

AMCAN™

Amlodipine Tablets USP 5 mg
Amlodipine Tablets USP 10 mg

1 COMPOSITION:**AMCAN™5**

Each uncoated tablet contains:
Amlodipine Besylate BP
Equivalent to Amlodipine 5 mg
Excipients q.s
Excipients with known effects
Each tablets contains 61.23 mg of lactose

AMCAN™10

Each uncoated tablet contains:
Amlodipine Besylate BP
Equivalent to Amlodipine 10 mg
Excipients q.s
Excipients with known effects
Each tablets contains 80.50 mg of lactose

2 LIST OF EXCIPIENTS

Amlodipine Besilate BP, Microcrsytalline cellulose PH 102 DC BP, Lactose BP, Microcrystalline cellulose PH 101 BP, Sodium starch glycolate BP, Magnesium stearate BP

3 DESCRIPTION:

Amlodipine is a Novel calcium channel antagonist from the family of dihydropyridines. The major advantages of amlodipine are a very long half-life, slow onset of action and a favorable effect on quality of life. The tablets of Amlodipine Besilate contain 2.5, 5 and 10 mg of amlodipine respectively.

4 PHARMACODYNAMIC PROPERTIES:**• MECHANISM OF ACTION:**

Amlodipine blocks slow calcium channels and therefore leads to inhibition of the transmembrane influx of calcium ions into vascular smooth muscle and cardiac smooth muscle. The effect is greater on vascular muscle. Amlodipine does not have negative inotropic effects in men at therapeutic doses. Amlodipine reduces blood pressure by reducing peripheral vascular resistance and reflex tachycardia does not occur. Moreover, due to the slow onset of action, acute hypotension does not occur. The antianginal effects of amlodipine are due to a primary reduction in cardiac afterload leading to improved myocardial oxygen supply and demand ratio at a given level of exercise. In Prinzmetal's (variant) angina due to coronary vasospasticity, amlodipine is effective because it blocks vasoconstriction mediated by calcium, potassium, serotonin, thromboxane A2 and epinephrine.

Amlodipine has no effect on the R-A-A (Renin-Angiotensin-Aldosterone) system, the sympathetic nervous system and the ANF (Atrial Natriuretic Factor). It has no adverse effects on plasma lipids, diabetes status and gout.

• PHARMACODYNAMICS:

Amlodipine maintains antihypertensive effects for at least 24 hours. It Does not alter blood pressure in normotensive individuals; magnitude of reduction in blood pressure with amlodipine correlates with pre-treatment blood pressure in moderate hypertension (diastolic 105 to 114 mm Hg) response was 50% greater than in mild hypertension (diastolic 90 -104 mm Hg). Amlodipine does not produce ECG changes or conduction blocks. Increased the treadmill or bicycle ergometry exercise time to develop ST segment deviation.

• PHARMACOKINETIC PROPERTIES:

Absorption following oral administration is slow (time to peak plasma levels: 6 to 12 hours after administration) and incomplete (up to 80%). Unlike its congeners, amlodipine has minimal (<4%) first-pass metabolism plasma proteins binding is high (95%). It has extensive distribution into tissues and body fluids. Amlodipine has an elimination half-life of 35 to 60 h. Steady-state levels are Reached 7 to 9 days after consecutive dosing. The drug has a wide therapeutic index, providing safety and efficacy in a wide range of concentrations.

5 INDICATIONS:

1. Amlodipine is a first-line antihypertensive either as monotherapy (majority of hypertensives) or in combination with ACE inhibitors, diuretics and beta-blockers.
2. Amlodipine is also the first-line treatment of stable angina pectoris, and
3. Prinzmetal's (variant) angina. It can be used as monotherapy or in combination with other antianginals in angina refractory to nitrates and beta-blockers.

6 CONTRAINDICATIONS:

Amlodipine tablets are contra-indicated in patients with known sensitivity to dihydropyridine, amlodipine, or any of the excipients.

7 WARNINGS AND PRECAUTIONS:

As there are no adequate and controlled trials on the use of amlodipine during pregnancy, and in the presence of evidence of teratogenicity in some animals during pre-clinical studies, amlodipine should not be administered during pregnancy, lactation and the patient should be advised to use effective contraception.

8 DOSAGE AND MODE OF ADMINISTRATION:**• FOR HYPERTENSION:**

The usual initial dose is 5 mg once daily orally; the maximum recommended dosage is 10 mg once daily. In the elderly (over 60 years), liver failure, liver insufficiency and thin/fragile individuals, the recommended starting dose is 2.5 mg once daily. When adding amlodipine to other antihypertensive therapy, the starting dose is 2.5 mg once daily. The dosage should be individualized over 7 to 14 days of dose-effect titration.

• FOR ANGINA:

The recommended dose is 5 to 10 mg once daily orally for both stable angina pectoris and Prinzmetals angina pectoris. The lowest dosage of 2.5 mg once a day orally is recommended in the case of elderly and in liver failure/insufficiency. Amlodipine may be administered with or without food. It has been safely administered with thiazides, ACE inhibitors, beta-blockers, sublingual

nitro glycerine, and long-acting oral nitrates.

• USE IN CHILDREN:

Since there is no clinical experience in patients less than 18 years, use in children is not currently recommended.

• USE WITH RENAL IMPAIRMENT:

Amlodipine is extensively metabolized to inactive metabolites, with 10% excreted as unchanged drug in the urine. Changes in amlodipine plasma concentration are not correlated with the degree of renal impairment, therefore normal dosage is recommended. Amlodipine is not dialyzable.

• USE PATIENTS WITH IMPAIRED HEPATIC FUNCTION:

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

9 PREGNANCY, LACTATION AND FERTILITY:**• PREGNANCY**

The safety of amlodipine in human pregnancy has not been established.

In animal studies, reproductive toxicity was observed at high doses.

Use in pregnancy is only recommended when there is no safer alternative and when the disease itself carries greater risk for the mother and fetus.

• BREAST-FEEDING

It is not known whether amlodipine is excreted in breast milk. A decision on whether to continue/discontinue breastfeeding or add to continue / discontinue therapy with amlodipine should be made taking into account the benefit of breastfeeding to the child and the benefit of amlodipine therapy to the mother.

• FERTILITY

Reversible biochemical changes in the head of spermatozoa have been reported in some patients treated with calcium channel blockers. Clinical data are insufficient regarding the potential effect of amlodipine on fertility. In one at rat study, adverse effects were found on male fertility.

10 DRUG INTERACTIONS:

Impact of Other Drugs on Amlodipine

• CYP3A inhibitors -

Co-administration with CYP3A inhibitors (moderate and strong) results in increased systemic exposure to amlodipine and may require dose reduction. Monitor for symptoms of hypotension and edema when amlodipine is co-administered with CYP3A inhibitors to determine the need for dosage adjustment.

• CYP3A inducers -

No information is available on the quantitative effects of CYP3A inducers on amlodipine. Blood pressure should be monitored closely when amlodipine is co-administered with CYP3A inducers.

11 SIDE EFFECTS:

Headache, peripheral edema, fatigue, nausea, flushing and dizziness are occasionally observed; Peripheral edema is the most unacceptable side effect. It is dose-dependent and totally reversible on dose reduction or cessation of therapy.

Concurrent administration of amlodipine with thiazide diuretics, beta blockers, ACE inhibitors, nitrates, NSAIDs, antibiotics, oral antidiabetics, digoxin, cimetidine, warfarin, phenytoin has been demonstrated to be safe.

12 OVERDOSAGE:

It is not fully known what effects an overdose can cause in humans. Based on the effects of an amlodipine overdose in animals and based on the way the medication works, symptoms may include:

- Low blood pressure
- Fast heart rate.

This may cause signs or symptoms that include:

- Lightheadedness
- Dizziness
- Fainting
- Feelings of a rapidly or forcefully beating heart.

13 PRESENTATION:

Pack of 3 x 10 tablets.

14 STORAGE :

Store below 30°C. Protect from light.

Keep out of the reach of children.



Manufactured & Exported By:
V. S. International Pvt. Ltd.
Plot No.: 17&18, Golden Indl. Estate,
Somnath Road, Dabhel, Daman- 396215, India.

Amlodipine Comprimé USP 5 mg
Amlodipine Comprimé USP 10 mg

Bésilate d'amlodipine USP
Équivalent à d'amlodipine Bésilate 5 mg
Excipients q.s
Excipients à effets notoires
Chaque comprimé contient 61,23 mg de lactose

Chaque comprimé non enrobé contient
Bésilyate d'amlopidine USP
Équivalent à d'amlopidine Bésilyate 10 mg
Excipients q.s
Excipients à effets notoires
Chaque comprimé contient 80,50 mg de lactose

Besilate d'amlopidine BP, Cellulose microcristalline PH 102 DC BP, Lactose BP, Cellulose microcristalline PH 101 BP, Glycolate d'amidon sodique BP, Stéarate de magnésium BP

L'amlopipine est un nouvel antagoniste des canaux calciques de la famille des dihydropyridines. Les principaux avantages de l'amlopipine sont une tres longue demi-vie, un debut d'action effet sur la qualilte de vie.

Les comprimés d'Amlodipine Besilate contiennent 2,5, 5 et 10 mg d'amlopipine, respectivement.

L'amlodipine bloque le canal calcique lent et conduit donc à l'inhibition de la transmission transmembranaire influx d'ions Ca^{2+} dans le muscle lisse vasculaire et le muscle lisse cardiaque. Le effet est plus important sur le muscle vasculaire. L'amlodipine n'a pas d'effets inotropes négatifs l'homme a des doses thérapeutiques. Amlodipine réduit la pression artérielle en réduisant périphérique la résistance vasculaire et la tachycardia reflexe ne se produisent pas. En outre, en raison de l'apparition lente de l'action, l'hypotension aiguë ne se prod uit pas. Les effets antiangineux de l'amlodipine sont dus à une réduction primaire de la post-charge cardiaque conduisant à une amélioration de l'apport en oxygène myocardique: rapport de demande, a niveau donne d'exercice. Dans Angine de Prinzmetal (variante) en raison de la vasospasmodie coronarienne, l'amlodipine est efficace parce que ça bloque Vasoconstriction medee par le calcium, le potassium, la serotonine, lethromboxane A 2 et epinephrine. L'amlodipine n'a aucun effet sur le système R-A-A (renine-angiotensine-aldosterone), sympathique système nerveux et ANF (facteur natriurique auriculaire). Il n'a pas d'effets indésirables sur le plasma lipides, est diabétique et goutte.

L'amlodipine maintient des effets antihypertenseurs pendant au moins 24 heures. Il n'altère pas le sang la pression chez les normotendus; amplitude de la réduction de la pression artérielle avec l'amlodipine corréle avec la pression artérielle prétraitement dans l'hypertension modérée (diastolique 105 à 114 mm Hg) était 50% plus élevée que dans l'hypertension légère (diastolique 90-104 mm Hg). L'amlodipine ne produit pas de changements d'ECG ou de blocs de conduction. Il a augmenté l'ergométrie du tapis roulant ou de la bicyclette fail de l'exercice pour développer une déviation du segment ST.

L'absorption après l'administration orale est lente (délai avant pic des concentrations plasmatiques: 6 à 12 h après administration) et incomplète (jusqu'à 80%). Contrairement à ses congénères, l'amlodipine a un minimum ($< 4\%$) le métabolisme de premier passage, la liaison aux protéines plasmatiques est élevée (95%). Il a étendu distribution dans les tissus et les fluides corporels. L'amlodipine a une demi-vie d'élimination de 35 à 60 h. Les niveaux d'état d'équilibre sont atteints 7 à 9 jours après l'administration consecutive. Le médicament a large index thérapeutique, assurant la sécurité et l'efficacité sur une large gamme de concentrations.

1. L'amlopidine est un antihypertenseur de première intention, soit en monothérapie hypertensives) ou en association avec des inhibiteurs de l'ECA, des diurétiques et des bêta-bloquants.
2. L'amlopidine est également un traitement de première intention de l'angine de poitrine stable, et
3. Angine de Prinzmetal (variante). Il peut être utilisé en monothérapie ou en combinaison avec d'autres antiangineux dans l'angine réfractaire aux nitrates et aux bêta-bloquants.

Les comprimés d'amlopipine sont contre-indiqués chez les patients présentant une sensibilité connue aux dihydropyridine, l'amlopipine ou l'un des excipients.

Comme il n'existe pas d'essais contrôlés adéquats sur l'utilisation de l'amlodipine pendant la grossesse et présence de signes de tératogénicité chez certains animaux lors d'études précliniques, L'amlodipine ne doit pas être administrée pendant la grossesse, l'allaitement et le patient doit être conseillé d'utiliser une contraception efficace.

La dose initiale habituelle est de 5 mg une fois par jour par voie orale; la dose maxi male recommandee est de 10 mg une fois par jour. Chez les personnes agees (plus de 60 ans), insuffisance hepatiche, insuffisance hépatique et Chez les individus, la dose initiale recommandee est de 2,5 mg une fois par jour. Lars de l'ajout d'amlopidine a autre traitement antihypertenseur, la dose initiale est de 2,5 mg une fois par jour. Le dosage



Product Name	AMCAN 5 & 10 MG		Item Code :	XXXXXXX	Reference Art. :	NA
Packaging Material	Pack Insert		Reason of Change :	NEW	Specification :	
Foil Width	NA		Country :	BENIN	GSM	NA
Blister Type	NA		Pack Size :	3 x 10's Tablets	Board / Paper	NA
Blister Size	NA		Barcode No :	NA	Varnish Type	NA
Foil Thickness	NA		Pharmacode :	NA	Grain Direction	NA
Carton Size	NA		Min. Font Size :	NA	Braille	NA
Leaflet Size	230 (L) x 180 (H) mm		Language :	NA	Finishing Operation	NA
No of Colors : 1	 Black				Brand Embossing	No
					Inside Printing	No
Remark (if Any) :				Change Part Layout No. :		
				Developed For :		
	PREPARED BY	CHECKED BY			APPROVED BY	AUTHORISED BY
SIGNATURE						
DATE						
NAME						
DEPARTMENT	GRAPHIC DESIGNER	PACKING DEV.	PACKING DEPT.	QUALITY ASSURANCE	REGULATORY AFFAIRS	QUALITY ASSURANCE