

# CORTEC<sup>®</sup> Tablets

(Enalapril Maleate Tablets USP)

**COMPOSITION:** Each film coated tablet contains:  
Enalapril Maleate USP ... 5mg or 10mg. [USP Specs.]

**DESCRIPTION:** CORTEC (Enalapril Maleate) is the Maleate Salt of Enalapril, a derivative of two amino-acids i.e L-alanine and L-Proline. After oral administration Enalapril is rapidly absorbed and then hydrolyzed to enalaprilat, which is highly specific, long acting, non-sulphydryl Angiotensin Converting Enzyme Inhibitor (ACEI).

**INDICATIONS AND USAGE:** **Hypertension:** CORTEC is indicated in the treatment of all grades of essential hypertension and in renovascular hypertension CORTEC is effective alone or in combination with other antihypertensive agents especially diuretics.

**Heart Failure:** CORTEC is indicated as adjunctive therapy in the management of heart failure, in patients who are not responding adequately to diuretic and digitalis. In patients with severe heart failure CORTEC improves survival. In patients with symptomatic heart failure CORTEC is also indicated to: Improve survival, retard the progression of heart failure, reduce hospitalization for heart failure and prevention of symptomatic heart failure. In asymptomatic patients with left ventricular dysfunction, CORTEC is indicated to: Retard the development of symptomatic heart failure, reduce hospitalization for heart failure, and prevention of coronary ischemic events in patients with left ventricular dysfunction. CORTEC is indicated to: Reduce the incidence of myocardial infarction and reduce hospitalization for unstable angina pectoris.

**DOSAGE AND ADMINISTRATION:** Since the absorption of CORTEC tablets is not affected by food, the tablets may be administered before, during or after meals.

**Essential Hypertension:** The initial dose is 10-20mg depending on the degree of hypertension and is given once daily. In mild hypertension the recommended initial dose is 10mg daily. For other degrees of hypertension the initial dose is 20mg, daily. The usual maintenance dose is 20mg taken once daily. The dosage should be adjusted according to requirements of patient to a maximum of 40mg daily.

**Renovascular Hypertension:** Because blood pressure and renal function in such patients may be particularly sensitive to ACE inhibitor, therapy should be initiated with lower starting dose (2.5mg or 5mg). The dosage should be adjusted to the needs of patient. Most patients may be expected to respond to 20mg taken once daily. For patients with hypertension who have been treated with diuretics, caution is recommended as there is likelihood of development of symptomatic hypotension.

**Concomitant Diuretic Therapy in Hypertension:** Symptomatic hypotension may occur following the initial dose of CORTEC this is more likely in patients who are being treated concomitantly with diuretics. Caution is therefore recommended, since these patients may be volume or salt depleted. The diuretic therapy should be discontinued for 2-3 days prior to initiation of therapy with CORTEC. If this is not possible, smallest initial dose (2.5mg) should be given to ascertain blood pressure response. Dosage should then be adjusted according to the needs of patient.

**Dosage in Renal Failure:** The intervals between the administration of CORTEC should be prolonged and/or dosage reduced. The dosage in renal failure is shown as per table given below:

Renal Status	Creatinine Clearance (ml/min)	Initial dose (mg/day)
Mild impairment	≤ 80 >30ml/min	5-10mg
Moderate impairment	≤ 30 >10ml/min	2.5-5mg
Severe Impairment. Normally, these patients will be on dialysis*	≤ 10ml/min	2.5mg on dialysis days**

\* See PRECAUTIONS - Hemodialysis patients.

\*\* Enalapril is dialyzable. Dosage on non-dialysis days should be adjusted depending on the blood pressure response.

**Dosage in Heart Failure:** CORTEC is indicated as adjunctive therapy with diuretic and digitalis. The recommended starting dose is 2.5mg once or twice daily. After the initial dose of CORTEC, the patient should be kept under medical supervision for at least two hours and until blood pressure has stabilized for at least additional one hour. If possible, dose of diuretic should be reduced. The usual therapeutic dosing range for treatment of heart failure is 5-20mg daily given in two divided doses; the maximum dose is 40mg. Dosage may be adjusted depending under clinical or hemodynamic response.

**CONTRA-INDICATIONS:** CORTEC is contra-indicated in patients who are hypersensitive to this product and in patients with a history of angioneurotic edema related to previous treatment with an angiotensin converting enzyme inhibitor (ACEI).

#### PRECAUTIONS:

**Symptomatic Hypotension:** Symptomatic hypotension was seen rarely in uncomplicated hypertensive patients. In hypertensive patients receiving CORTEC, hypotension is more likely to occur, if the patient has been volume depleted e.g., diuretic therapy, dietary salt restriction, dialysis, diarrhea or vomiting. In patients with heart failure with or without associated renal insufficiency, symptomatic hypotension has been observed. This is more likely to occur in those patients with more severe degree of heart failure, as reflected by the use of high doses of loop diuretics, hyponatremia or functional renal impairment. In these patients therapy should be started under medical supervision and patient should be followed closely whenever dose of CORTEC and/or diuretic is adjusted. Similar considerations may apply to patients with ischemic heart or cerebrovascular disease in whom an excessive fall in blood pressure could result in myocardial infarction or cerebrovascular accident. If hypotension occurs, patient should be placed in supine position and if necessary should receive an intravenous infusion of normal saline. A transient hypotensive response is not contra-indication to further doses, which can be given usually without difficulty once blood pressure has increased after volume expansion. In some patients with heart failure who have normal or low blood pressure, additional lowering of systemic blood pressure may occur with CORTEC. This effect is anticipated and usually is not a reason to discontinue treatment. If hypotension becomes symptomatic, a reduction of dose and/or discontinuation of diuretic or CORTEC may be necessary.

**Impaired Renal Function:** In some patients hypotension following the initiation of therapy with ACE inhibitors may lead to some further impairment in renal function. Acute renal failure usually reversible, has been noticed in this situation. Patients with renal insufficiency may require reduced and/or less frequent doses of CORTEC.

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In some patients with bilateral renal artery stenosis or stenosis of the artery to a solitary kidney, increases of blood urea and serum creatinine; usually reversible upon discontinuation of therapy, have been seen. This is especially likely in patients with renal insufficiency. Some patients with no apparent pre-existing renal disease have developed minor and transient increase of blood urea and serum creatinine when CORTEC has been given concomitantly with diuretic. Dosage reduction and/or discontinuation of the diuretic and/or CORTEC may be required.

**Surgery/Anesthesia:** In patients undergoing major surgery or during anesthesia with agents that produce hypotension, Enalapril blocks 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 Patients:** Anaphylactoid reactions have been reported in patients dialyzed with high-flux membrane and concomitantly treated with an ACEI. In these patients consideration should be given to use a different type of dialysis membrane or different class of antihypertensive agent.

**Use in Pregnancy & Lactation:** The use of CORTEC during pregnancy & lactation is not recommended.

**Angioedema:** Angioedema including laryngeal edema, may occur especially after the first dose of Enalapril. The patient should be advised to report immediately, if any signs or symptoms suggesting angioedema (Swelling of face, extremities, eyes, lips, tongue, difficulty in swallowing or breathing) and to take no more drug before consulting with prescribing physician.

**Hyperkalemia:** Patients should be told not to use salt substitutes containing potassium without consulting their physician.

**Neutropenia:** Patients should be told to report promptly, if any signs of infection (e.g. Sore throat, fever) which may be a sign of neutropenia.

**DRUG INTERACTIONS: Hypotension in Patient on Diuretic Therapy:** Patients on diuretic and especially those in whom diuretic therapy was recently instituted, may occasionally experience excessive reduction of blood pressure after initiation of therapy with Enalapril. The possibility of hypotensive effect with Enalapril can be minimized by either discontinuing diuretic or increasing salt intake prior to initiation of Enalapril.

**Agents Causing Renin Release:** The antihypertensive effect of CORTEC is additive by other antihypertensive agents that cause renin release, (e.g. diuretic)

**Other Cardiovascular Agents:** CORTEC when used concomitantly with  $\beta$ -adrenergic blocking agents, methyl dopa, nitrates, calcium blocking agents, hydralazine and digoxin has no adverse interactions.

**Agents Increasing Serum Potassium:** CORTEC attenuates the potassium loss, caused by thiazide type diuretics. Potassium sparing diuretic, potassium supplements or potassium containing salt substitutes may lead to significant increase in serum potassium. Therefore in concomitant use of these agents, caution and frequent monitoring of serum potassium is recommended.

**Lithium:** Lithium toxicity has been reported in patient receiving lithium with drugs, which cause elimination of sodium including Enalapril. Therefore monitoring of serum lithium is recommended.

**ADVERSE REACTIONS:** Enalapril has been found generally well tolerated in controlled clinical trials involving 2987 patients. For the most part adverse experiences were mild and transient in nature. Dizziness and headache were more commonly reported adverse effects. Fatigue and asthenia were reported in 2-3% of patients. Other side effects occurred in less than 2% of patients and included hypotension, muscle cramps, rash and cough, less frequently renal dysfunction and oliguria have been reported.

**Hypersensitivity/Angioneurotic Edema:** Angioneurotic edema of the face, extremities, lips, tongue, glottis and/or larynx has been reported rarely.

**Cardio-vascular:** Myocardial infarction or cerebrovascular accident, chest pain, palpitations, rhythm disturbance.

**Gastrointestinal:** Ileus, pancreatitis, hepatitis, jaundice, abdominal pain, vomiting, dyspepsia, constipation, anorexia.

**Skin:** Photosensitivity, erythema multiforme, exfoliative dermatitis, Stevens Johnson Syndrome, toxic epidermal necrolysis, pruritus, urticaria, and alopecia.

**Nervous System/Psychiatric:** Depression, confusion, somnolence, insomnia, nervousness, and vertigo.

**Respiratory:** Bronchospasm, dyspnea, rhinorrhea, sore throat/hoarseness.

**Others:** Impotence, flushing, taste alteration, tinnitus, glossitis, blurred vision.

**OVER DOSAGE:** The salient features of over dosage reported to date is hypotension, beginning about six hours after ingestion of tablets, along with blockade of the renin angiotensin system and stupor. The recommended treatment of over dosage is intravenous saline infusion. If ingestion is recent, induce emesis. Enalapril may be removed from general circulation by hemodialysis.

**INSTRUCTIONS:** Store below 30°C. Store in dry place away from children. Do not stop medication without medical advice.

**PRESENTATION:** CORTEC tablets 5mg and 10mg are available in a Alu Alu Blister pack of 10'sx2 tablets.

کورٹیک گولیاں  
(اینٹالاپریل ٹیبلیٹ)

اگر آپ کو کورٹیک کے ساتھ کوئی بھی دوا استعمال کر رہے ہیں تو ان کی دوا کے بارے میں جاننا ضروری ہے۔

نوٹ: اگر آپ کو کورٹیک کے ساتھ کوئی بھی دوا استعمال کر رہے ہیں تو ان کی دوا کے بارے میں جاننا ضروری ہے۔

خوراک و طریقہ استعمال: صرف صبح کی دوا کے ساتھ استعمال کریں۔

احتیاط: (1) اگر آپ کو کورٹیک کے ساتھ کوئی بھی دوا استعمال کر رہے ہیں تو ان کی دوا کے بارے میں جاننا ضروری ہے۔

(2) اگر آپ کو کورٹیک کے ساتھ کوئی بھی دوا استعمال کر رہے ہیں تو ان کی دوا کے بارے میں جاننا ضروری ہے۔

ضروریات: (1) دوا کے بارے میں جاننا ضروری ہے۔

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Manufactured by:  
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