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

ESAM

(S-Amlodipine Besylate Tablets, 2.5 mg and 5 mg)

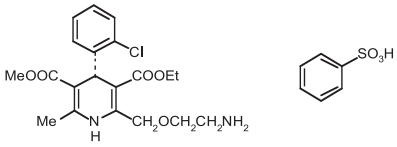
COMPOSITION

ESAM-2.5: Each uncoated tablet contains S-Amlodipine Besylate equivalent to S-Amlodipine.....2.5 mg

ESAM-5: Each uncoated tablet contains S-Amlodipine Besylate equivalent to S- Amlodipine.....5 mg

PROPERTIES

S-Amlodipine Besylate is a white to pale yellow powder, freely soluble in methanol. Chemically it is (S)-3-ethyl-5-methyl-2-(2-aminoethoxymethyl)-4-(2-chlorophenyl)1,4-dihydro-6-methyl-3,5-pyridinedicarboxylate benzenesulphonate. Its empirical formula is $C_{20}H_{25}ClN_2O_5$. C6H6O3S with a molecular weight of 567.1, and its structural formula is:



PHARMACOLOGICAL PROPERTIES

PHARMACODYNAMICS

S-Amlodipine is a long-acting calcium channel blocker that inhibits the transmembrane influx of calcium ions into vascular smooth muscle and cardiac muscle. The contractile process of cardiac muscle and vascular smooth muscle are dependent upon movement of extra cellular calcium ions into these cells through specific ion channels. By inhibiting calcium ion influx this product directly diastoles vascular smooth muscle, resisting hypertension. The mechanism of remitting angina pectoris with this product is not yet determined completely, but it is clear that this product can abate myocardial ischemia through the following functions:

1. Dilate the peripheral small artery, decreasing peripheral resistance, causing the reduction of energy consumption and oxygen requirement of cardiac muscle.
2. Dilate the coronary artery and the coronary small artery at normal and ischaemic areas, increasing the oxygen supply to cardiac muscle of the patients with coronary spasm

PHARMACOKINETICS

Absorption

After oral administration of S-Amlodipine besylate tablet, the blood-drug concentration reaches peak value within 6-12 hours. The absolute bioavailability has been estimated to be in between 64-80% and the apparent distribution volume is approximately 21 L/kg.

Distribution

The blood-drug concentration comes up to homeostasis after successive administration with once a day for 7-8 days. Approximately 93% of the circulating drug is bound to plasma proteins.

Metabolism

S-Amlodipine besylate is extensively converted to inactive metabolites via hepatic metabolism.

Elimination

S-Amlodipine is excreted out along with urine, with 10% of the parent, and 60% of the metabolites. The terminal elimination half-life for S-Amlodipine is 35-50 hours. The average final elimination half-life period of S-Amlodipine is 49.6 hours while for R-Amlodipine it is 34.9 hours.

INDICATIONS

ESAM is indicated in the treatment of essential hypertension and angina pectoris.

CONTRAINDICATIONS

ESAM is contraindicated in patients allergic to dihydropyridine calcium antagonist.

PRECAUTIONS

Hepatic failure patients: Similar to other calcium antagonist, the half-life of S-Amlodipine is prolonged in patients with impaired liver function. So, caution should be exercised in such patients.

Renal failure patients: The normal dose may be adopted. This product is not dialyzed.

Use in Pregnancy, Nursing mothers and Children:

Pregnant Women & Nursing Mothers: S-Amlodipine should be recommended only while there is no other safer alternative and the potential benefit outweighs the potential risk to the fetus. In the absence of this information, it is recommended that nursing should be discontinued while this product is administered.

Children: Safety and effectiveness of S - Amlodipine in children have not been established.

ADVERSE REACTIONS

S-Amlodipine is generally well tolerated.

The most commonly observed side effects are headache, edema, fatigue, flushing and dizziness.

Less common side effects include nausea, abdominal pain, somnolence and palpitations.

Rare side effects include muscle cramps, frequency of micturition or nocturia, coughing, breathlessness, epistaxis, impotence, nervousness and conjunctivitis.

No clinically significant pattern of laboratory test abnormalities related to S-Amlodipine has been observed.

S-Amlodipine has not been associated with any adverse metabolic effects or changes in plasma lipids. S-Amlodipine has been used safely in patients with well-compensated congestive heart failure, peripheral vascular disease, chronic obstructive pulmonary disease, abnormal lipid profiles and diabetes mellitus. Like other calcium antagonist, adverse reaction seldom causes myocardial infarction and pectoralgia, which cannot be clearly distinguished from fundamental diseases of patients.

DRUG INTERACTIONS

S-Amlodipine has been safely administered with thiazide diuretics, beta adrenoceptor blocking drugs, angiotensin converting enzyme inhibitors, long acting nitrates, sublingual glyceryl trinitrate, nonsteroidal anti-inflammatory drugs, antibiotics, and oral hypoglycemic agents.

Co administration of S-Amlodipine 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 S-Amlodipine.

In healthy volunteers, co administration of S-Amlodipine did not significantly alter the effect of warfarin on prothrombin time. The introduction of S-Amlodipine is not likely to result in the need for modification of an established warfarin regimen.

DOSAGE AND ADMINISTRATION

The recommended dose is 2.5 mg once daily taken with or without food, which may be increased to a maximum dose of 5 mg depending on the individual patient s response.

No dosage adjustment is necessary for elderly patients or patients with renal disease. The half-life of S-Amlodipine is prolonged in patients with impaired liver function. ESAM should therefore be administered with caution in such patients.

OVERDOSAGE

Symptoms: Available data suggests that the gross overdosage could result in excessive peripheral vasodilation with subsequent marked and probably prolonged hypotension.

Treatment: Since absorption of S-Amlodipine is slow, gastric lavage should be performed. Active cardiovascular support including monitoring of cardiac and respiratory function, elevation of extremities, and attention to circulating fluid volume and urine output should be given. Intravenous calcium gluconate may help to reverse the effects of calcium entry blockade. A vasoconstrictor agent may be helpful in restoring vascular tone and blood pressure provided that there is no contraindication to its use. Since S-Amlodipine is highly protein bound, dialysis is unlikely to be of benefit.

PRESENTATION

ESAM-2.5: It is available as white to off white, square shape, flat uncoated tablets with torrent logo on one side, in strips of 10 tablets.

ESAM-5: It is available as yellow coloured, square shape, flat uncoated tablets with torrent logo on one side; in strips of 10 tablets.

torrent PHARMA

Manufactured by :
TORRENT PHARMACEUTICALS LTD.
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