Anapril®

Enalapril Maleate Tablet

DESCRIPTION

Anapril® is a preparation of Enalapril Maleate, an anti-hypertensive agent. Following oral administration, **Anapril®** is rapidly absorbed and hydrolysed to enalapril at a highly specific, long acting angiotensin-converting enzyme inhibitor. Onset of action of **Anapril®** begins smoothly and gradually within one hour and its effects continue usually for 24 hours after a single daily dose, Data indicate no loss of effect during long-term therapy.

INDICATIONS

Hypertension: All grades of essential hypertension and renovascular hypertension. **Heart failure:** In heart failure, **Anapril®** should be used as an adjunctive therapy with non-potassium-sparing diuretics and, where appropriate, digitalis. **Severe heart failure:** Treatment with **Anapril®** should always be initiated in hospital under close medical supervision. When used as an adjunct to conventional therapy in these patients, **Anapril®** improves symptoms, and reduces mortality and hospitalization. **Mild to moderate heart failure:** Treatment with **Anapril®** should always be initiated under close medical supervision. When used as an adjunct to conventional therapy in these patients, **Anapril®** improves symptoms, and reduces mortality and hospitalization.

DOSAGE AND ADMINISTRATION

The maximum daily dose is 40 mg. The absorption of **Anapril®** is not affected by food. **Essential and renovascular hypertension:** Treatment should be initiated with 5 mg once a day. Where concomitant therapy is a diuretic, the recommended initial dose of **Anapril®** 2.5 mg. The dose should be titrated to give optimum control of blood pressure. The usual maintenance dose is 10-20 mg given once daily. In severe hypertension, the dosage may be increased incrementally to a maximum of 40 mg once daily. The dosage of other antihypertensive agents being used together with **Anapril®** may need to be adjusted. Where **Anapril®** replaces a beta-blocking drug in the therapeutic regimen, the beta-blocking agent should not be discontinued abruptly; the dosage should be titrated down after commencing therapy with **Anapril®**.

With concomitant diuretic therapy: The recommended initial dose of **Anapril®** is 2.5 mg. Symptomatic hypotension can occur following the initial dose of **Anapril®**; this is more likely when **Anapril®** is added to previous diuretic therapy. Caution is recommended, therefore, since these patients may be volume or salt depleted. If possible,the diuretic therapy should be discontinued for 2-3 days prior to initiation of therapy with **Anapril®**. **Anapril®** minimises the development of thiazide-induced hypokalaemia and hyperuricaemia.

Use in the elderly (over 65 years): The starting dose should be 2.5 mg. **Anapril®** is effective in the treatment of hypertension in the elderly. Some elderly patients may be more responsive to **Anapril®** than younger patients. The dose should be titrated according to need for the control of blood pressure.

Heart failure: Anapril® can be used as an adjunctive therapy with non-potassium-sparing diuretics and /or digitalis. **Anapril®** should be introduced for the treatment of heart failure following stabilisation of the patient on diuretic therapy. Therapy with **Anapril®** should be initiated under close medical supervision (in hospital for severe heart failure) with a recommended starting dose of 2.5 mg once daily. The dose of **Anapril®** should be gradually increased depending upon tolerability to the recommended maintenance dose (10-20 mg) given as a single or twice daily dose. This dosage schedule has been shown to improve survival. In order to decrease the possibility of symptomatic hypotension, patients on previous high dose diuretics should have the diuretic dose reduced before introducing **Anapril®**, The appearance of hypotension after the initial dose of **Anapril®** dose not preclude subsequent careful dose titration with the drug, following effective treatment of the hypotension.

Use in impaired renal function: Anapril® is excreted by kidney. It should be used with caution in patients with renal impairment. The recommended starting dose is 2.5 mg. The dose should be titrated against the response, and should be kept as low as possible to maintain adequate control of blood pressure or heart failure. **Anapril®** is dialysable. Dialysis patients may be given the usual dose of **Anapril®**on dialysis. On the days when patients are not on dialysis the dosage should be tailored to the blood pressure response.

Children: The paediatric use of **Anapril®** has not been studied.

CONTRAINDICATIONS

Pregnancy: Anapril® has been shown to be fetotoxic in rabbits during middle and late pregnancy. Because of these findings **Anapril®** is contra-indicated in pregnancy. Hypersensitivity to the product or any of its components, and in patients with a history of angioneurotic oedema relating to previous treatment with an ACE inhibitor.

PRECAUTIONS

Pretreatment assessment of renal function: Assessment of renal function prior to initiation of therapy, and during treatment where appropriate. Symptomatic hypotension was seen rarely in uncomplicated hypertensive patients. It has been reported mainly in patients with severe heart failure and who have been volume-depleted by diuretic therapy. By initiating therapy with a small dose (2.5 mg **Anapril®**) the duration of any hypotensive effect may be lessened.

Similar considerations in terms of initiating therapy with a small dose may apply also to patients with ischaemic heart or cerebrovascular disease in whom severe hypotension could result in a myocardial infarct or cerebrovascular accident. Severe hypotension has been reported, mainly in patients with severe heart failure with or without associated renal insufficiency. This is most likely in those patients on high doses of loop diuretics, or with hyponatraemia or functional renal impairment. The appearance of hypotension after the initial dose of **Anapril®** does not preclude subsequent careful dose titration with the drug after effective management of the hypotention.

Impaired renal function: Anapril® should be used with caution in patients with renal insufficiency as they may require reduced or less frequent doses. As with all antihypertensive agents, renal function should be assessed in patients with hypertension or congestive heart failure before initiating therapy. Angioneurotic oedema has been reported with angiotensin-converting enzyme inhibitors, including Enalapril. In such cases, **Anapril®** should be discontinued immediately and appropriate monitoring should be instituted to ensure complete resolution of symptoms prior to dismissing the patient. **Haemodialysis patients:** A high incidence of anaphylactoid reactions have been reported in patients dialyzed with high flux membranes (e.g., AN 69) and treated concomitantly with an ACE inhibitor. This combination should therefore be avoided. Cough: Cough has been reported with the use of ACE inhibitors. Characteristically, the cough is non-productive, persistent and resolves after discontinuation of therapy. **Surgery / Anaesthesia:** In patients undergoing major surgery or during anaesthesia with agents that produce hypotension. **Anapril®** blocks angiotensin II formation secondary to compensatory renin release. This may lead to hypotension which can be corrected by volume expansion. **Anapril®** should not be used in patients with aortic stenosis or outflow obstruction. L**actating mothers:** Enalapril and enalaprilat are excreted in human milk; caution should be exercised if **Anapril®** is given to lactating mothers.

DRUG INTERACTIONS

Combination with other antihypertensive agents such as beta-blockers, methyldopa, calcium antagonists, and diuretics may increase the antihypertensive efficacy. Adrenergic - blocking drugs should only be combined with **Anapril®** under careful supervision, Concomitant propranolol may reduce the bioavailability of **Anapril®**, but this does not appear to be of any clinical significance. Plasma potassium usually remains within normal limits, although cases of hyperkalaemia have been reported. If **Anapril®** is given with potassium losing diuretic, the likelihood of diuretic-induced hypokalaemia may be lessened. **Anapril®** may elevate plasma potassium levels in patients with renal failure. Potassium supplements, potassium -containing saft substitutes are not recommended, particularly in patients with impaired renal function, since they may lead to significant increases in plasma potassium.

SIDE-EFFECTS

Severe hypotension and renal failure have occurred in association with therapy with **Anapril®**. These appear to occur in certain specific sub-groups. Other adverse reactions include dizziness, headache, fatigue, asthenia, orthostatic hypotension, syncope, nausea, diarrhoea, muscle cramps, rash, cough. Less frequently renal dysfunction, renal failure, and oliguria have been reported. Less common side- effects include: Myocardial infarction, chest pain, palpitations, rhythm disturbances, angina pectoris, pancreatitis, hepatitis-either hepatocellular or cholestatic, jaundice, abdominal pain, vomiting, dyspepsia, constipation, anorexia. stomatitis, depression, confusion, somnolence, insomnia, nervousness, paraesthesiae, vertigo, bronchospasm, asthma, dyspnoea, rhinorrhoea, sore throat and hoarseness. diaphoresis, erythema multiforme, exfoliative dermatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis, pruritus, urticaria, alopecia, impotence, flushing, taste alteration, tinnitus, glossitis, blurred vision,etc. Angioneurotic oedema of the face, extremities, lips, tongue, glottis, and /or larynx has been reported rarely.

OVERDOSAGE

Limited data are available for overdosage in humans. The most prominent features of overdosage reported to date are marked hypotension, beginning some six hours after ingestion of tablets, concomitant with blockage of the renin - angiotensin system, and stupor. The recommended treatment of overdosage is intravenous infusion of normal saline solution. If ingestion is recent, induce emesis. **Anapril®** can be removed from the general circulation by haemodialysis.

PHARMACEUTICAL PRECAUTIONS

Do not store above 25 °C. Keep away from light and wet place. Keep out of reach of children.

PACKAGING

Anapril® 5 tablet: Box containing 10 strips of 10 tablets each. Each tablet contains Enalapril Maleate USP 5 mg.
Anapril® 10 tablet: Box containing 10 strips of 10 tablets each. Each tablet contains Enalapril Maleate USP 10 mg.

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