

Zeglopin

(Amlodipine Besylate U.S.P.)

زیگلوپین
(ایملوڈیپین بے سیلیٹ یو ایس پی)

COMPOSITION

Each **Zeglopin** 5mg tablet contains Amlodipine Besylate eq. to 5mg of Amlodipine.
Each **Zeglopin** 10mg tablet contains Amlodipine Besylate eq. to 10mg of Amlodipine.
"Product contains Lactose"

MECHANISM OF ACTION

Amlodipine Besylate inhibits calcium ion influx across cell membranes selectively, with a greater effect on vascular smooth muscle cells than on cardiac muscle cells. Negative inotropic effects can be detected in vitro but such effects have not been seen in intact animals at therapeutic doses. Amlodipine Besylate is a peripheral arterial vasodilator that acts directly on vascular smooth muscle to cause a reduction in peripheral vascular resistance and reduction in blood pressure. The precise mechanisms by which Amlodipine Besylate relieves angina have not been fully delineated, but are thought to include the following:

Exertional Angina: In patients with exertional angina, Amlodipine Besylate reduces the total peripheral resistance (afterload) against which the heart works and reduces the rate pressure product, and thus myocardial oxygen demand, at any given level of exercise.

Vasospastic Angina: Amlodipine Besylate has been demonstrated to block constriction and restore blood flow in coronary arteries and arterioles in response to calcium, potassium epinephrine, serotonin, and thromboxane A2 analog in experimental animal models and in human coronary vessels in vitro. This inhibition of coronary spasm is responsible for the effectiveness of Amlodipine Besylate in vasospastic (Prinzmetal or variant) angina.

PHARMACOKINETICS

Absorption

After oral administration of therapeutic doses of Amlodipine Besylate, absorption produces peak plasma concentrations between 6 and 12 hours. Absolute bioavailability has been estimated to be between 64 and 90%. The bioavailability of Amlodipine Besylate is not altered by the presence of food. Steady-state plasma levels of Amlodipine Besylate are reached after 7 to 8 days of consecutive daily dosing.

Distribution

Ex vivo studies have shown that approximately 93% of the circulating drug is bound to plasma proteins in hypertensive patients.

Metabolism

Amlodipine Besylate is extensively (about 90%) converted to inactive metabolites via hepatic metabolism.

Excretion

10% of the parent compound and 60% of the metabolites excreted in the urine. Elimination from the plasma is biphasic with a terminal elimination half-life of about 30-50 hours.

Renal Dysfunction

The pharmacokinetics of Amlodipine Besylate are not significantly influenced by renal impairment. Patients with renal failure may therefore receive the usual initial dose.

Hepatic Dysfunction

Elderly patients and patients with hepatic insufficiency have decreased clearance of Amlodipine Besylate with a resulting increase in AUC of approximately 40-60%, and a lower initial dose may be required. A similar increase in AUC was observed in patients with moderate to severe heart failure.

Pediatric Patients

Hypertensive patients aged 6 to 17 years received doses of Amlodipine Besylate between 1.25 mg and 20 mg. Weight-adjusted clearance and volume of distribution were similar to values in adults.

INDICATIONS

Hypertension

It may be used alone or in combination with other antihypertensive agents.

Coronary Artery Disease (CAD)

Chronic Stable Angina: Amlodipine Besylate may be used alone or in combination with other antianginal agents.

Vasospastic Angina (Prinzmetal's or Variant Angina): Amlodipine Besylate is indicated for the treatment of confirmed or suspected vasospastic angina. Amlodipine Besylate may be used as monotherapy or in combination with other antianginal agents.

Angiographically Documented CAD: In patients with recently documented CAD by angiography and without heart failure or an ejection fraction < 40%, Amlodipine Besylate is indicated to reduce the risk of hospitalization due to angina and to reduce the risk of a coronary revascularization procedure.

DOSAGE AND ADMINISTRATION

Adults: The usual initial antihypertensive oral dose of Amlodipine Besylate is 5 mg once daily with a maximum dose of 10 mg once daily. Small, fragile, or elderly patients, or patients with hepatic insufficiency may be started on 2.5 mg once daily and this dose may be used when adding Amlodipine Besylate to other antihypertensive therapy.

Adjust dosage according to each patient's need. In general, titration should proceed over 7 to 14 days so that the physician can fully assess the patient's response to each dose level. Titration may proceed more rapidly, however, if clinically warranted, provided the patient is assessed frequently. The recommended dose for chronic stable or vasospastic angina is 5-10 mg, with the lower dose suggested in the elderly and in patients with hepatic insufficiency. Most patients will require 10 mg for adequate effect. The recommended dose range for patients with coronary artery disease is 5-10 mg once daily. In clinical studies, the majority of patients required 10 mg.

Children: The effective antihypertensive oral dose in pediatric patients ages 6-17 years is 2.5 mg to 5 mg once daily. Doses in excess of 5 mg daily have not been studied in pediatric patients.

SIDE EFFECTS

The most common side effects are headache and edema.

Cardiovascular: Palpitation, flushing, postural dizziness, arrhythmia (including ventricular tachycardia and atrial fibrillation), bradycardia, chest pain, hypotension, peripheral ischemia, syncope, tachycardia, postural hypotension, vasculitis.

Central and Peripheral Nervous System: Somnolence, hypoesthesia, neuropathy peripheral, paresthesia, tremor, vertigo.

Gastrointestinal: Nausea, abdominal pain, anorexia, constipation, dyspepsia, dysphagia, diarrhea, flatulence, pancreatitis, vomiting, gingival hyperplasia.

General: Fatigue, allergic reaction, asthenia, back pain, hot flushes, malaise, pain, rigors, weight gain, weight decrease.

Musculoskeletal System: Arthralgia, arthrosis, muscle cramps, myalgia.

Psychiatric: Sexual dysfunction (male and female), insomnia, nervousness, depression, abnormal dreams, anxiety, depersonalization.

Respiratory System: Dyspnea, epistaxis.

Skin and Appendages: Angioedema, erythema multiforme, pruritus, rash, rash erythematous, rash maculopapular.

Special Senses: Abnormal vision, conjunctivitis, diplopia, eye pain, tinnitus.

Urinary System: Micturition frequency, micturition disorder, nocturia.

Autonomic Nervous System: Dry mouth, sweating increased.

Metabolic and Nutritional: Hyperglycemia, thirst.

Hemopoietic: Leukopenia, purpura, thrombocytopenia.

Other reactions occurred sporadically and cannot be distinguished from medications or concurrent disease states such as myocardial infarction and angina.

Amlodipine Besylate therapy has not been associated with clinically significant changes in routine laboratory tests.

Amlodipine Besylate has been used safely in patients with chronic obstructive pulmonary disease, well-compensated congestive heart failure, coronary artery disease, peripheral vascular disease, diabetes mellitus, and abnormal lipid profiles.

DRUG INTERACTIONS

In Vitro Data: In vitro data indicate that Amlodipine Besylate has no effect on the human plasma protein binding of digoxin, phenytoin, warfarin, and indomethacin.

Cimetidine: Co-administration did not alter the pharmacokinetics of Amlodipine Besylate.

Magnesium and Aluminum Hydroxide Antacid: Co-administration had no significant effect on the pharmacokinetics of Amlodipine Besylate.

Sildenafil: A single 100 mg dose of sildenafil in subjects with essential hypertension had no effect on the pharmacokinetic parameters of Amlodipine Besylate.

Atorvastatin: Co-administration resulted in no significant change in the steady-state pharmacokinetic parameters of atorvastatin.

Simvastatin: Co-administration resulted in a 77% increase in exposure to simvastatin compared to simvastatin alone. Limit the dose of simvastatin in patients on Amlodipine Besylate to 20 mg daily.

Digoxin: Co-administration did not change serum digoxin levels or digoxin renal clearance in normal volunteers.

Ethanol (Alcohol): Amlodipine Besylate had no significant effect on the pharmacokinetics of ethanol.

Warfarin: Co-administration did not change the warfarin prothrombin response time.

CYP3A4 Inhibitors: Monitor for symptoms of hypotension and edema when Amlodipine Besylate is co-administered with CYP3A4 inhibitors.

CYP3A4 Inducers: No information is available on the quantitative effects of CYP3A4 inducers on Amlodipine Besylate. Blood pressure should be closely monitored when Amlodipine Besylate is co-administered with CYP3A4 inducers.

PRECAUTIONS

Hypotension: Symptomatic hypotension is possible, particularly in patients with severe aortic stenosis. Because of the gradual onset of action, acute hypotension is unlikely.

Increased Angina or Myocardial Infarction: Worsening angina and acute myocardial infarction can develop after starting or increasing the dose of Amlodipine Besylate, particularly in patients with severe obstructive coronary artery disease.

Beta-Blocker Withdrawal: Amlodipine Besylate is not a beta-blocker and therefore gives no protection against the dangers of abrupt beta-blocker withdrawal; any such withdrawal should be by gradual reduction of the dose of beta-blocker.

Patients with Hepatic Failure: Because Amlodipine Besylate is extensively metabolized by the liver and the plasma elimination half-life ($t_{1/2}$) is 56 hours in patients with impaired hepatic function, titrate slowly when administering Amlodipine Besylate to patients with severe hepatic impairment.

Pregnancy: Pregnancy Category C- There are no adequate and well-controlled studies in pregnant women. Amlodipine Besylate should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether Amlodipine Besylate is excreted in human milk. In the absence of this information, it is recommended that nursing be discontinued while Amlodipine Besylate is administered.

Pediatric Use: Effect of Amlodipine Besylate on blood pressure in patients less than 6 years of age is not known.

Geriatric Use: Reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

OVERDOSE

Overdosage might be expected to cause excessive peripheral vasodilation with marked hypotension and possibly a reflex tachycardia.

If massive overdose should occur, initiate active cardiac and respiratory monitoring. Frequent blood pressure measurements are essential. Should hypotension occur, provide cardiovascular support including elevation of the extremities and the judicious administration of fluids. If hypotension remains unresponsive to these conservative measures, consider administration of vasopressors (such as phenylephrine) with attention to circulating volume and urine output. As Amlodipine Besylate is highly protein bound, hemodialysis is not likely to be of benefit.

CONTRAINDICATIONS

Zeglopin is contraindicated in patients with known sensitivity to Amlodipine Besylate.

PRESENTATION

Zeglopin 5mg tablet: 2x10's/pack.

Zeglopin 10mg tablet: 2x10's/pack.

خوراک:

ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

DOSAGE

As directed by the physician.

ہدایات:

دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

INSTRUCTIONS

Store below 30°C.

Protect from sunlight & moisture.

Keep out of reach of children.

دھوپ اور نمی سے بچائیں۔

بچوں کی پہنچ سے دور رکھیں۔

Detailed prescribing information is available on request.



Manufactured by:
AsianContinental (Pvt.) Ltd.
D-32, S.I.T.E. II, Super Highway,
Karachi-Pakistan.



An ISO Certified Company

LFT/051/00