CAPTOPRIL

Tablets

USE IN PREGNANCY

When used in pregnancy during the second & third trimesters, ACE inhibitors can cause injury and even death to the developing fetus. When pregnancy is detected, captopril should be discontinued as soon as possible. **See WARNINGS : Fetal / Neonatal Morbidity & Mortality.**

DESCRIPTION

Each tablet contains: Captopril 25 mg or 50 mg.
Inactive Ingredients: Lactose, Micro Crystalline Cellulose 102, Sodium Starch Glycolate, Magnesium stearate

CLINICAL PHARMACOLOGY

The beneficial effects of captopril, in hypertension and heart failure, appear to result primarily from suppression of the rennin-angiotensin-aldosterone system. Captopril prevents the conversion of angiotensin I to angiotensin II by inhibition of ACE, a peptidyldipeptide carboxy hydrolase. Administration of captopril results in a reduction of peripheral arterial resistance in hypertensive patients with either no change, or an increase, in cardiac output. There is an increase in renal blood flow following administration of captopril and glomerular filtration rate is usually unchanged.

INDICATIONS AND USAGE

Hypertension : Captopril tablets are indicated for the treatment of hypertension.

Heart failure : Captopril tablets are indicated in the treatment of congestive heart failure usually in combination with diuretics and digitalis.

CONTRAINDICATIONS

Captopril tablets are contraindicated in patients who are hypersensitive to this product or any other angiotensin-converting enzyme inhibitor.

WARNINGS

Angioedema : Angioedema involving the extremities, face, lips, mucous membranes, tongue, glottis or larynx has been seen in patients treated with captopril.
Swelling confined to the face, mucous membranes of the mouth, lips and extremities are usually resolved with discontinuation of captopril; some cases required medical therapy.

Neutropenia / Agranulocytosis : Neutropenia (< 1000 / mm^3) with myeloid hypoplasia has resulted from use of captopril.
The neutropenia has usually been detected within three months after captopril was started.
In general, neutrophils returned to normal in about two weeks after captopril was discontinued.

Evaluation of the hypertensive or heart failure patient should always include assessment of renal function.

All patients treated with captopril should be told to report any signs of infections (e.g., sore throat, fever). If infection is suspected, white cell counts should be performed without delay. Since discontinuation of captopril & other drugs has generally led to prompt return of the white count to normal upon confirmation of neutropenia, the physician should withdraw captopril and closely follow the patient's course.

Hypotension : Excessive hypotension was rarely seen in hypertensive patients but is a possible consequence of captopril use in salt / volume depleted persons (such as those treated vigorously with diuretics), patients with heart failure or those patients undergoing renal dialysis.

Fetal / Neonatal Morbidity & Mortality: ACE inhibitors can cause fetal & neonatal morbidity and death when administered to pregnant women. When pregnancy is detected, ACE inhibitors should be discontinued as soon as possible.

Hepatic Failure : Rarely, ACE inhibitors have been associated with a syndrome that starts with cholestatic jaundice and progresses to fulminant hepatic necrosis and (sometimes) death.

PRECAUTIONS

Hyperkalemia : Elevations in serum potassium have been observed in some patients treated with captopril.

Cough : Presumably due to the inhibition of the degradation of endogenous bradykinin, persistent nonproductive cough has been reported with all ACE inhibitors, always resolving after discontinuation of therapy.

Valvular Stenosis : There is concern, on theoretical grounds, that patients with aortic stenosis might be at particular risk of decreased coronary perfusion when treated with vasodilatators because they do not develop as much afterload reduction as others.

Surgery / Anesthesia : In patients undergoing major surgery or during anesthesia with agents that produce hypotension, captopril will block angiotensin II formation secondary to compensatory renin release. If hypotension occurs and is considered to be due to this mechanism, it can be corrected by volume expansion

Patients should be advised to immediately report to their physician any signs or symptoms suggesting angioedema (e.g., swelling of face, eyes, lips, tongue, larynx and extremities; difficulty in swallowing or breathing; hoarseness) and to discontinue therapy.

Patients should be told to report promptly any indication of infection (e.g., sore throat, fever), which may be a sign of neutropenia, or of progressive edema which might be related to proteinuria and nephrotic syndrome.

All patients should be cautioned that excessive perspiration and dehydratation may lead to an excessive fall in blood pressure because of reduction in fluid volume. Other causes of volume depletion such as vomiting or diarrhea may also lead to a fall in blood pressure; patients should be advised to consult with the physician.

Patients should be advised not to use potassium-sparing diuretics, potassium supplements or potassium -containing salt substitutes without consulting their physician.

Patients should be warned against interruption or discontinuation of medication unless instructed by the physician.

Heart failure patients on captopril therapy should be cautioned against rapid increases in physical activity

Patients should be informed that captopril should be taken one hour before meals.

DRUG INTERACTIONS

Agents Having Vasodilatator Activity : Nitroglycerin or other nitrates or other drugs having vasodilatator activity should, if possible, be discontinued before starting **Captopril** tablets. If resumed during **Captopril** treatment, such agents should be administered cautiously, and perhaps at lower dosage.

Agents Causing Renin Release : Captopril's effect will be augmented by antihypertensive agents that cause renin release.

Agents Affecting Sympathetic Activity : Agents affecting sympathetic activity (e.g., ganglionic blocking agents or adrenergic neuron blocking agents) should be used with caution. Beta-adrenergic blocking drugs add some further antihypertensive effect to captopril, but the overall response is less than additive.

Agents Increasing Serum Potassium : Since **Captopril** decreases aldosterone production, elevation of serum potassium may occur. Potassium-sparing diuretics such as spironolactone, triamterene, or amiloride, or potassium supplements should be given only for documented hypokalemia, and then with caution, since they may lead to a significant increase of serum potassium. Salt substitutes containing potassium should also be used with caution.

Inhibitors of Endogenous Prostaglandin Synthesis : It has been reported that indomethacin may reduce the antihypertensive effect of **Captopril**, especially in cases of low renin hypertension. Other nonsteroidal anti-inflammatory agents (e.g., aspirin) may also have this effect.

Lithium : Increased serum lithium levels and symptoms of lithium toxicity have been reported in patients receiving concomitant lithium and ACE inhibitor therapy. These drugs should be co-administered with caution and frequent monitoring of serum lithium levels is recommended. If a diuretic is also used, it may increase the risk of lithium toxicity.

Drug / Laboratory Test Interactions : Captopril tablets may cause a false-positive urine test for acetone.

ADVERSE REACTIONS

Renal : Proteinuria and rarely renal insufficiency, renal failure, nephrotic syndrome, polyuria, oliguria, and urinary frequency.

Hematologic : Neutropenia / agranulocytosis has occurred. Cases of anemia (including aplastic and hemolytic), thrombocytopenia, pancytopenia, and a positive ANA have been reported.

Dermatologic : Rash, often with pruritis, and sometimes with fever, arthralgia, and eosinophilia have occurred. It is usually maculopapular and rarely urticarial. The rash is usually mild and disappears within a few days of dosage reduction, short-term treatment with an antihistaminic agent, and / or discontinuing therapy; remission may occur even if **Captopril** is continued. A reversible associated pemphigoid-like lesion, photosensitivity, erythema multiforme (including Stevens-Johnson syndrome), and exfoliative dermatitis have also been reported.

Dysgeusia : Taste impairment is reversible and usually self-limited (2 to 3 months) even with continued drug administration. Weight loss may be associated with the loss of taste.

Angioedema : Angioedema involving the extremities, face, lips, mucous membranes, tongue, glottis or larynx has been reported. Angioedema involving the upper airways has caused fatal airway obstruction.

Respiratory : A persistent dry cough has been reported. Bronchospasm, eosinophilic pneumonitis, and rhinitis.

Cardiovascular : Cardiac arrest, cerebrovascular accident / insufficiency, rhythm disturbances, orthostatic hypotension, syncope.

Body as a whole : Anaphylactoid reactions.

General : Asthenia, gynecomastia.

Gastrointestinal : Pancreatitis, glossitis, dyspepsia.

Hepatobiliary : Jaundice, hepatitis, including rare cases of necrosis, cholestasis.

Metabolic : Symptomatic hyponatremia.

Musculoskeletal : Myalgia, myasthenia.

Special senses : Blurred vision.

Urogenital : Impotence.

Liver Function Tests : Elevations of liver transaminases, alkaline phosphatase, and serum bilirubin have occurred.

OVERDOSAGE

Correction of hypotension would be of primary concern . Volume expansion with an intravenous infusion of normal saline is the treatment of choice for restoration of blood pressure.

While captopril may be removed from the adult circulation by hemodialysis, there is inadequate data concerning the effectiveness of hemodialysis for removing it from the circulation of neonates or children. Peritoneal dialysis is not effective for removing captopril; there is no information concerning exchange transfusion for removing captopril from the general circulation.

DOSAGE AND ADMINISTRATION

Captopril tablets should be taken one hour before meals & may be used in combination with diuretics, as well as with other antihypertensive agents. Dosage must be individualized. Reduced dosages are indicated for patients with impaired renal function, the elderly and those receiving diuretics.

Hypertension : Initiation of therapy requires consideration of recent antihypertensive drug treatment, the extent of blood pressure elevation, salt restriction, and other clinical circumstances. If possible, discontinue the patient's previous antihypertensive drug regimen for one week before starting **Captopril** tablets.

The usual dose range is 25 to 150 mg two or three times daily. A maximum daily dose of 450 mg **Captopril** should not be exceeded.

For patients with severe hypertension (e.g., accelerated or malignant hypertension), when temporary discontinuation of current antihypertensive therapy is not practical or desirable, or when prompt titration to more normotensive blood pressure levels is indicated, diuretic should be continued but other current antihypertensive medication stopped and **Captopril** dosage promptly initiated at 25 mg two or three times daily, under close medical supervision.

When necessitated by the patient's clinical condition, the daily dose of **Captopril** may be increased every 24 hours or less under continuous medical supervision until a satisfactory blood pressure response is obtained or the maximum dose of **Captopril** is reached. In this regimen, addition of a more potent diuretic, e.g., furosemide, may also be indicated.

Beta-blockers may also be used in conjunction with **Captopril** therapy, but the effects of the two drugs are less than additive.

Heart Failure : Initiation of therapy requires consideration of recent diuretic therapy and the possibility of severe salt / volume depletion. For most patients the usual initial daily dosage is 25 mg three times daily. After a dose of 50 mg three times daily is reached , further increases in dosage should be delayed, where possible, for at least two weeks to determine if a satisfactory response occurs. Most patients studied have had a satisfactory clinical improvement at 50 or 100 mg three times daily. A maximum daily dose of 450 mg of **Captopril** should not be exceeded. **Captopril** should generally be used in conjunction with a diuretic and digitalis. **Captopril** therapy must be initiated under very close medical supervision.

Left Ventricular Dysfunction after Myocardial Infarction : The recommended dose for long-term use in patients following a myocardial infarction is a target maintenance dose of 50 mg three times daily.

Diabetic Nephropathy : The recommended dose of **Captopril** for long-term use to treat diabetic nephropathy is 25 mg three times daily. Other antihypertensives such as diuretics, beta blockers, centrally acting agents or vasodilators may be used in conjunction with **Captopril** if additional therapy is required to further lower blood pressure.

Dosage Adjustment in Renal Impairment : Because **Captopril** is excreted primarily by the kidneys, excretion rates are reduced in patients with impaired renal function. These patients will take longer to reach steady-state captopril levels and will reach higher steady- state levels for a given daily dose than patients with normal renal function. Therefore, these patients may respond to smaller or less frequent doses.

HOW SUPPLIED

Captopril tablets, containing 25 or 50 mg, are available in pack of 500 tablets.

Store at controlled room temperature, between 15°C and 25°C.

Protect from light and moisture.

Keep out of the reach of children.

THIS IS A MEDICINE

- Medicines are products which affect your health, and failure to follow the instructions may be dangerous for you.
- Follow your doctor's advice carefully, the method of use, and the instructions of the pharmacist who sold you the medicine.
- Your doctor and pharmacist are expert in the use of medicines, and their benefits and risks.
- Do not stop your course of treatment early unless advised to do so by your doctor or pharmacist.
- Do not repeat the same prescription without consulting your doctor.

KEEP MEDICINES OUT OF THE REACH OF CHILDREN

Revised 07 / 2014

PHARMADEX S.A.L.
KAHALE - LEBANON