For the use of a Registered Medical Practitioner or a Hospital or a Laboratory.

AMLODIPINE BESILATE TABLETS

AMDEPIN

COMPOSITION :
Each tablet of Amdepin 5 contains :
Amlodipine Besilate equivalent to Amlodipine 5 mg
White to off white, octagonal shaped, uncoated tablets, debossed with "AM 5" on one side and plain on other side.

Each tablet of Amdepin 10 contains :
Amlodipine Besilate equivalent to Amlodipine 10 mg
White to off white, octagonal shaped, uncoated tablets, debossed with "AM 10" on one side and plain on other side.

PHARMACOLOGY :
Amdepin is a calcium antagonist calcium (slow channel blocker) of the dihydropyridine group, It inhibits the transmembrane influx of calcium ions into cardiac and smooth muscles.
The mechanism of the anti-hypertensive action of Amdepin is due to a direct relaxant effect on vascular smooth muscles. The precise mechanism by which Amdepin relieves angina has not been fully determined, but Amdepin reduces total ischaemic burden by the following two actions :

1. Amdepin dilates peripheral arterioles and thus reduces the total peripheral resistance (after load) against which the heart works. Since there is no associated reflex tachycardia, this unloading of the heart reduces myocardial energy consumption and oxygen requirements and probably accounts for the effectiveness of Amdepin in myocardial ischaemia.
2. The mechanism of action of Amdepin probably involves dilation of the main coronary arteries and coronary arterioles, both in normal and ischaemic regions. This dilation increases myocardial oxygen delivery in patients with coronary artery spasm (Prinzmetal's or variant angina).

CLINICAL PHARMACOLOGY :
After oral administration of therapeutic doses, amlodipine is well absorbed with peak blood levels between 6-12 hour post-dose. The terminal plasma elimination half-life is about 35-50 hours and is consistent with once-daily administration. Steady state plasma level are reached after 7-8 days.
Amlodipine is predominantly cleared by metabolism to inactive metabolites with most metabolites excreted in the urine. Amlodipine is approximately 97.5% plasma protein bound.
In patients with hypertension, once daily dosing provides clinically significant reductions of blood pressure in both the supine and standing positions throughout the 24 hour interval. Due to the slow onset of action, acute hypotension is not a feature of Amdepin administration.
In patients with angina, once daily administration of Amdepin increases total exercise time and decreases both angina attack frequency and glyceryl trinitrate tablet consumption.
Amdepin has not been associated with any adverse metabolic effects or changes in plasma lipids and is suitable for use in patients with asthma, diabetes, and gout.

INDICATIONS :
Amdepin is indicated for the first-line treatment of hypertension and can be used as the sole agent to control blood pressure in a majority of the patients. Patients not adequately controlled on a single anti-hypertensive agent may benefit from the addition of Amdepin, which has been used in combination with a thiazide diuretic, beta-adrenoceptor blocking agent, or an angiotensin converting enzyme inhibitor.
Amdepin is indicated for the first-line treatment of myocardial ischaemia, whether due to fixed obstruction (stable angina) and/or vasospasm/vasoconstriction (Prinzmetal's or variant angina) of the coronary vasculature. Amdepin may also be used where the clinical presentation suggests a possible vasospastic/vasoconstrictive component but where vasospasm/vasoconstriction has not been confirmed. Amlodipine may be used alone, as monotherapy, or in combination with other antianginal drugs in patients with angina that is refractory to nitrates and/or adequate doses of beta blockers.

DOSAGE AND ADMINISTRATION :
Adults : For both hypertension and angina, the recommended initial dose is 5 mg. Amdepin orally once daily which may be increased to a maximum dose of 10 mg depending on the individual patient's response.
The dose does not need adjusting when Amdepin is given concurrently with thiazide diuretics, beta adrenoceptor blocking agents or angiotensin converting enzyme inhibitors. Amdepin can be administered with or without food.

Use in Children : Children and adolescents with hypertension from 6 years to 17 years of age. The recommended antihypertensive oral dose in pediatric patients aged 6 -17 years is 2.5 mg once daily as a starting dose, up-titrated to 5 mg once daily if blood pressure goal is not achieved after 4 weeks. Doses in excess of 5 mg daily have not been studied in pediatric patients.
Children under 6 years old : No data are available.

Use in elderly : Although elderly patients may have higher plasma concentrations of amlodipine than younger patients, the terminal elimination half-lives are similar. Amdepin is similarly well tolerated elderly or younger patients. Therefore the normal dosage is recommended.
Use in renal impairment : Amlodipine is extensively metabolised 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 the normal dosage is recommended, Amlodipin is not dialysable.

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

CONTRA-INDICATIONS :
Amdepin is contra-indicated in patients with a known sensitivity to dihydropyridines e.g. nifedipine, nicardipine, isradipine.

WARNING AND PRECAUTIONS :
Patients with heart failure
Patients with cardiac failure should be treated with caution. In a long-term study including patients suffering from severe heart failure (NYHA grade III and IV) the reported incidence of pulmonary oedema was higher in the amlodipine treated group than in the placebo group, but this was not indicating an aggravation of the heart failure.
Use in patients with impaired hepatic function
The half-life of amlodipine is prolonged in patients with impaired liver function; dosage recommendations have not been established. Amlodipine should therefore be administered with caution in these patients.

DRUG INTERACTIONS :
Amdepin has been safely administered with thiazide diuretics, beta-adrenoceptor blocking drugs, angiotensin-converting enzyme inhibitors, long-acting nitrates, sublingual glyceryl trinitrate, non-steroidal anti-inflammatory drugs, antibiotics and oral hypoglycemic agents.
Co-administration of Amdepin with digoxin did not change serum digoxin levels or digoxin renal clearance in normal volunteers. Co-administration of cimetidine did not alter the pharmacokinetics of amlodipine.
In healthy volunteers, co-administration of Amdepin did not significantly alter the effect of warfarin on prothrombin time. The introduction of Amdepin is not likely to result in the need for modification of an established warfarin regimen.
In vitro data from studies with human plasma indicate that amlodipine has no effect on protein binding of digoxin, phenytoin, warfarin or indomethacin.

PREGNANCY AND LACTATION :
Although some dihydropyridine compounds have been found to be teratogenic in animals, studies in rat and rabbit for amlodipine provide no evidence for a teratogenic effect. There is however, no clinical experience with Amdepin in pregnancy or lactation. Accordingly, Amdepin should not be administered during pregnancy or lactation, or to women of child-bearing potential unless effective contraception is used.

SIDE-EFFECTS:
The most commonly observed side effects were headache, oedema, fatigue, sommolence, nausea, flushing, palpitations and dizziness. Vomiting and abdominal pain have occured. Less commonly observed side effects include alopecia, altered bowel habits, arthralgia, asthenia, back pain, dyspepsia, dyspnea, gingival hyperplasia, gynecomastia, hyperglycemia, impotence, increased urinary frequency, leucopenia, malaise, mood changes and depression, dry mouth, muscle cramps, myalgia, peripheral neurophathy, pancreatitis, increased sweating, syncope, thrombocytopenia, vasculitis, and visual disturbances. Allergic reactions including pruritus, rash, angioedema and erythema multiforme have also been observed. The following adverse events have been reported but cannot be distinguished from the natural history of the underlying disease: myocardial infarction, arrhythmia (including ventricular tachycardia and atrial fibrillation) and chest pain. Hepatitis and jaundice and hepatic enzyme elevations have been reported (mostly consistent with cholestasis). Some cases severe enough to require hospitalisation have been reported in association with use of amlodipine.

OVERDOSAGE :
There is no well documented experience with Amdepin overdosage. Since amlodipine absorption is slow, gastric lavage may be worthwhile in some cases. Available data suggest that gross overdosage could result in excessive peripheral vasodilation with subsequent marked and probably prolonged systemic hypotension. Clinically significant hypotension due to Amdepin overdosage calls for active cardiovascular support including monitoring of cardiac and respiratory function, elevation of extremities, and urine output. A vasoconstrictor agent may be helpful in restoring vascular tone and blood pressure provided that there is no contra-indication to its use. Since amlodipine is highly protein-bound, dialysis is unlikely to be of benefit.

Pack Size : 10x10 Blister's in carton.

STORAGE : STORE BELOW 30°C. PROTECT FROM LIGHT

Revision of Package Insert : 23-MAY-2022

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Manufactured by :
CADILA PHARMACEUTICALS LIMITED
1389, Dholka-382 225, India.

Front **Back**

Size : 120 x 240 mm
Export : Malaysia
Pantone P Black C

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DG-23/05/22-V01