

# PREFACE - H TABLETS

## Composition

### PREFACE - H Tablets

Each uncoated tablet contains Ramipril USP equivalent to Ramipril (anhydrous) 2.5 mg and Hydrochlorothiazide I.P. 12.5 mg

## Description

**PREFACE - H** is a combination of Ramipril and hydrochlorothiazide. Ramipril is a long acting specific inhibitor of angiotensin converting enzyme, which catalyses the conversion of the inactive decapeptide angiotensin I to the active angiotensin II. Inhibition of ACE results in decreased angiotensin II which leads to decreased vasopressor activity and aldosterone secretion. Thus, Ramipril reduces both cardiac output and peripheral resistance, and thus reduces blood pressure.

Hydrochlorothiazide is a thiazide diuretic. It has a complex mechanism of action, including natriuresis and vasodilation. Reduction in blood volume brought about by hydrochlorothiazide activates the renin-angiotensin system. Hydrochlorothiazide also decreases serum potassium, as a result of its diuretic effects.

Administration of Ramipril blocks the activation of the renin-angiotensin system and reverses the potassium loss associated with the diuretic.

The combination of Ramipril and hydro-chlorothiazide has an additive effect on blood pressure control. The antihypertensive effect is sustained for at least 24 hours.

## Indications

Hypertension not responding to monotherapy with ACE inhibitors or diuretics.

## Dosage and Administration

The usual initial dosage is one or two tablets of **PREFACE - H** daily. The dosage however should be individualised. The combination is not meant for initial therapy. It may be substituted for the titrated individual components.

## Contraindications

Hypersensitivity to either component, hypersensitivity to other sulfonamide derived drugs, history of angioedema related to previous treatment with an ACE inhibitor, anuria, patients on lithium therapy, pregnancy.

## Warnings and Precautions

### DRUG INTERACTIONS

*Agents increasing serum potassium:* Ramipril attenuates potassium loss caused by thiazide-type diuretics. Use of **PREFACE - H** with potassium sparing diuretics, potassium supplements, or potassium containing salt substitutes may lead to significant increases in serum potassium. Therefore, if concomitant use of these agents is indicated, they should be used with caution and with frequent monitoring of serum potassium.

*Lithium:* Lithium toxicity has been reported in patients receiving lithium concomitantly with drugs which cause elimination of sodium. Both, Ramipril and

hydrochlorothiazide increase sodium excretion. Also, diuretic agents reduce the renal clearance of lithium and add a high risk of lithium toxicity.

*Alcohol, barbiturates or narcotics:* Potentiation of orthostatic hypotension may occur.

*Antidiabetic drugs (oral agents and insulin):* Dosage adjustment of the antidiabetic agent may be required.

*Corticosteroids, ACTH:* Intensified electrolyte depletion, particularly, hypokalaemia may occur.

*Nondepolarizing skeletal muscle relaxants:* Responsiveness to the muscle relaxant may be increased.

*Nonsteroidal anti-inflammatory drugs:* In some patients, the administration of a non-steroidal anti-inflammatory agent can reduce the antihypertensive effects of **PREFACE - H**. Patients receiving these medications concomitantly should be observed closely to determine if the desired antihypertensive effect is obtained.

#### ANGIOEDEMA

Angioedema of the face, extremities, lips, tongue, glottis and/or larynx has been reported in patients treated with Ramipril. In such cases, **PREFACE - H** should be promptly discontinued.

#### HYPOTENSION

Excessive hypotension has been rarely seen in uncomplicated hypertensive patients but is a possible consequence. In patients with severe congestive heart failure, with or without associated renal insufficiency, excessive hypotension has been observed following administration of such combination therapy. Because of the potential fall in blood pressure in these patients, therapy should be started under very close medical supervision. Similar considerations apply to patients with ischemic heart disease or cerebrovascular disease in whom an excessive fall in blood pressure could result in a myocardial infarction or cerebrovascular accident.

#### PREGNANCY

When used in pregnancy during the second and third trimester, ACE inhibitors can cause injury and death to the developing foetus. Hence the combination is contraindicated in pregnancy.

#### NURSING MOTHERS

The combination should not be administered to nursing mothers, unless the benefits highly outweigh the risks.

#### PAEDIATRIC USE

Safety and effectiveness of the combination in children have not been established.

#### RENAL IMPAIRMENT

**PREFACE - H** should be used with caution in patients with severe renal disease. As a consequence of inhibition of the renin-angiotensin-aldosterone system (RAAS), changes in renal function may be anticipated in susceptible individuals. In hypertensive patients with unilateral or bilateral renal stenosis, increases in blood urea nitrogen and serum creatinine may occur which is usually reversible. When such patients are treated with the combination, renal function should be monitored

during the first few weeks of therapy.

The use of thiazides in patients with impaired renal function may precipitate azotemia.

#### **HEPATIC IMPAIRMENT**

Caution needs to be exercised since thiazides may precipitate hepatic coma in patients with hepatic impairment.

#### **Side effects**

The combination of Ramipril and hydrochloro-thiazide is well tolerated. Angioneurotic edema has been reported with ACE inhibitors. In such cases, the combination should be discontinued immediately. Other frequent side effects include dizziness, headache, fatigue, cough and orthostatic effects.

#### **Overdosage**

The treatment of overdosage with the combination is symptomatic and supportive. Therapy with the combination should be discontinued and the patient observed closely. Suggested measures include induction of emesis and/or gastric lavage, and correction of dehydration, electrolyte imbalance and hypotension by established procedures.

#### **Presentation**

**PREFACE - H** Blister pack of 10 tablets