Summary of Product Characteristics for Pharmaceutical Products

1.Name of the medicinal product

Esem Tablet 2.5mg

Esem Tablet 5.0mg

2.Qualitative and quantitative composition

Each uncoated tablet contains S-Amlodipine Besylate

Equivalent to S-Amlodipine 2.5/5.0 mg

For the full list of excipients, see section 6.1.

3.Pharmaceutical form

Un coated tablets.

S-Amlodipine Besylate Tablets 2.5/5.0 mg: Yellow colored round shaped smooth flat bevel edged plain uncoated tablet.

4.Clinical particulars

4.1 Therapeutic indications Hypertension

Prophylaxis of chronic stable angina pectoris

Prinzmetal's (variant) angina when diagnosed by a cardiologist

In hypertensive patients, S-Amlodipine tablet has been used in combination with a thiazide diuretic, alpha blocker, beta-adrenoceptor blocking agent, or an angiotensin converting enzyme inhibitor. For angina, S-Amlodipine tablet may be used 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. S Amlodipine tablet is well tolerated in patients with heart failure and a history of hypertension or ischaemic heart disease.

4.2 Posology and method of administration

In adults: For both hypertension and angina the usual initial dose is 5mg Amlodpine tablet once daily which may be increased to a maximum dose of 10 mg depending on the individual patient's response.
No dose adjustment of S-Amlodipine tablet is required upon concomitant administration of thiazide diuretics, beta blockers, and angiotensin-converting enzyme inhibitors.

Use in children: Not recommended.

Use in the elderly: S-Amlodipine tablet, used at similar doses in elderly or younger patients, is equally well tolerated. Therefore normal dosage regimens are recommended.
Patients with hepatic impairment: See section Special warnings and precautions for use.

Patients with renal impairment: Changes in S-Amlodipine plasma concentrations are not correlated with degree of renal impairment, therefore the normal dosage is recommended. S Amlodipine is not dialysable.

4.3 Contraindications

Hypersensitivity to any of the components of the formulation.

S-Amlodipine tablet is contra-indicated in patients with a known sensitivity to dihydropyridines, S Amlodipine or any of the excipients.
S-Amlodipine tablet should not be used in cardiogenic shock, clinically significant aortic stenosis, unstable angina (excluding Prinzmetal's angina). Pregnancy and lactation.

4.4 Special warnings and precautions for use

Use in patients with Heart Failure: In a long-term, placebo controlled study (PRAISE-2) of Amlodpine tablet in patients with NYHA III and IV heart failure of nonischaemic aetiology, S Amlodipine was associated with increased reports of pulmonary oedema despite no significant difference in the incidence of worsening heart failure as compared to placebo. See section 5.1 “Pharmacodynamic Properties”.
No controlled clinical study of S-amlodipine has been performed in patients with hepatic impairment and renal impairment. Clinical studies in patients with normal liver function have shown that there is no elevation in the hepatic enzymes with the use of S-amlodipine. However, caution should be taken while administering S-amlodipine to such patients.
Pregnant Women & Nursing Mothers

There is no data available on the use of (S) - amlodipine in pregnant and lactating women, hence the drug should be administered only when the potential benefits outweighs the risk to the patient.
Children

Safety and effectiveness of this product in children have not been established.

Use in patients with impaired hepatic function: As with all calcium antagonists, Samlodipine'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.
There are no data to support the use of S-Amlodipine tablet alone, during or within one month of a myocardial infarction.

The safety and efficacy of S-Amlodipine tablet in hypertensive crisis has not been established.

4.5 Interaction with other medicinal products and other forms of interaction

Amlodpine tablet has been safely administered with thiazide diuretics, alpha blockers, beta blockers, angiotensin-converting enzyme inhibitors, long-acting nitrates, sublingual glyceryl trinitrate, non-steroidal anti-inflammatory drugs, antibiotics, and oral hypoglycaemic drugs.
In vitro data from studies with human plasma, indicate that S-Amlodipine has no effect on protein binding of digoxin, phenytoin, warfarin or indometacin.
Special Studies: Effect of other agents on S-Amlodipine Cimetidine:

Co-administration of Amlodpine tablet with cimetidine did not alter the pharmacokinetics of S-Amlodipine tablet.
Grapefruit Juice: Co-administration of 240ml of grapefruit juice with a single oral dose of Amlodpine tablet 10mg in 20 healthy volunteers had no significant effect on the pharmacokinetics of S-Amlodipine tablet.
Sildenafil: When Amlodpine tablet and sildenafil were used in combination, each agent independently exerted its own blood pressure lowering effect.
Special Studies: Effect of S-Amlodipine on other agents

Atorvastatin: Co-administration of multiple 10mg doses of Amlodpine tablet with 80mg of atorvastatin resulted in no significant change in the steady state pharmacokinetic parameters of atorvastatin.
Digoxin: Co-administration of Amlodpine tablet with digoxin did not change serum digoxin levels or digoxin renal clearance in normal volunteers.
Warfarin: In healthy male volunteers, the co-administration of Amlodpine tablet does not significantly alter the effect of warfarin on prothrombin response time. Coadministration of Amlodpine tablet with warfarin did not change the warfarin prothrombin response time.
Ciclosporin: Pharmacokinetic studies with ciclosporin have demonstrated that Amlodpine tablet does not significantly alter the pharmacokinetics of ciclosporin.

4.6 Fertility, pregnancy and lactation

Although some dihydropyridine compounds have been found to be teratogenic in animals, data in the rat and rabbit for S-Amlodipine provide no evidence for a teratogenic effect. There is, however, no clinical experience with the preparation in pregnancy or lactation. Accordingly, S-Amlodipine tablet should not be administered during pregnancy, or lactation, or to women of childbearing potential unless effective contraception is used.

4.7 Effects on ability to drive and use machines

Clinical experience with Amlodpine tablet indicates that therapy is unlikely to impair a patient's ability to drive or use machinery.

4.8 Undesirable effects

Adverse events that have been reported in S-Amlodipine trials are categorised below, according to system organ class and frequency. Frequencies are defined as: very common (>10%); common (>1%, <10%); uncommon (>0.1%, <1%); rare (>0.01%, <0.1%) and very rare (<0.01%).
Very rare

Blood and the Lymphatic System Disorders:- thrombocytopenia Immune System Disorders: allergic reaction
Metabolism and Nutrition Disorders: hyperglycaemia
Nervous System Disorders: peripheral neuropathy
Cardiac Disorders: Myocardial infarction, arrhythmia, ventricular tachycardia and atrial fibrillation)
Vascular Disorders: vasculitis

Respiratory, Thoracic and Mediastinal Disorders: coughing

Gastrointestinal Disorders: pancreatitis, gastritis, gingival hyperplasia

Hepato-biliary Disorders: hepatitis, jaundice and hepatic enzyme elevations (mostly consistent with cholestasis)
Skin and Subcutaneous Tissue Disorders: angioedema, erythema multiforme, urticaria

Uncommon

Psychiatric Disorders: insomnia, mood changes

Nervous System Disorders: tremor, taste perversion, syncope, hypoaesthesia,

Eye Disorders: visual disturbances

Ear and Labyrinth Disorders: tinnitus

Vascular Disorders: hypotension
Respiratory, Thoracic and Mediastinal Disorders: dyspnoea, rhinitis Gastrointestinal Disorders: vomiting, dyspepsia, altered bowel habits, dry mouth
Skin and Subcutaneous Tissue Disorders: alopecia, purpura, skin discolouration, increased sweating, pruritus, rash
Musculoskeletal and Connective Tissue Disorders: arthralgia, myalgia, muscle cramps, back pain *Renal and Urinary Disorders:* micturition disorder,nocturia, increased urinary frequency
Reproductive System and Breast Disorders: impotence, gynaecomastia

General Disorders and Administration Site Conditions: chest pain, asthenia, pain, malaise

Investigations: weight increase, weight decrease

Common

Nervous System Disorders: somnolence, dizziness, headache

Cardiac Disorders: Palpitations

Vascular Disorders: flushing

Gastrointestinal Disorders: abdominal pain, nausea

General Disorders and Administration Site Conditions: oedema, fatigue.

Reporting of suspected adverse reactions:
Healthcare professionals are requested to report any suspected adverse reactions via national Pharmacovigilance Electronic Reporting Systems' to the respective national regulatory authorities.

4.9 Overdose

There are no reported cases of overdosage with the use of S-amlodipine.

Overdosage with racemic amlodipine may cause excessive peripheral vasodilation with marked hypotension and possibly a reflex tachycardia. Hence, caution should be taken in case of an overdosage with Samlodipoine. If massive overdose occurs, active cardiac and respiratory monitoring should be instituted. Frequent blood pressure measurements should be performed. Should hypotension occur, cardiovascular support including elevation of the extremities and the judicious administration of fluids should be initiated. If hypotension remains unresponsive to these conservative measures, administration of vasopressors (such as phenylephrine) should be considered with attention to circulating. If massive overdose occurs, gastric lavage should be employed. As this product is highly plasma protein bound, hemodialysis is not likely to be of benefit.

5.Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Calcium channel blockers – Dihydropyridine derivatives.

ATC Code: C08CA01.

S-Amlodipine tablet 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 S Amlodipine tablet is due to a direct relaxant effect on vascular smooth muscle. The precise mechanism by which SAmlodipine tablet relieves angina has not been fully

determined but S-Amlodipine tablet reduces total ischaemic burden by the following two actions.

1) S-Amlodipine tablet 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 S-Amlodipine tablet 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).

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 S-Amlodipine tablet administration.

In patients with angina, once daily administration of S-Amlodipine tablet increases total exercise time, time to angina onset, and time to 1mm ST segment depression, and decreases both angina attack frequency and glyceryl trinitrate tablet consumption.

In a follow-up, long term, placebo controlled study (PRAISE-2) of S-Amlodipine tablet in patients with NYHA III and IV heart failure without clinical symptoms or objective findings suggestive or underlying ischaemic disease, on stable doses of ACE inhibitors, digitalis, and diuretics, S Amlodipine tablet had no effect on total cardiovascular mortality. In this same population S Amlodipine tablet was associated with increased reports of pulmonary oedema despite no significant difference in the incidence of worsening heart failure as compared to placebo.

A randomized double-blind morbidity-mortality study called the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) was performed to compare newer drug therapies: S-Amlodipine 2.5-10 mg/d (calcium channel blocker) or lisinopril 10-40 mg/d (ACE inhibitor) as first-line therapies to that of the thiazidediuretic, chlorthalidone 12.5-25 mg/d in mild to moderate hypertension."

A total of 33,357 hypertensive patients aged 55 or older were randomized and followed for a mean of 4.9 years. The patients had at least one additional CHD risk factor, including: previous myocardial infarction or stroke > 6 months prior to enrollment) or documentation of other atherosclerotic CVD (overall 51.5%), type 2 diabetes (36.1%), HDL-C < 35 mg/dL (11.6%), left ventricular hypertrophy diagnosed by electrocardiogram or echocardiography (20.9%), current cigarette smoking (21.9%). The primary endpoint was a composite of fatal CHD or non-fatal myocardial infarction. There was no significant difference in the primary endpoint between S-Amlodipinebased therapy and chlorthalidone-based therapy: RR 0.98 95% CI(0.90-1.07) p=0.65.Among Secondary Endpoints, the incidence of heart failure (component of a composite combined cardiovascular endpoint) was significantly higher in the SAmlodipine group as compared to the chlorthalidone group (10.2% % vs 7.7%, RR 1.38, 95% CI [1.25-1.52] p<0.001). However,

there was no significant difference in allcause mortality between S-Amlodipine-based therapy and chlorthalidone-based therapy. RR 0.96 95% CI [0.89-1.02] p= 0.20.
In a study involving 268 children aged 6 -17 years with predominantly secondary hypertension, comparison of a 2.5 mg dose, and 5.0 mg dose of S-Amlodipine with placebo, showed that both doses reduced Systolic Blood Pressure significantly more than placebo. The difference between the two doses was not statistically significant. The long-term effects of S-Amlodipine on growth, puberty and general development have not been studied. The long-term efficacy of S-Amlodipine on therapy in childhood to reduce cardiovascular morbidity and mortality in adulthood have also not been established.

5.2 Pharmacokinetic properties

Administration of (S) - amlodipine 2.5 mg as a single dose in the fasting state produced maximum plasma concentration (Cmax) of 8.30 ± 1.071 ng/ ml in 2.73 ± 0.88 hrs. (Tmax). Amlodipine is extensively (about 90%) converted to inactive metabolites via hepatic metabolism with 10% of the parent compound and 60% of the metabolites excreted in the urine. Ex vivo studies have shown that approximately 93% of the circulating drug is bound to plasma proteins in hypertensive patients. The mean AUC0-t value (t= 48 hrs.) of Tablet Samlodipine (2.5mg) is 95.33 ± 14.45 ng.hr/ml. The AUC0 ∞ value is recorded to be 140.91± 28.06 ng.hr/ml. The plasma elimination half life of (S)-amlodipine has been found to be 31.09 ± 12.65 hrs.

5.3 Preclinical safety data

None

6.Pharmaceutical particulars

6.1 List of excipients

Microcrystalline Cellulose (PH 102), Sodium Starch Glycollate, Iron Oxide Yellow, Collodial Silicon Dioxide, Povidone K 30, Isopropyl alcohol, Magnesium Stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 30°C. Protect from light and moistrure. Keep out of reach of children.

6.5 Nature and contents of container

Alu-Alu blister pack of 10 Tablets.

6.6 Special precautions for disposal and other handling

No special requirements

7.Marketing authorisation holder

MSN LABORATORIES PRIVATE LIMITED

MSN House, Plot No. : C-24, Sanathnagar Industrial Estate, Sanath Nagar, Hyderabad – 500 018

Telangana, India.

8. Market Authorization Number

H2017/3766/121

9. Date of First Authorization/Renewal

August 2026

10. Date of revision of the text

August 2026