Azapril®

Anti-hypertension

Composition:

* Each tablet of **Azapril 20** contains:
  Lisinopril USP 20 mg (As lisinopril dihydrate)
* Each tablet of **Azapril 10** contains:
  Lisinopril USP 10 mg (As lisinopril dihydrate)
* Each tablet of **Azapril 5** contains:
  Lisinopril USP 5 mg (As lisinopril dihydrate)
* Each tablet of **Azapril 2.5** contains:
  Lisinopril USP 2.5 mg (As lisinopril dihydrate)

Pharmacotherapeutic group

Angiotensin- converting enzyme inhibitor.

Indications:

Azapril is used in the treatment of:
- Hypertension.
- Heart failure.
- Haemodynamically stable patients within 24 hours of an acute myocardial infarction (as short treatment).
- Renal disease in hypertensive patients with Type II diabetes mellitus.
- Diabetic nephropathy in patients with Type I diabetes mellitus.

Dosage and Administration:

* **Azapril** should be administered orally in a single daily dose with or without food.
***Adult**:
Hypertension:
Initial dose of **Azapril** is 10mg orally once a day, if **Azapril** is used in addition to diuretic or in cardiac decomposition or in volume depletion, initially (2.5-5 mg) once a day, the maintenance dose is 20 mg once a day and the maximum dose is 80mg once daily.
Heart failure:
Initial dose of **Azapril** is 2.5-5 mg per day under closed medical supervision, increased in steps no greater than 10 mg at intervals of at least 2 weeks up to max 35 mg once daily if tolerated.
Acute myocardial infarction:
- The initial dose of **Azapril** is 5mg given orally within 24 hours if the systolic blood pressure is over 120 mm Hg, followed by further 5 mg after 24 hours, then 10 mg after a further 24 hours and continuing with 10 mg once daily for 6 weeks. If the systolic pressure (100-120 mm Hg), the starting dose will be 2.5mg once a day, increased to maintenance dose of 5 mg once daily.
- If hypotension occurs (SBP < 100 mmHg), a daily maintenance dose of 5mg may be given with temporary reduction to 2.5mg if needed.
- In prolonged hypotension (SBP < 90 mmHg for more than 1 hour), **Azapril** should be withdrawn.
Diabetic Nephropathy:
- The recommended initial dose is (2.5-5 mg) daily, adjusted according to response. The usual dosage is 10-20 mg daily.
- Dosage of **Azapril** should be adjusted in patients with renal impairment as shown below**:**

Creatinine clearance (ml/min)	initial dose (mg/day)
≤ 70 > 30 ml / min	5-10 mg
≤ 30 ≥10 ml / min	2.5-5 mg
< 10 ml / min	2.5 mg

Use in hypertensive pediatric patients (6–16) years:
The recommended initial dose is 2.5 mg once daily in patients 20 to <50 kg, and 5 mg once daily in patients ≥ 50 kg.
The use of **Azapril** is not recommended for children under 6 years or in any children with severe kidney problems.

Contraindications:

Azapril is contraindicated in patients with:
- Hypersensitivity to lisinopril, other ACE inhibitors or to any other component of **Azapril** tablets.
- History of angioedema related to previous treatment with ACE inhibitors.
- Hereditary or idiopathic angioedema.
- Second and third trimesters of pregnancy.
- Combination with aliskiren-containing medicines in patients with diabetes mellitus (type I or II) or with moderate to severe renal impairment (GFR < 60 ml/min/1.73 m^2).

Side Effects:

- **The most frequent side effects include**: dizziness, headache, fatigue, cough, diarrhea and nausea.
- **Other side effects include**: orthostatic effects (including hypotension), rash and asthenia.
- **Rare side effects include**: palpitations, abdominal pain, jaundice, mood alterations, pruritus, urticaria , fever , dry mouth , gynaecomastia, alopecia, psoriasis, tachycardia, cerebrovascular accident, myocardial infarction, elevation of liver enzymes, sleep disturbances, impotence, confusion and Raynaud's syndrome.
- **Very rare side effects include**: allergic alveolitis, profuse sweating, angioedema, pemphigus, Stevens - Johnsons syndrome and toxic epidermal necrolysis.

Precautions:

- Lisinopril should be used with caution in patients receiving diuretics, high dose vasodilator therapy, immunosuppressant therapy, desensitisation treatment , low-sodium diet, potassium supplements, undergoing major surgery, dialysis, patients with dehydration, heart failure, cerebrovascular disease, renovascular diseases, hypovolaemia, hyponatraemia, hyperkalaemia, diabetes mellitus, hypotension, peripheral vascular disease, generalised atherosclerosis, collagen vascular disease, severe aortic stenosis or hypertrophic cardiomyopathy.
- ACE inhibitors-induced cough should be considered as part of the differential diagnosis of cough.
- Lisinopril may be less effective in lowering blood pressure in black patients than in non-blacks and it cause a higher rate of angioedema in black patients than in non-black patients.
- Patients receiving lisinopril who develop jaundice, marked elevation of hepatic enzymes or angioedema of face, extremities, lips, tongue, glottis and/or larynx should discontinue lisinopril and receive appropriate medical follow-up.

Overdose:

- Symptoms associated with over dosage of ACE inhibitors may include:
Hypotension, circulatory shock, electrolyte disturbances, renal failure, hyperventilation, tachycardia, palpitations, bradycardia, dizziness, anxiety and cough.
- The recommended treatment of overdose is intravenous infusion of normal saline solution.

Drug Interactions:

- Drugs that enhance hypotensive effect of lisinopril when co administered are: (aldesleukin, alpha blockers, general anaesthetics drugs, MAOIs, antipsychotic, anxiolytics, hypnotics, beta blockers, CCBs, clonidine, diazoxide, diuretics, levodopa, methyldopa, moxisylyte, moxonidine, baclofen, tizanidine, nitrates, alprostadil, hydralazine, minoxidil and sodium nitroprusside).
- Drugs that antagonized the hypotensive effect of lisinopril when co administered are: (Corticosteroids, NSAIDs and oestrogens).
- Drugs that increase risk of hyperkalaemia when co administered with lisinopril are: (Angiotensin-II receptor antagonists, trimethoprim, heparin, ciclosporin and potassium salts).
- Concomitant use of lisinopril with:
Lithium: reduce the excretion of lithium.
Allopurinol: increased risk of leucopenia and hypersensitivity reactions especially in renal impairment.
NSAIDs: increased risk of renal impairment.
Insulin, metformin and sulfonylureas: enhance their hypoglycaemic effect.

Pregnancy and Lactation:

- **Pregnancy:** The use of lisinopril during pregnancy is not recommended and when pregnancy is detected, lisinopril treatment should be discontinued as soon as possible. Because, It may adversely affect fetal and neonatal blood pressure control and renal functions, also skull defects and oligohydramnios cases have been reported.
- **Lactation:** The use of lisinopril is not recommended in women who are breast feeding.

Driving and using machines:

When driving vehicles or operating machines, it should be taken in to account that occasionally dizziness or tiredness may occur.

Properties:

- **Pharmacodynamic Properties:**
- Lisinopril is a peptidyldipeptidase enzyme inhibitor. It inhibits the angiotensin converting enzyme (ACE) that catalyses the conversion of angiotensen I to the vasoconstrictor peptide angiotensin II. Angiotensin II also stimulates aldosterone secretion by the adrenal cortex.
- Inhibition of the angiotensin converting enzyme (ACE) results in decreased concentrations of angiotensen II which result in an increase in serum potassium concentration. Whilst the mechanism through which lisinopril lowers blood pressure is believed to be primarily supression of the renin-angiotensin-aldosterone system.
- Angiotensin converting enzyme (ACE) inhibitors including lisinopril inhibit the formation of angiotensin II and break down bradykinin and hence ameliorate endothelial dysfunction.
Pharmacokinetic Properties:
Absorption: following oral administration of lisinopril, peak serum concentrations occur within about 7 hours, although there was a small delay in time taken to reach peak serum concentrations in acute myocardial infarction patients.
The mean extent of absorption of lisinopril is approximately 25% .The absolute bioavailability is reduced to approximately 16% in patients with heart failure. Lisinopril absorption is not affected by the presence of food.

Distribution: Lisinopril does not appear to be bound to serum proteins other than to circulating angiotensin converting enzyme (ACE).
Elimination: Lisinopril does not undergo metabolism and is execreted entirely unchanged in urine. The clearance of lisinopril in healthy subjects is approximately 50 ml/min.
Hepatic impairement: Impairement of hepatic function (cirrohotic patients), results in a decrease in lisinopril absorption but an increase in exposure (approximately 50 %) compared to healthy subjects due to decreased clearance.
Heart failure: Patients with heart failure have a greater exposure of lisinopril when compared to healthy subjects, but there is reduced absorption of approxamitly 16 % compared to healthy subjects.
Renal impairemiant: impaired renal function decreases elemination of lisinopril, which is execreted via the kidneys, but this decrease becomes clinically important only when the glomerular filteration rate is below 30ml /min.
Elderly: Older patients have higher blood levels and higher values for the area under the plasma concentration time curve (AUC) (increase approximately 60 %) compared with younger subjects.

List of excipients:

Azapril 20: Dibasic calcium phosphate, maize starch, povidone, mg stearate, talc and sun set yellow dye.
Azapril 10: Dibasic calcium phosphate, maize starch, povidone, mg stearate, talc and erythrocin red.
Azapril 5: Dibasic calcium phosphate, maize starch, povidone, mg stearate, talc and erythrocin red.
Azapril 2.5: Dibasic calcium phosphate, maize starch, povidone, mg stearate and talc.

Incompatibilities:

Un Known.

Shelf life:

24 months.

Special precaution for storage:

- Keep out of the reach and sight of children.
- Do not use **Azapril** tablet after the expiry date which is stated on the container.
- They should be stored in a cool, dry place, not exceed 30°C.
- Keep in original container.

Nature and contents of container:

- Box of 3 blisters.
- Each blister contains 10 tablets.

Special precaution for disposal:

- Medicines should not be disposed of via wastewater or household waste.
- Ask the pharmacist how to dispose of medicines no longer required.
- These measures will help to protect the environment.

Marketing Authorization holder and manufacturer:

Azal Pharma.
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To report any Side effect
National Medicines and Poisons Board (NMPB)
Fax (+249)183522263
E-mail: inf@nmpb.gov.sd
Website: www.nmpb.gov.sd

THIS IS A MEDICAMENT

- Medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consultation your doctor.
- Keep medicament out of reach of children.

Produced By:
Azal Pharma
Khartoum - Sudan

051215

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Tec. Manager		