

Amloc 5 mg

Amloc 10 mg

SCHEDULING STATUS:

S3

PROPRIETARY NAME AND DOSAGE FORM:

Amloc 5 mg tablets

Amloc 10 mg tablets

COMPOSITION:

Each **Amloc 5 mg** contains Amlodipine maleate equivalent to 5 mg amlodipine.

Each **Amloc 10 mg** contains Amlodipine maleate equivalent to 10 mg amlodipine.

PHARMACOLOGICAL CLASSIFICATION:

A: 7.1 Vasodilators, hypotensive medicines.

PHARMACOLOGICAL ACTION:

Amlodipine is a dihydropyridine calcium channel blocker. It inhibits the transmembrane influx of calcium ions into cardiac and vascular smooth muscle without affecting serum calcium concentrations. Direct relaxation of vascular smooth muscle forms the basis of the antihypertensive action.

In angina pectoris, amlodipine acts as a peripheral arteriolar vasodilator resulting in a reduction in total peripheral resistance (afterload). Myocardial energy and oxygen requirements are reduced. Amlodipine exerts its activity by binding to the dihydropyridine binding sites. It exerts minimal action on cardiac conduction, contraction and heart rate.

Pharmacokinetics:

Complete absorption of amlodipine is slow following oral administration with peak plasma levels being attained after 6 to 12 hours. Amlodipine has a bioavailability of about 64% and a plasma elimination half-life of 35 to 50 hours, allowing for once-daily oral dosing. Steady state plasma concentrations are achieved after 7 to 8 days of consecutive dosing. The volume of distribution is about 20 L/kg. Metabolism is via the liver and is extensive with less than 10% of amlodipine appearing unchanged in the urine. Metabolites are inactive and primarily (up to 60%) excreted via the kidney.

INDICATIONS:

Amloc is indicated for the:

- Treatment of angina pectoris.
- Treatment of mild-to moderate hypertension, alone or in combination with other antihypertensives.

CONTRA-INDICATIONS:

Hypersensitivity to any of the ingredients.

Hypersensitivity to dihydropyridines.

WARNINGS:

Use in the Elderly:

Amlodipine clearance is decreased (40-60%) in the elderly, which results in increases of amlodipine concentration in the area under the concentration-time curve (AUC) and elimination half-life. Therefore, elderly patients should start **Amloc** therapy at a lower dose.

Use in Renal Failure:

Although **Amloc** is excreted primarily via the kidney, mild renal impairment does not appear to have an effect on the plasma concentrations. Severe renal impairment may however require a dosage reduction. Amlodipine is not dialysable.

Use in Impaired Hepatic Function:

The half-life of **Amloc** is significantly prolonged in patients with impaired hepatic function. **Amloc** should therefore be administered at lower doses in these patients.

Use in Children:

Safety and efficacy has not been established.

Use in Heart Failure:

An increased incidence of pulmonary oedema has been reported. **Amloc** may have a negative inotropic effect. AUC of **Amloc** may increase in patients with heart failure.

Porphyria:

Safety has not been established.

INTERACTIONS:

Concurrent administration of sublingual nitroglycerin, long acting nitrates, beta-blockers or other antianginal agents with amlodipine may produce additive antihypertensive and antianginal effects. Sublingual nitroglycerin may be used as needed to abort acute angina attacks during amlodipine therapy. Nitrate medication may be used during amlodipine therapy for angina prophylaxis. Amlodipine will not protect against the consequences of abrupt beta-blocker withdrawal; gradual beta-blocker dose reduction is recommended. Although no “rebound effect” has been reported upon discontinuation of amlodipine, a gradual decrease of dosage with medical practitioner supervision is recommended.

PREGNANCY AND LACTATION:

Safety in pregnancy and lactation has not been established (see **CONTRA-INDICATIONS**).

DOSAGE AND DIRECTIONS FOR USE:

Hypertension and Angina Pectoris:

Adults:

An initial dose of 5 mg **Amloc** once daily is recommended which may be increased to 10 mg once a day after 10 -14 days of therapy if there is no improvement.

No dose reduction is required when adding **Amloc** to thiazide diuretics, beta-blockers, or angiotensin-converting enzyme inhibitors.

SIDE EFFECTS AND SPECIAL PRECAUTIONS:

Side effects:

Cardiovascular:

Frequent: Peripheral oedema, palpitations.

Less Frequent: Hypotension (including orthostatic hypotension), syncope, vasculitis, myocardial infarction, arrhythmia (including ventricular tachycardia and atrial fibrillation), chest pain.

Neurological:

Frequent: Dizziness, headache, somnolence.

Less Frequent: Hypertonia, hypoesthesia/paresthesia, peripheral neuropathy, tremor, insomnia, mood changes.

Gastro-intestinal:

Frequent: Nausea, abdominal pain.

Less Frequent: Altered bowel habits, vomiting, dyspepsia, gingival hyperplasia, pancreatitis.

Musculoskeletal:

Frequent: Fatigue.

Less Frequent: Arthralgia, asthenia, back pain, muscle cramps, myalgia.

Autonomic Nervous system:

Frequent: Flushing.

Less Frequent: Dry mouth, increased sweating.

Hepatobilliary:

Less Frequent: Hepatitis, jaundice, raised liver enzymes (mostly consistent with cholestasis).

Haematological:

Less Frequent: Purpura, thrombocytopenia, leucopenia.

Genito-urinary:

Less Frequent: Increased urinary frequency, impotence.

Body as whole:

Less Frequent: Pain, weight increase/decrease.

Endocrine:

Less frequent: Gynaecomastia.

Metabolic:

Less frequent: Hyperglycemia

Skin and Appendages:

Less frequent: Alopecia.

Respiratory:

Less frequent: Coughing, dyspnoea.

Vision:

Less Frequent: Visual disturbances.

Special Senses:

Less Frequent: Taste perversion, tinnitus.

Hypersensitivity reactions:

Less Frequent: Allergic reactions with pruritus, rash, angioedema and erythema multiforme.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

There is no documented experience with **Amloc** over-dosage. Gastric lavage may be of benefit. Gross over-dosage could result in excessive peripheral vasodilatation, resulting in marked and probably prolonged systemic hypotension. Clinically significant hypotension due to **Amloc** over-dosage requires active cardiovascular support. Intravenous calcium gluconate may be of benefit in reversing the effects of calcium channel blockade. Since amlodipine is highly protein-bound, dialysis is not likely to be of benefit.

TREATMENT IS SYMPTOMATIC AND SUPPORTIVE.

IDENTIFICATION:

Amloc 5 mg: A white, round, slightly biconvex, bevelled edge tablet scored on one side.

Diameter: 8,0 mm

Amloc 10 mg: A white, round, slightly biconvex, bevelled edge tablet scored on one side.

Diameter: 10,0 mm.

PRESENTATION:

Amloc 5 mg: Opaque PVC / Aluminium foil blisters of 30 tablets.

Amloc 10 mg: Opaque PVC / Aluminium foil blisters of 30 tablets.

STORAGE INSTRUCTIONS:

Store in a cool (below 25°C), dry place. Protect from light.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS:

Amloc 5 mg: 38/7.1/0183

Amloc 10 mg: 38/7.1/0147

**NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF
REGISTRATION:**

Pharma Dynamics (Pty) Ltd.

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DATE OF PUBLICATION OF THE PACKAGE INSERT:

12 August 2004

Amloc 5 mg

Amloc 10 mg

SKEDULERINGSTATUS:

S3

EIENDOMSNAAM EN DOSEERVORM:

Amloc 5 mg tablette

Amloc 10 mg tablette

SAMESTELLING:

Elke **Amloc 5 mg** tablet bevat amlodipienmaleaat ekwivalent aan 5 mg amlodipien.

Elke **Amloc 10 mg** tablet bevat amlodipienmaleaat ekwivalent 10 mg amlodipien.

FARMAKOLOGIESE KLASSIFIKASIE:

A: 7.1 Vasodilatore, hipotensiewe medisyne.

FARMAKOLOGIESE WERKING:

Amlodipien is 'n dihidropiridien kalsiumkanaalblokkeerder. Dit rem die transmembraan invloei van kalsiumione in gladdespier van die hart en bloedvate sonder dat dit die konsentrasie van kalsium in die serum affekteer. Direkte verslapping van vaskulêre gladdespier vorm die basis van die antihipertensiewe werking.

Tydens angina pectoris werk amlodipien as 'n vasodilator van perifere bloedvate wat tot 'n afname in totale perifere weerstand (nabelading) lei. Die behoefte van die hart aan energie en suurstof word verminder. Amlodipien oefen sy aktiwiteit uit deur aan die dihidropiridienbindingsentrums te bind. Dit het 'n minimale effek op geleiding, kontrakisie en polsslag van die hart.

Farmakokinetika:

Na orale toediening geskied volledige absorpsie van amlodipien stadig en piekplasmavlakke word na 6 tot 12 uur bereik. Amlodipien het 'n biobeskikbaarheid van ongeveer 64% en die eliminasihalfleeftyd uit die plasma is 35 tot 50 uur wat dosering teen een keer per dag moontlik maak. Gelykvlakke in die plasma word na 7 tot 8 dae van opeenvolgende toediening bereik. Die volume van verspreiding is ongeveer 20 L/kg. Metabolisme geskied in die lewer en tot 'n groot mate met minder as 10% amlodipien wat onveranderd in die urien

uitgeskei word. Die metaboliete is onaktief en word hoofsaaklik (tot 60%) deur die niere uitgeskei.

INDIKASIES:

Amloc is aangedui vir die:

- Behandeling van angina pectoris
- Behandeling van ligte tot matige hipertensie, alleen of in kombinasie met ander antihipertensiewe middels.

KONTRA-INDIKASIES:

Hipersensitiwiteit teenoor enige van die bestanddele.

Hipersensitiwiteit teenoor dihidropiridien.

WAARSKUWINGS:

Gebruik in bejaardes:

Die opruiming van amlodipien is stadiger (40-60%) in bejaardes wat tot toename in die hoeveelheid amlodipien in die oppervlak onder die konsentrasie-tyd kurwe (AOK) en eliminasihalfleeftyd lei. Daarom moet behandeling van bejaarde pasiënte met **Amloc** teen 'n laer dosis begin word.

Gebruik in nierversaking:

Hoewel **Amloc** hoofsaaklik deur die niere uitgeskei word, lyk dit nie of matige aantasting van die niere 'n effek op die plasmakonsentrasies het nie. 'n Vermindering in die dosis kan egter met erge verswakte nierfunksie nodig wees. Amlodipien is nie dialiseerbaar nie.

Gebruik in swak lewerfunksie:

Die halfleeftyd van **Amloc** is beduidend langer in pasiënte met swak lewerfunksie. **Amloc** moet daarom teen laer dosisse aan hierdie pasiënte gegee word.

Gebruik in kinders:

Die veiligheid en effektiwiteit is nie bepaal nie.

Gebruik in hartversaking:

'n Hoër insidensie van pulmonêre edeem is aangemeld. **Amloc** kan 'n negatiewe inotropiese effek uitoefen. Die AOK van **Amloc** kan hoër wees in pasiënte met hartversaking.

Porfirie:

Die veiligheid is nie bepaal nie.

INTERAKSIES:

Gelyktydige toediening van ondertongse nitrogliserien, langwerkende nitrate, betablokkeerders of ander middels teen angina saam met amlodipien kan bykomende effekte teen hipertensie en angina veroorsaak. Ondertongse nitrogliserien kan soos nodig saam met amlodipien gebruik word om akute angina-aanvalle te voorkom. Nitrate kan tydens behandeling met amlodipien gebruik word vir die profilakse van angina. Amlodipien sal die pasiënt nie teen die gevolge van skielike staking van behandeling met betablokkeerders beskerm nie; geleidelike vermindering in die dosis van die betablokkeerder word aanbeveel. Hoewel geen “terugslageffek” na staking van amlodipien aangemeld is nie, word ‘n geleidelike afname in die dosis onder toesig van ‘n mediese praktisyn aanbeveel.

SWANGERSKAP EN LAKTASIE:

Die veiligheid tydens swangerskap en laktasie is nie bepaal nie (kyk **KONTRA-INDIKASIES**).

DOSIS EN GEBRUIKSAANWYSINGS:

Hipertensie en angina pectoris:

Volwassenes:

‘n Aanvanklike dosis van 5 mg **Amloc** een keer per dag word aanbeveel wat na 10 – 14 dae van behandeling tot 10 mg een keer per dag verhoog kan word as daar geen verbetering is nie.

Geen afname in die dosis is nodig as **Amloc** saam met tiasieddiuretika, betablokkeerders of AOE-remmers gegee word nie.

NEWE-EFFEKTE EN SPESIALE VOORSORGMAATREËLS:

Neuwe-effekte:

Kardiovaskulêr:

Dikwels: Perifere edeem, palpitasies

Minder dikwels: Hipotensie (waaronder ortostatiese hipotensie), sinkopee, vaskulitis, miokardiale infarksie, aritmie (waaronder ventrikulêre tagikardie en atriale fibrillasie), pyn in die bors

Neurologies:

Dikwels: Duiseligheid, hoofpyn, lomerigheid

Minder dikwels: Hipertonie, hipoëstesie/parestesie, perifere neuropatie, tremor, slaaploosheid, gemoedsversteurings

Gastro-intestinaal:

Dikwels: Naarheid, buikpyn

Minder dikwels: Verandering in dermgewoontes, braking, slegte spysvertering, gingivale hiperplasie, pankreatitis

Muskuloskeletaal:

Dikwels: Moegheid

Minder dikwels: Artralgie, astenie, rugpyn, spierkrampe, mialgie

Outonome senustelsel:

Dikwels: Blosing

Minder dikwels: Droë mond, meer sweet

Hepatobilliêr:

Minder dikwels: Hepatitis, geelsug, hoër vlakke lewerensieme (gewoonlik saam met cholestase)

Hematologies:

Minder dikwels: Purpura, trombositopenie, leukopenie

Genito-urinêr:

Minder dikwels: Toename in frekwensie van urinering, impotensie

Liggaam as geheel:

Minder dikwels: Pyn, toename/afname in gewig

Endokrien:

Minder dikwels: Ginekomastie

Metabolies:

Minder dikwels: Hiperglisemie

Vel en aanhangsels:

Minder dikwels: Alopesie

Respiratories:

Minder dikwels: Hoes, dispnee

Visie:

Minder dikwels: Versteurings in visie

Spesiale sintuie:

Minder dikwels: Smaakversteuring, tinnitus

Hipersensitiwiteitsreaksies:

Minder dikwels: Allergiese reaksies met pruritus, veluitslag, angioedeem en multivorme eriteem

**BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VIR DIE
BEHANDELING DAARVAN:**

Daar is geen gedokumenteerde ondervinding van oordosering met **Amloc** nie.

Maagspoeling kan nuttig wees. Grootskaalse oordosering kan tot oormatige perifere vasodilatasie lei wat tot uitgesproke en moontlik langdurige sistemiese hipotensie lei. Klinies beduidende hipotensie vanweë oordosering met **Amloc** vereis aktiewe kardiovaskulêre ondersteuning. Intraveneuse kalsiumglukonaat kan voordelig wees om die effekte van blokkade van die kalsiumkanale om te keer. Omdat amlodipien sterk aan proteïene bind, is dit onwaarskynlik dat dialise sal help.

BEHANDELING IS SIMPTOMATIES EN ONDERSTEUNEND.

IDENTIFIKASIE:

Amloc 5 mg: 'n Wit, ronde, effens bikonvekse tablet met skuins kante en 'n breeklyn op een kant. Deursnit: 8,0 mm.

Amloc 10 mg: 'n Wit, ronde, effens bikonvekse tablet met skuins kante met 'n breeklyn op een kant. Deursnit: 10,0 mm.

AANBIEDING:

Amloc 5 mg: Ondeursigtige PVC/aluminiumfoeliestulppakke met 30 tablette.

Amloc 10 mg: Ondeursigtige PVC/aluminiumfoeliestulppakke met 30 tablette.

BEWARINGSINSTRUKSIES:

Bêre op 'n koel (onder 25 °C), droë plek. Beskerm teen lig.

HOU BUIITE BEREIK VAN KINDERS.

REGISTRASIENOMMERS:

Amloc 5 mg: 38/7.1/0183

Amloc 10 mg: 37/7.1/0147

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE**REGISTRASIESERTIFIKAATS:**

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