# Actapin
## Amlodipine

**Composition :**
Actapin 5 mg Tablet : Each tablet contains Amlodipine besilate corresponding to amlodipine base 5 mg.
Actapin 10 mg Tablet : Each tablet contains Amlodipine besilate corresponding to amlodipine base 10 mg.

**Pharmacological Properties**
**Pharmacodynamic properties :**
Dihydropyridine derivative with long half life. Eases cardiac work and lowers peripheral resistance. No effect on supraventricular arrhythmias.
*Mechanism of action :*
Inhibits calcium ion influx in cardiac muscle cells and vascular smooth muscle.
*Pharmacodynamic effects :*
Vasodilatation with reduction of peripheral vessel resistance reduces afterload and lowers raised blood pressure. As the heart rate is unaffected, reduction of cardiac work reduces cardiac energy consumption and oxygen need. This, and dilatation of the coronary vessels, explains the effect of amlodipine in angina pectoris.
In patients with hypertension, a once daily dose gives a clinically significant reduction of both supine and standing blood pressure over 24 hours. Due to slow initial effect there is little danger of acute hypotension. Taken daily by patients with angina pectoris, amlodipine increases total exercise capacity, and increases the time to an angina attack and to 1 mm ST augment depression. Frequency of anginal attacks and use of nitroglycerine are reduced. Amlodipine has not been shown to cause metabolic side effects or changes in plasma lipids. It may be used by patients with asthma, diabetes and gout. In cardiac failure patients with NYHA classes II-IV amlodipine has not been shown to cause clinical deterioration as measured by exercise tolerance, left ventricular ejection fraction and clinical symptomatology. In patients with NYHA classes III-IV, treated with digitalis, diuretics and ACE inhibitors, amlodipine has not been shown to lead to an increased risk of mortality or morbidity, but it associated with increased incidence of pulmodary oedema.

**Pharmacokinetic properties**
*Absorption:*
Peak plasma concentration is reached after 6 - 12 hours. Bioavailability is 64 - 80%.
*Distribution:*
The distribution volume is approx.. 21 l/kg. Protein binding is approx.. 97.5% in vitro.
*Biotransformation:*
Mainly metabolized to inactive metabolites in the liver.
*Elimination:*
The half life is 35 - 50 hours. Effective plasma concentration are maintained for 24 hours with one dose daily. Steady state is reached after 7 - 8 days. 10% is excreted unchanged and 60% as metabolites in the urine.
*Use in elderly patients*
Time to peak plasma concentration of amlodipine is the same in younger and elderly patients. Amlodipine clearance tends to be reduced, with a resulting increase in UAC and half life in elderly patients. An increase in AUC and half life in patients with cardiac failure is as expected considering the patients age.

**Preclinical safety data**
Amlodipine has been studied in rats and habbits. Perinatal doses of up to 50 times the human dose showed prolonged birth time and an increased rate of stillbirths.

**Indications**
- Hypertension
- Chronic Stable angina and/or Prizmetal/variant angina.

**Posology**
Posology and method of administration
The usual starting dose is 5 mg daily. May if necessary be increased to 10 mg daily. It is not necessary to adjust the dose of amlodipine during co-administration of thiazides, beta-blockers or ACE inhibitors (angiotensin-converting enzymes). Normal dosage regimens are recommended. Amlodipine, used at similar doses in elderly and younger patients, is equally well tolerated. The efficacy and safety in children has not been investigated.

**Contraindications**
Hypersensitivity to dihydropyridines (amlodipine, nifedipine, felodipine, isradipine). Or any of the excipients.
Pregnancy (see Pregnancy and Lactation)
Severe hypertension.

**Drug Interaction**
Amlodipine has been safely administered with Thiazide diuretics, beta - blockers, angiotensin converting enzyme inhibitors long-acting Nitrates, sublingual Nitroglycerine, NSAIDs (non-steroidal anti-inflammatory drugs), antibiotics and oral hypoglycemic drugs. Special studies have indicated that the co-administration of Amlodipine with 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, Phenyton, Warfarin, or Indomethacin). In healthy male volunteers, the co-administration of Amlodipine does not significantly alter the effect of Warfarin on prothrombin response time.

**Warnings and Precautions**
- Caution is recommended with high doses in elderly patients, as clearace appears to be reduced, resulting in higher plasma concentrations. The half life is prolonged in patients with hepatic impairment and the preparation must therefore be used with caution in these patients.
- Use in patients with impaired hepatic function : As with all Calcium antagonists. Amlodipine

PHARMACODE AREA


**AAAM3081** - Amlodipine All strengths -, PIL, Singapore

| GENERAL INFORMATION | | | |
|---|---|---|---|
| **Proof Round:** | 4 | **Dimensions:** | 248x146 mm |
| **Origination Date:** | 4.8.2020 | **Manuf. site:** | Actavis Jakarta |
| **Originated by:** | V.Baksanov | **Min pt size*:** | 8 |
| Revision Date: | 26.8.2020 | **SAP Code:** | |
| Revised by: | VB | | |

| TECHNICAL CHECK | | COLOURS/PLATES |
|---|---|---|
| **Date Sent:** | 4.8.2020 | 1. black |
| **Resent Date:** | | 2. |
| **Approval Date:** | 5.8.2020 | 3. |
| **NON-PRINTING COLOURS** | 1. Profile | 4. |
| | 2. | 5. |
| | 3. | 6. |

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half life is prolonged in patients with impaired liver function and dosage recommendations have not been established. The drug should therefore be administered with caution in these patients.

- Use in patients with impaired renal function : Amlodipine is extensively metabolized to inactive metabolites with 10% excreted as unchanged drug in the urine. Amlodipine may be used in such patients at normal doses. Changes in amlodipine plasma concentration are not correlated with degree of renal impairment. Amlodipine is not dialyzable.

*Patients with heart failure :*
An association between amlodipine and increased incidence of pulmonary oedema has been seen in patients with NYHA III and IV heart failure of non – ischemic etiology (see pharmacodynamic properties).
*Interaction with other medicinal products and other forms of interaction*
See Drug Interaction

**Pregnancy and lactation**
Pregnancy : See Contra indications
Pharmacodynamic effects associated with hypotension in the mother may lead to foetal hypoxia. In high perinatal doses prolonged birth time and an increased rate of stillbirths have been observed in rats.
Lactation :
It is not known whether breast – fed children can be harmful affected. The preparation should therefore not be used during lactation.

*Effects on ability to drive and use machines*
Amlodipine is normally considered to have no or insignificant effects on the ability to drive or operate machinery.

**Undesirable Effects**
Amlodipine is usually well tolerated. In placebo – controlled studies in patients with hypertension or angina the commonest adverse reactions were :
Neurological reactions : Dizziness, headache, facial redness, flushing, somnolence.
General reactions : Muscle fatigue.
Cardiovascular reactions : Peripheral oedema (mainly of the ankles), palpitations.
Gastrointestinal reactions : Abdominal pain, nausea.
Psychiatric reactions : Drowsiness.
Less common adverse reactions seen after marketing were :
Neurological reactions : hypertonia, hypoesthesia/paraesthesia, peripheral neuropathy, tremor, dry mouth.
General reactions : asthenia, back pain, malaise, pain, weight gain/loss.
Cardiovascular reactions : hypotension, syncope, vasculitis.
Endocrinal reactions : gynecomastia, increased sweating.
Gastrointestinal reactions : altered bowel habit, dyspepsia (including gastritis), gingival hyperplasia, pancreatitis, vomiting.
Metabolic and nutritional disorders : hyperglycemia.
Reactions in muscles, connective tissue and skeleton : arthralgia, muscle cramps, myalgia.
Reactions in the blood and lymph system : purpura, thrombocytopenia, leucopenia.
Psychiatric reactions : impotence, insomnia, mood changes.
Respiratory reactions : cough, dyspnea, rhinitis.
Reactions in skin and subcutaneous tissues : alopecia, skin discolouration, urticarial.
Special senses : taste changes.
Reactions in the ear and labyrinth : tinnitus.
Eye reactions : visual disturbances.
Reactions in the kidney and urinary track : increased urinary frequency, micturition disorder, nocturia
Rare allergic reactions including pruritus, rash, angioedema and erythema multiforme.
Hepatitis jaundice, and raised liver enzymes have also been reported in rare cases (usually with cholestasis) occasionally serious enough to require hospitalization, In several cases the causal association with amlodipine was uncertain.
Myocardial infarction, arrhythmias (including bradycardia, ventricular tachycardia and atrial fibrillation) and chest pain have been reported in rare cases, but a definite association with the treatment has not been established.

**Overdose**
Experience of overdose in human is limited.
Gastric lavage may be effective in some cases.
Patients with clinically significant hypotension should be monitored and given vasoconstrictors if necessary. As amlodipine in highly bound to plasma proteins, dialysis is not indicated. Slow intravenous calcium may be useful in reversing the calcium entry blockade. Should be given as chloride, or if acidosis is present, as gluconate.

List of excipients:
Microcrystalline cellulose, dibasic calcium phosphate anhydrous, sodium starch glycolate, magnesium stearate

ATC Code : C08CA01

**Storage**
Do not store above 30°C

**Presentation**
Actapin 5 mg Tablets :
Available in box of 3 blisters @ 10 tablets and 10 blisters @ 10 tablets
Actapin 10 mg Tablets :
Available in box of 3 blisters @ 10 tablets and 10 blisters @ 10 tablets

*This leaflet was last revised in August 2020*

Manufactured by:
PT Actavis Indonesia
Jl. Raya Bogor Km. 28,
Jakarta 13710, Indonesia

PHARMACODE AREA

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AAAM3081

## AAAM3081 - Amlodipine All strengths -, PIL, Singapore

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