

CAPTOPRIL TABLETS BP

COMPOSITION:

Each uncoated tablet contains:
Captopril BP 25 mg
Excipients Q.S.

POM

Each uncoated tablet contains:
Captopril BP 50 mg
Excipients Q.S.

PHARMACOLOGICAL CLASS:

Angiotensin-Converting Enzyme Inhibitors

PHARMACOLOGICAL ACTION:

Captopril is an angiotensin converting enzyme (ACE) inhibitors of angiotensin I to angiotensin II vasoconstrictor substance. It reduced aldosterone secretion, an increase in plasma renin activity, aldosterone no longer carrying negative feedback and decrease in total peripheral resistance with a preferential action on muscle and renal territories, although this decrease is accompanied by fluid retention or reflex tachycardia. The treatment of hypertension with captopril increases arterial compliance, increased renal blood flow without significant decrease in glomerular filtration rate and a reduction in left ventricular hypertrophy. In heart failure patients it reduces the workload of the heart by venous vasodilator effect probably due to a change in prostaglandin metabolism; decreased preload and by decreasing total peripheral resistance; decreased afterload.

Pharmacokinetic: Oral captopril is rapidly absorbed (peak blood levels in the first hour). The amount absorbed is 75% of the administered dose is reduced by 30 to 35% by food intake, without affecting efficiency. In plasma, 30% are attached to plasma albumin. The half-life of unchanged captopril is close to 2 hours. Captopril excreted in urine is approximately 95% (40 to 50% in unchanged form) of the administered dose of captopril. Patients with renal impairment, plasma concentrations of captopril were significantly higher in patients with a creatinine clearance less than or equal to 40 ml/min, the half-life up to 30 hours. Captopril crosses the placenta. Passage into breast milk occurs in very small amounts.

INDICATIONS:

Captopril used in the treatment of hypertension; congestive heart failure; myocardial infarction within the first 24 hours in patients with hemodynamically stable condition and post-myocardial infarction patients with left ventricular dysfunction (ejection fraction \leq 40%). It is also used for diabetic nephropathy.

CONTRAINDICATIONS:

Captopril is contraindicating in the patient with known hypersensitivity to captopril, to any of the excipients or any other ACE inhibitor. History of angioedema associated with the intake of an ACE inhibitor; hereditary / idiopathic angioneurotic oedema; second and third trimester of pregnancy, lactation.

SPECIAL PRECAUTIONS AND WARNING:

Risk of symptomatic hypotension is more likely to occur in hypertensive patients who are volume and/or sodium depleted by vigorous diuretic therapy, dietary salt restriction, diarrhoea, vomiting or haemodialysis. Myocardial infarction or stroke in patients with ischemic heart disease or cerebral circulatory insufficiency; angioedema of the extremities (i.e. face, lips, mucous membranes, tongue, glottis or larynx) may occur any time during treatment; elevations in serum potassium (Hyperkalaemia); neutropenia/agranulocytosis, thrombocytopenia and anaemia; Proteinuria; non-productive cough; anaphylactoid reactions during high-flux dialysis/lipoprotein apheresis membrane exposure, sustained life-threatening anaphylactoid reactions for patients undergoing desensitising treatment with hymenoptera venom has been reported with the use of ACE inhibitor including captopril. Patients with heart failure are at higher risk of hypotension. There is an increased risk of hypotension and renal insufficiency when patients with bilateral renal artery stenosis or stenosis of the artery to a single functioning kidney are treated with ACE inhibitors. Patients undergoing major surgery or during treatment with anesthetic agents are risk of hypotension. ACE inhibitors should be used with caution in patients with left ventricular valvular and outflow tract obstruction and avoided in cases of cardiogenic shock and haemodynamically significant obstruction.

Renal impairment: In cases of renal impairment (creatinine clearance \leq 40 ml/min), the initial dosage of captopril must be adjusted according to the patient's creatinine clearance, and then as a function of the patient's response to treatment. The dose should not exceed that necessary for adequate control and should be reduced in patients with impaired renal function.

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

Diabetic patients: The glycaemia levels should be closely monitored in diabetic patients previously treated with oral antidiabetic drugs or insulin, namely during the first month of treatment with an ACE inhibitor.

Pregnancy: ACE inhibitors should not be initiated during pregnancy. Unless continued ACE inhibitor therapy is considered essential, patients planning pregnancy should be changed to alternative antihypertensive treatments which have an established safety profile for use in pregnancy. When pregnancy is diagnosed, treatment with ACE inhibitors should be stopped immediately, and, if appropriate, alternative therapy should be started.

Lactation: The use of Captopril in breastfeeding is not recommended for preterm infants and for the first few weeks after delivery, because of the hypothetical risk of cardiovascular and renal effects and because there is not enough clinical experience.

DOSAGE AND DIRECTIONS FOR USE:

Adults:

Hypertension:

The recommended starting dose is 25-50 mg daily in two divided doses. The dose may be increased incrementally, with intervals of at least 2 weeks, to 100-150mg/day in two divided doses as needed to reach target blood pressure. Captopril may be used alone or with

other antihypertensive agents, especially thiazide diuretics. A once-daily dosing regimen may be appropriate when concomitant antihypertensive medication such as thiazide diuretics is added.

In patients with a strongly active renin-angiotensin-aldosterone system (hypovolaemia, renovascular hypertension, cardiac decompensation) it is preferable to commence with a single dose of 6.25 mg or 12.5 mg. The inauguration of this treatment should preferably take place under close medical supervision. These doses will then be administered at a rate of two per day. The dosage can be gradually increased to 50mg per day in one or two doses and if necessary to 100mg per day in one or two doses.

Heart Failure:

The usual starting dose is 6.25mg - 12.5mg BID or TID. Titration to the maintenance dose (75 - 150mg per day) should be carried out based on patient's response, clinical status and tolerability, up to a maximum of 150mg per day in divided doses. The dose should be increased incrementally, with intervals of at least 2 weeks to evaluate patient's response.

Myocardial Infarction:

Acute phase: Treatment with captopril will be initiated in the hospital as soon as possible after the onset of signs and/or symptoms in hemodynamically stable patients. A test dose of 6.25 mg is administered, then 2 hours after a dose of 12.5 mg, and 12 hours after a dose of 25 mg. The next day, captopril is administered at a dose of 100 mg per day in 2 divided doses daily for 4 weeks if the patient's hemodynamic tolerance permits. At the end of 4 weeks of treatment, the patient will be reassessed before the therapeutic decision to phase post-myocardial infarction.

Chronic treatment: If treatment with captopril did not begin in the acute phase of myocardial infarction in the first 24 hours, it is suggested to begin treatment between the 3rd and 16th day of infarction as soon as conditions initiation of treatment are met (hemodynamic stability support a possible residual ischemia). The initial dose should be low 6.25 mg followed by 12.5 mg 3 times daily for 2 days, then 25 mg 3 times daily if the patient's hemodynamic tolerance permits. The recommended dose for effective cardioprotection in the long-term treatment is 75 mg to 150 mg per day in 2 or 3 doses.

If symptomatic hypotension, as in heart failure, the dose of diuretics and/or other vasodilators may be associated with reduced dose to achieve the balance of captopril. If necessary, the dose of captopril is adjusted according to the tolerance of the patient.

Diabetic nephropathy: The recommended dose of captopril for long term use to treat diabetic nephropathy is 25 mg t.i.d.

Renal Impairment: captopril is excreted primarily via the kidneys, dosage should be reduced or the dosage interval should be increased in patients with impaired renal function. When concomitant diuretic therapy is required, a loop diuretic (e.g. furosemide), rather than a thiazide diuretic, is preferred in patients with severe renal impairment. In patients with renal insufficiency, the dose of captopril is adjusted to the degree of impairment:

Creatinine clearance (ml/min/1,73 m ²)	Daily starting dose (mg)	Daily maximum dose (mg)
> 40	25-50	150
21-40	25	100
10-20	12.5	75
< 10	6.25	37.5

Elderly patients:

As with other antihypertensive agents, consideration should be given to initiating therapy with a lower starting dose (6.25 mg BID) in elderly patients who may have reduced renal function and other organ dysfunctions. Dosage should be titrated against the blood pressure response and kept as low as possible to achieve adequate control.

Children and adolescents: The efficacy and safety of captopril have not been fully established.

ADVERSE EFFECTS:

The adverse effects of captopril are neutropenia/agranulocytosis, hyperkalaemia, hypoglycaemia, sleep disorders, taste impairment, dizziness, drowsiness, headache and paraesthesia, tachycardia or tachyarrhythmia, angina pectoris, palpitations, dry and irritating non-productive cough, dyspnoea, nausea, vomiting, abdominal pain, diarrhoea, constipation, dry mouth, impaired hepatic function and cholestasis (including jaundice), pruritus with or without a rash, alopecia, angioedema, polyuria, oliguria, increased urine frequency, nephrotic syndrome, chest pain, fatigue, malaise, fever.

DRUG INTERACTIONS:

Captopril may interact with Potassium sparing diuretics (e.g. spironolactone, triamterene or amiloride), potassium supplements, or potassium-containing salt; Lithium; Estramustine; Antidiabetic agents (insulin, sulphonylureas); other anti-hypertensive agents (e.g. beta-blockers and long-acting calcium channel blockers); NSAIDs, salicylates in high doses (>3 g per day); Antidepressants Imipramine (tricyclics), neuroleptics; Corticosteroids, Tetracosactide (route), except hydrocortisone; Allopurinol, procainamide, cytostatic or immunosuppressive agents.

OVERDOSAGE:

Overdose symptoms include severe hypotension, shock, lethargy, bradycardia, electrolyte disturbance and renal failure. If hypotension occurs, patient should be placed in supine position and sodium supplements as well as fluids should be administered immediately. Parasympathetic nervous system side effects should be treated with atropine administration. In this case cardiac pacing may be considered. Captopril may be eliminated from the circulation with haemodialysis.

PRESENTATION:

Blister pack/Jar Pack.

STORAGE INSTRUCTIONS:

Store below 30 C. Protect from light.

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