

AMPER

(As per Innovator's Specification)

Amlodipine as Besylate (USP Specs.)

Perindopril tert-butylamine (Manufacturer Specs.)

5 / 4mg, 5 / 8mg, 10 / 4mg & 10 / 8mg Film Coated Tablets

COMPOSITION

Amper 5/4mg Tablets: Each film coated tablet contains:

Amlodipine as besylate 5 mg
Perindopril tert-butylamine 4 mg.
(As per Innovator's specification)

Amper 5/8mg Tablets: Each film coated tablet contains:

Amlodipine as besylate 5 mg
Perindopril tert-butylamine 8 mg.
(As per Innovator's specification)

Amper 10/4mg Tablets: Each film coated tablet contains:

Amlodipine as besylate 10 mg
Perindopril tert-butylamine 4 mg.
(As per Innovator's specification)

Amper 10/8mg Tablets: Each film coated tablet contains:

Amlodipine as besylate 10 mg
Perindopril tert-butylamine 8 mg.
(As per Innovator's specification)

DESCRIPTION

Amlodipine is a calcium channel blocker. Perindopril is an angiotensin converting enzyme (ACE) inhibitor.

CLINICAL PARTICULARS

Therapeutic Indications:

Essential hypertension.

Dosage and administration:

One tablet once daily.

The usual dose of **AMPER** is Amlodipine 5mg and Perindopril 4mg. The maximum daily dose is Amlodipine 10mg and Perindopril 8mg. The increase in the dosage should be adjusted to individual patient's need to attain the control of the elevated blood pressure. The increments should be spaced over the time intervals of 1 to 2 weeks.

Contraindications:

This medicine should not be used in the following cases:

- Patients with known allergy to perindopril and/or amlodipine
- Children under 15 years of age

Precautions:

Caution should be exercised while prescribing **AMPER** to patients with impaired hepatic and renal functions. Renal function should be assessed before and during treatment where appropriate. In patients with renovascular hypertension, surgery/anaesthesia, renal failure, the dose should be cautiously adjusted in accordance with the creatinine clearance. There is a risk of allergic reactions and angioneurotic oedema. The doctor should be informed about the treatment if the patient has to undergo haemodialysis.

AMPER does not contain a beta-blocker and therefore gives no protection against the dangers of abrupt beta-blocker withdrawal; any such withdrawal should be performed by gradual reduction of the dose of beta-blocker.

Combination with beta-blockers must be avoided in patients with markedly impaired left ventricular function. Combination with neuroleptics or imipramine-type drugs may increase the hypotensive effect. Serum lithium concentrations may rise during lithium therapy.

Acute hypotension has rarely been reported with Amlodipine. However, caution should be exercised when administering

AMPER as with any other peripheral vasodilator particularly in patients with severe aortic stenosis. In general, calcium channel blockers should be used with caution in patients with heart failure. Symptomatic hypotension is rarely seen but is more likely in volume-depleted patients, those receiving diuretics, or with the first two doses. A diuretic may later be given in association if necessary; potassium-sparing diuretics are not recommended.

Co-administration with other hypertensives and/or antianginal drugs:

AMPER can be co-administered with other hypertensive (potassium-sparing diuretics are not recommended) and/or antianginal drugs. However care should be exercised before prescribing to avoid any possibility of hypotension.

Drug Interactions:

Special attention is needed while prescribing other medications such as lithium salts, estramustine, potassium salts or a potassium-sparing diuretic and drugs that are likely to affect the drug displacements and potentiate the drug action.

Pregnancy and lactation:

As with other medicines, use of this medicine is contraindicated during pregnancy. There are no data about the passage of this medicine into maternal milk. Therefore, administration of this medicine is not recommended in women who are breast-feeding.

Effects on ability to drive and use machines:

Drivers and machine operators should take special care due to the risk of dizziness.

Side effects:

As with active products, this drug may cause undesirable effects of varying severity in certain patients. The reported side-effects include headache, oedema, fatigue, somnolence, flushing, palpitations, dizziness, mood and/or sleep disturbances, gastrointestinal pain, taste disturbances and dry cough. The doctor should be consulted if any undesirable effect is noted.

Overdosage:

Hypotension is the most likely result of overdosage. If significant hypotension occurs, it may be countered by making the patient lie down with the legs elevated. Gastric lavage should be performed if necessary. For any emergency the doctor should be contacted immediately.

CLINICAL PHARMACOLOGY

Pharmacodynamics:

Amlodipine: Amlodipine inhibits the transmembrane influx of calcium ions into vascular smooth muscle and cardiac muscle. Amlodipine inhibits calcium ion influx across cell membranes selectively, with a greater effect on vascular smooth muscle cells than on cardiac muscle cells. Within the physiologic pH range, amlodipine is an ionized compound (pKa = 8.6), and its kinetic interaction with the calcium channel receptor is characterized by a gradual rate of association and dissociation with the receptor binding site, resulting in a gradual onset of effect.

Following administration of therapeutic doses to patients with hypertension, amlodipine produces vasodilation, resulting in a reduction of supine and standing blood pressures. With chronic once daily oral administration, antihypertensive effectiveness is maintained for at least 24 hours.

Perindopril: Perindopril is an inhibitor of the enzyme that converts angiotensin I into angiotensin II (Angiotensin Converting Enzyme ACE). Inhibition of ACE results in decreased plasma angiotensin II, leading to decreased vasoconstriction, increased plasma renin activity and decreased aldosterone secretion. The latter results in diuresis and natriuresis and may be associated with a small increase of serum potassium. Since ACE inactivates bradykinin, inhibition of ACE also results in

an increased activity of circulating and local kallikrein-kinin systems (and thus also activation of the prostaglandin system). It is possible that this mechanism contributes to the blood pressure-lowering action of ACE inhibitors and is partially responsible for certain of their side effects (e.g. cough). Perindopril acts through its active metabolite, perindoprilat. The other metabolites show no inhibition of ACE activity *in vitro*. Perindopril is active in all grades of hypertension : mild, moderate, severe ; a reduction in systolic and diastolic blood pressures in both supine and standing positions is observed. Perindopril reduces peripheral vascular resistance, leading to blood pressure reduction. As a consequence, peripheral blood flow increases, with no effect on heart rate.

Renal blood flow increases as a rule, while the glomerular filtration rate (GFR) is usually unchanged. The antihypertensive activity is maximal between 4 and 6 hours after a single dose and is sustained for at least 24 hours: trough effects are about 87-100 % of peak effects. The decrease in blood pressure occurs rapidly. In responding patients, normalisation is achieved within a month and persists without the occurrence of tachyphylaxis. Discontinuation of treatment does not lead to a rebound effect.

Pharmacokinetics:

The rate and extent of absorption of perindopril and amlodipine from **AMPER** are not significantly different, respectively, from the rate and extent of absorption of perindopril and amlodipine from individual tablet formulations.

Amlodipine: After oral administration of therapeutic doses of amlodipine, 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 is not altered by the presence of food. 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.

The terminal elimination half-life of amlodipine is about 30-50 hours. Steady-state plasma levels of amlodipine are reached after 7 to 8 days of consecutive daily dosing.

The pharmacokinetics of amlodipine is not significantly influenced by renal impairment. Elderly patients and patients with hepatic insufficiency have decreased clearance of amlodipine with a resulting increase in the area under the plasma concentration time curve (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.

Perindopril: After oral administration, the absorption of perindopril is rapid and the peak concentration complete within 1 hour. Bioavailability is 65 to 70 %. About 20 % of the total quantity of perindopril absorbed is converted into perindoprilat, the active metabolite. In addition to active perindoprilat, perindopril yields five metabolites, all inactive. The plasma half-life of perindopril is equal to 1 hour. As ingestion of food decreases conversion to perindoprilat, hence bioavailability, it should be administered orally in a single daily dose in the morning before a meal.

Protein binding is slight (binding of perindoprilat to angiotensin converting enzyme is less than 30 %), but is concentration-dependent. Perindoprilat is eliminated in the urine and the half-life of the unbound fraction is approximately 3 to 5 hours. Dissociation of perindoprilat bound to angiotensin converting

enzyme leads to an effective elimination half-life of 25 hours, resulting in steady-state within 4 days. After repeated administration, no accumulation of perindopril is observed.

Elimination of perindoprilat is decreased in the elderly, and also in patients with heart or renal failure. Dosage adjustment in renal insufficiency is desirable depending on the degree of impairment (creatinine clearance). Dialysis clearance of perindoprilat is equal to 70 ml/min. Perindopril kinetics are modified in patients with cirrhosis: hepatic clearance of the parent molecule is reduced by half. However, the quantity of perindoprilat formed is not reduced.

STORAGE

Store below 30°C. Protect from light and moisture.

HOW SUPPLIED

Amper 5/4mg Tablets: Pack of 10 film coated tablets.

Amper 5/8mg Tablets: Pack of 10 film coated tablets.

Amper 10/4mg Tablets: Pack of 10 film coated tablets.

Amper 10/8mg Tablets: Pack of 10 film coated tablets.

TO BE SOLD ON THE PRESCRIPTION OF A REGISTERED MEDICAL PRACTITIONER ONLY.

KEEP ALL MEDICINES OUT OF THE REACH OF CHILDREN.

Lactose & Gluten Free

ایمپر

(ایملوڈیپین ہیسالکینٹ)

(پرنڈوپریل ٹریٹری ہیوٹائل امین)

5 ملی گرام + 4 ملی گرام، 5 ملی گرام + 8 ملی گرام،

10 ملی گرام + 4 ملی گرام اور 10 ملی گرام + 8 ملی گرام

فلم کوٹڈ گولیاں

خوراک و ہدایات

ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔

صرف مستند ڈاکٹر کے نسخے کے مطابق ہی دوا فروخت کی جائے۔

تمام ادویات بچوں کی پہنچ سے دور رکھیں۔

دوا کو 30°C سے کم درجہ حرارت پر، نمی اور روشنی سے محفوظ رکھیں۔

NEXT
PHARMACEUTICAL

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