related to **vasodilation** and tend to resolve with time:

- **Common** : Edema (especially ankles), dizziness, flushing, headache, palpitations
- **Others** : Fatigue, nausea, abdominal pain, constipation
- **Rare/Serious** :
 - **Hypotension** , **Reflex tachycardia**
 - **Angina exacerbation** , **Myocardial ischemia**
 - **Gingival hyperplasia** , **Skin rash (e.g., erythema multiforme)**

- **Liver enzyme elevation** , **Jaundice**
- **Psychiatric symptoms** : depression, anxiety
- **Sexual dysfunction**

Contraindications & Precautions

Contraindications

- Cardiogenic shock
- Severe aortic stenosis
- Unstable angina
- Recent myocardial infarction (with caution)
- Known hypersensitivity

Caution In

- **Heart failure** (may worsen symptoms)
- **Severe hepatic impairment**
- **Elderly patients** (lower starting dose recommended)

?? **Avoid sudden discontinuation** ? may cause rebound angina or hypertensive crisis.

Drug Interactions

- **CYP3A4 inhibitors** (e.g., azole antifungals, macrolides) ? amlodipine levels
- **CYP3A4 inducers** (e.g., rifampin, carbamazepine) ? effectiveness
- **Enhanced hypotension** with beta-blockers, nitrates, diuretics
- **Diabetic patients** : Monitor for altered insulin/glucose response
- **NSAIDs** : May attenuate antihypertensive effect

Special Considerations

- Once-daily dosing due to long half-life
- Suitable for use in asthma or COPD patients (unlike non-dihydropyridines)
- Safe in renal impairment (no dosage adjustment needed)

Mnemonic for Amlodipine Adverse Effects

"**HEAD**ache **DAMPEN**ed blood pressure"

- **H** eadache
- **E** dema
- **A** ltered flushing
- **D** izziness
- **A** ngina (worsening)
- **M** yalgia
- **P** alpitations

- **E** levated LFTs
- **N** ausea
- **B** lood pressure low