SUMMARY OF PRODUCTS CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT:

AMLODIPINE BESYLATE TABLETS USP 10 MG **(AMLOTRIX 10)**

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each uncoated tablet contains:

Amlodipine Besylate USP	
Eq. to Amlodipine	10 mg
Excipients	Q.S.

3. PHARMACEUTICAL FORM

Uncoated Tablets

4. CLINICAL PARTICULARS

4.1 Therapeutic Indication

It is used in the management of Hypertension, Chronic Stable angina pectoris and Vasospastic (Prinzmental's) angina.

4.2 Posology and Method of Administration

Adults & Elderly:

For both ***hypertension and angina*** the usual initial dose is 5 mg amlodipine once daily which may be increased to a maximum dose of 10 mg depending on the individual patient's response. In hypertensive patients, Amlodipine has been used in combination with a thiazide diuretic, alpha blocker, beta blocker, or an angiotensin converting enzyme inhibitor. For angina, Amlodipine may be used as monotherapy or in combination with other antianginal medicinal products in patients with angina that is refractory to nitrates and/or to adequate doses of beta blockers. No dose adjustment of Amlodipine is required upon concomitant administration of thiazide diuretics, beta blockers, and angiotensin-converting enzyme inhibitors.

Paediatric population: *Children and adolescents with hypertension from 6 years to 17 years of age:* The recommended antihypertensive oral dose in paediatric patients ages 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 paediatric patients.

Children under 6 years old: The effect of Amlodipine on blood pressure in patients less than 6 years of age is not known.

Method of administration

Tablet for oral administration.

4.3 Contraindications

Amlodipine is contraindicated in patients with hypersensitivity to dihydropyridine derivatives or Amlodipine, severe hypotension, shock (including cardiogenic shock), obstruction of the outflow tract of the left ventricle (e.g., high grade aortic stenosis) and haemodynamically unstable heart failure after acute myocardial infarction.

4.4 Special warnings and precautions for use

Calcium channel blockers, including Amlodipine, should be used with caution in patients with congestive heart failure, as they may increase the risk of future cardiovascular events and mortality. Amlodipine's 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.

4.5 Interaction with other medicinal products and other forms of Interaction

Effects of other medicinal products on Amlodipine:
CYP3A4 inhibitors*:* Concomitant use of Amlodipine with strong or moderate CYP3A4 inhibitors (protease inhibitors, azole antifungals, macrolides like Erythromycin or Clarithromycin, Verapamil or Diltiazem) may give rise to significant increase in Amlodipine exposure resulting in an increased risk of hypotension.
CYP3A4 inducers: Upon co-administration of known inducers of the CYP3A4, the plasma concentration of Amlodipine may vary. Therefore, blood pressure should be monitored and dose regulation considered both during and after concomitant medication particularly with strong CYP3A4 inducers (e.g. Rifampicin, Hypericum Perforatum). Administration of Amlodipine with grapefruit or grapefruit juice is not recommended as bioavailability may be increased in some patients resulting in increased blood pressure lowering effects.
Effects of Amlodipine on other medicinal products:
Tacrolimus: There is a risk of increased tacrolimus blood levels when co-administered with Amlodipine.
Mechanistic Target of Rapamycin (mTOR) Inhibitors*:* MTOR inhibitors such as sirolimus, temsirolimus, and everolimus are CYP3A substrates. Amlodipine is a weak CYP3A inhibitor. With concomitant use of mTOR inhibitors, Amlodipine may increase exposure of mTOR inhibitors.
Simvastatin*:* Co-administration of multiple doses of 10 mg of Amlodipine with 80 mg simvastatin resulted in a 77% increase in exposure to simvastatin compared to simvastatin alone. Limit the dose of simvastatin in patients on Amlodipine to 20 mg daily.

4.6 Pregnancy and lactation

Pregnancy: The safety of Amlodipine in human pregnancy has not been established. Use in pregnancy is only recommended when there is no safer alternative and when the disease itself carries greater risk for the mother and foetus.
Lactation: Amlodipine is excreted in human milk. The effect of Amlodipine on infants is unknown. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with Amlodipine should be made taking into account the benefit of breast-feeding to the child and the benefit of Amlodipine therapy to the mother.

4.7 Effects on ability to drive and use machines

Amlodipine can have minor or moderate influence on the ability to drive and use machines. If patients taking Amlodipine suffer from dizziness, headache, fatigue or nausea the ability to react may be impaired. Caution is recommended especially at the start of treatment.

4.8 Undesirable effects

Following adverse effects have been observed and reported during treatment with Amlodipine.

***Common or very common*:** Abdominal pain, dizziness, fatigue, flushing, headache, nausea, oedema, palpitation, sleep disturbances

***Uncommon*:** Alopecia, arthralgia, asthenia, back pain, chest pain, dry mouth, dyspnoea, gastro-intestinal disturbances, gynaecomastia, hypotension, impotence, mood changes, muscle cramps, myalgia, paraesthesia, pruritus, purpura, rashes, rhinitis, skin discolouration, sweating, syncope, taste disturbances, tinnitus, tremor, urinary disturbances, visual disturbances, weight changes.

***Very rare*:** Angioedema, arrhythmias, cholestasis, coughing, gastritis, gingival hyperplasia, hepatitis, hyperglycaemia, jaundice, myocardial infarction, pancreatitis, peripheral neuropathy, tachycardia, thrombocytopenia, urticaria, vasculitis.

***Frequency not known*:** Erythema multiforme.

4.9 Overdose

Symptoms: Available data suggest that gross overdosage could result in excessive peripheral vasodilatation and possibly reflex tachycardia. Marked and probably prolonged systemic hypotension up to and including shock with fatal outcome have been reported.

Treatment: Clinically significant hypotension due to Amlodipine overdosage calls for active cardiovascular support including frequent monitoring of cardiac and respiratory function, elevation of extremities and attention to circulating fluid volume and urine output. A vasoconstrictor may be helpful in restoring vascular tone and blood pressure, provided that there is no contraindication to its use. Intravenous calcium gluconate may be beneficial in reversing the effects of calcium channel blockade. Gastric lavage may be worthwhile in some cases. In healthy volunteers the use of charcoal up to 2 hours after administration of Amlodipine 10 mg has been shown to reduce the absorption rate of Amlodipine. Since Amlodipine is highly protein-bound, dialysis is not likely to be of benefit.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Amlodipine is a Calcium ion influx inhibitor of the dihydropyridine group (slow channel blocker or calcium ion antagonist) and inhibits the transmembrane influx of calcium ions into cardiac and vascular smooth muscle. The mechanism of the antihypertensive action of Amlodipine is due to a direct relaxant effect on vascular smooth muscle. The precise mechanism by which Amlodipine relieves angina has not been fully determined but Amlodipine reduces total ischaemic burden by the following two actions.

1) Amlodipine dilates peripheral arterioles and thus, reduces the total peripheral resistance (afterload) against which the heart works. Since the heart rate remains

stable, this unloading of the heart reduces myocardial energy consumption and oxygen requirements.
2) The mechanism of action of Amlodipine also probably involves dilatation of the main coronary arteries and coronary arterioles, both in normal and ischaemic regions. This dilatation increases myocardial oxygen delivery in patients with coronary artery spasm (Prinzmetal's or variant angina).

5.2 Pharmacokinetic properties

Amlodipine is well absorbed after oral doses with peak blood concentrations occurring after 6 to 12 hours. The bioavailability varies but is usually about 60 to 65%. Amlodipine is reported to be about 97.5% bound to plasma proteins. It has a prolonged terminal elimination half-life of 35 to 50 hours and steady-state plasma concentrations are not achieved until after 7 to 8 days of use. Amlodipine is extensively metabolised in the liver; metabolites are mostly excreted in urine together with less than 10% of a dose as unchanged drug. Amlodipine is not removed by dialysis.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipient(s)

Microcrystalline Cellulose (200), Dibasic Calcium Phosphate, Sodium Starch Glycolate (Type A), Colloidal Anhydrous Silica and Magnesium Stearate.

6.2 Shelf-life

36 months

6.3 Special precautions for storage

Store below 30°C. Protect from light. Store in the original package.

6.4 Nature and contents of container

10 Tablets are Blister packed. Such 10 Blisters are packed in a Printed Carton with packing insert.

7. MARKETING AUTHORISATION HOLDER

BIOMATRIX HEALTHCARE PVT LTD.
Survey No. 624, Sarkhej – Bavla Highway, Vil.: Rajoda,
Tal.: Bavla, Dist.: Ahmedabad – 382220, Gujarat, INDIA.

8. Marketing authorisation number(s)

10934/NMR/2023

9. Date of first authorisation/renewal of the authorisation

Jan 7, 2024

10. Date of revision of the text