CAPTACE® Tablets
captopril

USE IN PREGNANCY
When used in pregnancy during the second and third trimesters, ACE inhibitors can cause injury and even death to the developing fetus. When pregnancy is detected, CAPTACE® should be discontinued as soon as possible.

DESCRIPTION
Captopril is the first of a new class of antihypertensive agents, a specific competitive inhibitor of angiotensin I converting enzyme (ACE), the enzyme responsible for the conversion of angiotensin I to angiotensin II. Captopril is also effective in the management of heart failure.
CAPTACE® (captopril) is available as 12.5 mg white round, double break-line tablets, 25 mg white square, scored tablets and 50 mg white oval shaped, scored tablets, for oral administration.
Inactive ingredients: microcrystalline cellulose, corn starch, lactose and stearic acid.

INDICATIONS AND USAGE
Hypertension: Captopril is indicated for the treatment of hypertension.
Captopril may be used as initial therapy for patients with normal renal function, in whom the risk is relatively low. In patients with impaired renal function, particularly those with collagen vascular disease, captopril should be reserved for hypertensives who have either developed unacceptable side effects on other drugs, or have failed to respond satisfactorily to drug combinations.
Captopril is effective alone, and in combination with other antihypertensive agents, especially thiazide-type diuretics. The blood pressure lowering effects of captopril and thiazides are approximately additive.
Heart failure: Captopril is indicated in the treatment of congestive heart failure in combination with diuretics and digitalis.
Myocardial Infarction: Captopril is indicated following myocardial infarction in clinically stable patients with asymptomatic and symptomatic left ventricular dysfunction to improve survival, delay the onset of symptomatic heart failure, reduce hospitalizations for heart failure and reduce recurrent myocardial infarction and coronary revascularization procedures.
Diabetic Nephropathy: Captopril is indicated for the treatment of diabetic nephropathy (microalbuminuria greater than 30 mg/day) in insulin dependent diabetics. In these patients captopril prevents the progression of renal disease and reduces associated clinical events dialysis, renal transplantation and death.

CONTRAINDICATIONS
Captopril is contraindicated in patients who are hypersensitive to this product or any other angiotensin-converting enzyme inhibitor (e.g. a patient who has experienced angioedema during therapy with any other ACE inhibitor).

WARNINGS
Angioedema: Angioedema involving the extremities, face, lips mucous membranes, tongue, glottis or larynx, has been seen in patients treated with ACE inhibitors, including captopril. If angioedema involves the tongue, glottis or larynx, airway obstruction may occur and be fatal. Emergency therapy, including but not necessarily limited to, subcutaneous administration of a 1:1000 solution of epinephrine should be promptly instituted. Swelling confined to the face, mucous membranes of the mouth, lips and extremities has 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.
Evaluation of the hypertensive or heart failure patient should always include assessment of renal function.
If captopril is used in patients with impaired renal function, white blood cell and differential counts should be evaluated prior to starting treatment and at approximately two-week intervals for about three months, then periodically.
In patients with collagen vascular disease or who are exposed to other drugs known to affect the white cells or immune response particularly when there is impaired renal function, captopril should be used only after an assessment of benefit and risk, and then with caution.
All patients treated with captopril should be told to report any signs of infection (e.g. sore throat, fever). If infection is suspected, white cell counts should be performed without delay.
Proteinuria
Total urinary proteins greater than 1g per day were seen in about 0.7 percent of patients receiving captopril. Since most cases of proteinuria occured by the eighth month of therapy with captopril, patients with prior renal disease or those receiving captopril at doses greater than 150 mg per day, should have urinary protein estimations (dipstick on first morning urine) prior to treatment, and periodically thereafter.
Hypotension
Excessive hypotension was rarely seen in hypertensive patients but is a possible consequence of captopril use in salt/volume depleted persons, patients with heart failure or those patients undergoing renal dialysis.
BECAUSE OF THE POTENTIAL FALL IN BLOOD PRESSURE IN THESE PATIENTS, THERAPY SHOULD BE STARTED UNDER VERY CLOSE MEDICAL SUPERVISION.
A starting dose of 6.25 or 12.5 mg tid may minimize the hypotensive effect. Patients should be followed closely for the first two weeks of treatment and whenever the dose of captopril and/or diuretic is increased.

PRECAUTIONS
General
Impaired Renal Function.
Hypertension: Some patients with renal disease, particularly those with severe renal artery stenosis, have developed increases in BUN and serum creatinine after reduction of blood pressure with captopril. Captopril dosage reduction and/or discontinuation of diuretic may be required. For some of these patients, it may not be possible to normalize blood pressure and maintain adequate renal perfusion.
Heart Failure: About 20 percent of patients develop stable elevation of BUN and serum creatinine greater than 20 percent above normal of baseline upon long-term treatment with captopril.
Hyperkalemia: Elevations in serum potassium have been observed in some patients treated with ACE inhibitors, including captopril. When treated with ACE inhibitors, patients at risk for the development of hyperkalemia include those with renal insufficiency, diabetes mellitus, and those using concomitant potassium-sparing diuretics, potassium supplements, potassium-containing salt substitutes or other drugs associated with increases in serum potassium.
Cough: Cough has been reported with the use of ACE inhibitors. Characteristically, the cough is nonproductive, persistent and resolves after discontinuation of therapy. ACE inhibitor-induced cough should be considered as part of the differential diagnosis of cough.
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 vasodilators 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.
Hemodialysis
Recent clinical studies have shown an association of hypersensitivity - like (anaphylactoid) reactions during hemodialysis with high-flux dialysis membranes (e.g. AN69) in patients receiving ACE inhibitors. In these patients, consideration should be given to using a different type of dialysis membrane or a different class of medication.
Information for Patients
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 dehydration 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.
Drug Interactions
Diuretics: Patients on Diuretic Therapy and especially those in whom diuretic therapy was recently instituted, as well as those on severe dietary salt restriction or dialysis, may occasionally experience a precipitous reduction of blood pressure usually within the first hour after receiving the initial dose of captopril.
The possibility of hypotensive effects with captopril can be minimized by either discontinuing the diuretic or increasing the salt intake approximately one week prior to initiation of treatment with Captopril or initiating therapy with small doses (6.25 or 12.5 mg).
Agents Having Vasodilator Activity: Data on the effect of concomitant use of other vasodilators in patients receiving Captopril for heart failure are not available; therefore, nitroglycerin or other nitrates (used for management of angina) or other drugs having vasodilator activity should, if possible, be discontinued before starting.
Agents Causing Renin Release: Captopril's effect will be augmented by antihypertensive agents that cause renin release.
Agents Affecting Sympathetic Activity: The sympathetic nervous system may be especially important in supporting blood pressure in patients receiving captopril alone or with diuretics. Therefore, agents affecting sympathetic activity 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 the same effect.
Lithium: Increased serum lithium level and symptoms of lithium toxicity have been reported in patients receiving concomitant lithium and ACE inhibitor therapy. These drugs should be coadministered with caution and frequent monitoring of serum lithium level is recommended. If a diuretic is also used, it may increase the risk of lithium toxicity.
Drug / Laboratory Test Interaction
Captopril may cause a false-positive urine test for acetone.
Carcinogenesis, Mutagenesis and Impairment of Fertility
Two-year studies with doses of 50 to 1350 mg/Kg/day in mice and rats failed to show any evidence of carcinogenic potential.
Studies in rats have revealed no impairment of fertility.
Nursing Mothers
Concentrations of captopril in human milk are approximately one percent of those in maternal blood. Because of the potential for serious adverse reactions in nursing infants from captopril, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of Captopril to the mother.
Pediatric Use
Safety and effectiveness in children have not been established.
Captopril should be used in children only if other measures for controlling blood pressure have not been effective.

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 should be taken one hour before meals. Dosage must be individualized.
Hypertension - The initial dose of Captopril is 25 mg bid or tid. If satisfactory reduction of blood pressure has not been achieved after one or two weeks, the dose may be increased to 50 mg tid. Therefore, if the blood pressure has not been satisfactorily controlled after one to two weeks at this dose, (and the patient is not already receiving a diuretic), a modest dose of a thiazide-type diuretic (e.g. hydrochlorothiazide, 25 mg daily), should be added. The diuretic dose may be increased at one - to two week intervals until its highest usual antihypertensive dose is reached.
If Captopril is being started in a patient already receiving a diuretic, Captopril therapy should be initiated under close medical supervision.
If further blood pressure reduction is required, the dose of Captopril may be increased to 100 mg bid or tid and then, if necessary, to 150 mg bid or tid (while continuing the diuretic). The usual dose range is 25 to 150 mg bid or tid. A maximum daily dose of 450 mg Captopril should not be exceeded.
Heart failure - For most patients the usual initial daily dosage is 25 mg tid. After a dose of 50 mg tid is reached, further increase 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 tid. A maximum daily dose of 400 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.
Dosage Adjustment in Renal Impairment - For patients with significant renal impairment, initial daily dosage of Captopril should be reduced, and smaller increments utilized for titration, which should be quite slow (one - to two - week intervals). After the desired therapeutic effect has been achieved, the dose should be slowly back - titrated to determine the minimal effective dose. When concomitant diuretic therapy is required, a loop diuretic (e.g. furosemide), rather than thiazide diuretic, is preferred in patients with severe renal impairement.
Storage conditions
Store in a dry place below 30°C protected from light.
Do not refrigerate
Do not use after expiry date.
Packaging quantities:
Tablet 12.5 mg - blister pack of 30's
Tablet 25 mg - blister pack of 30's
Tablet 50 mg - blister pack of 30's

THIS IS A MEDICAMENT
- A 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 the 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.
- Do not repeat the same prescription without consulting your doctor.

KEEP MEDICAMENT OUT OF REACH OF CHILDREN

Manufactured in Zouk Mosbeh Lebanon by
ALGORITHM S.A.L.

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