SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

FINAPRIL 10
Enalapril Maleate Tablets USP

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each uncoated tablet contains:

Enalapril Maleate USP	:	10 mg
Excipients	:	Q.S.

For excipients, see 6.1.

3. PHARMACEUTICAL FORM

Tablet
For oral administration.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

FINAPRIL 10 is indicated for;

- **Treatment of hypertension:** All grades of essential hypertension and renovascular hypertension.
- **Treatment of heart failure:** Enalapril is indicated for the treatment of symptomatic congestive heart failure, usually in combination with diuretics and digitalis. In these patients Enalapril improves symptoms, increases survival, and decreases the frequency of hospitalization.
- **Asymptomatic left ventricular dysfunction:** In clinically stable asymptomatic patients with left ventricular dysfunction (ejection fraction <35%), Enalapril decreases the rate of development of overt heart failure and decreases the incidence of hospitalization for heart failure.

4.2 Posology and method of administration

Adults
Heart Failure
Initial dosage is 2.5 mg twice daily. Usual dosage is 2.5 to 20 mg/day in 2 divided doses (max, 40 mg/day). Titrate doses upward as tolerated over a period of a few days or weeks. The max daily dose is 40 mg in divided doses.

Hypertension
The initial dose is 5 to maximally 20 mg, depending on the degree of hypertension and the condition of the patient (see below). Enalapril maleate is given once daily. In mild hypertension, the recommended initial dose is 5 to 10 mg. Patients with a strongly activated renin-angiotensin-aldosterone system (e.g., renovascular hypertension, salt and/or volume depletion, cardiac decompensation, or severe hypertension) may experience an excessive blood pressure fall following the initial dose. A starting dose of 5 mg or lower is recommended in such patients and the initiation of treatment should take place under medical supervision.

The usual maintenance dose is 20 mg daily. The maximum maintenance dose is 40 mg daily.

Left Ventricular Dysfunction
Initial dosage is 2.5 mg twice daily. Titrate to targeted daily dose of 20 mg in divided doses.

Use in Paediatrics
For patients who can swallow tablets, the dose should be individualised according to patient profile and blood pressure response. The recommended initial dose is 2.5 mg in patients 20 to <50 kg and 5 mg in patients ≥50 kg. Enalapril maleate is given once daily. The dosage should be adjusted according to the needs of the patient to a maximum of 20 mg daily in patients 20 to <50 kg and 40 mg in patients ≥50 kg.

Method of administration: Oral

4.3 Contraindications

Hypersensitivity to the product or any of the components and in patients with a history of angioneuroticoedema relating to previous ACE inhibitor treatment.
Lactation - Enalapril and Enalaprilat are secreted into the breast milk.

4.4 Special warnings and precautions for use

- A woman become pregnant while receiving FINAPRIL, the treatment must be stopped promptly and switched to a different medicine.
- A woman contemplate pregnancy, the doctor should institute alternative medication.
- FINAPRIL can cause foetal and neonatal morbidity and mortality when administered to pregnant women during the 2nd and 3rd trimesters.
- FINAPRIL pass through the placenta and can be presumed to cause disturbance in foetal blood pressure regulatory mechanisms. Oligohydramnios, which may result in limb contractures, craniofacial deformities and hypoplastic lung development, as well as hypotension, hyperkalemia, oliguria and anuria in newborns have been reported after

administration of FINAPRIL in the second and third trimester. Cases of defective skull ossification have been observed. Prematurity and low birth mass can occur.

- Infants whose mothers have taken Enalapril should be closely observed for hypotension, oliguria and hyperkalemia. These adverse effects to the embryo and foetus do not appear to have resulted from intra-uterine FINAPRIL exposure limited to the first trimester.
- FINAPRIL, which crosses the placenta, has been removed from the neonatal circulation by peritoneal dialysis with some clinical benefit.

4.5 Interaction with other medicinal products and other forms of interaction

Hypotension-Patients on Diuretic Therapy: Patients on diuretics and especially those in whom diuretic therapy was recently instituted, may occasionally experience an excessive reduction of blood pressure after initiation of therapy with enalapril. The possibility of hypotensive effects with enalapril can be minimized by either discontinuing the diuretic or increasing the salt intake prior to initiation of treatment with Enalapril.

Agents Increasing Serum Potassium: Since enalapril decreases aldosterone production, elevation of serum potassium may occur. Potassium-sparing diuretics such as spironolactone, eplerenone, triamterene or amiloride, potassium supplements or other drugs that may increase serum potassium (e.g., trimethoprim-containing products) should be given only for documented hypokalemia and with caution and frequent monitoring of serum potassium particularly in patients with impaired renal function since they may lead to a significant increase in serum potassium. Salt substitutes which contain potassium should also be used with caution.

Agents Causing Renin Release: The antihypertensive effect of FINAPRIL is augmented by antihypertensive agents that cause renin release (e.g., diuretics).

Agents Affecting Sympathetic Activity: Agents affecting sympathetic activity (e.g., ganglionic blocking agents or adrenergic neuron blocking agents) may be used with caution. Beta- adrenergic blocking drugs add some further antihypertensive effect to enalapril.

Lithium Salts: As with other drugs which eliminate sodium, lithium clearance may be reduced. Therefore, the serum lithium levels should be monitored carefully if lithium salts are to be administered.

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) Including Selective Cyclooxygenase-2 Inhibitors: The antihypertensive effect of enalapril may be diminished with concomitant non- steroidal anti-inflammatory drug use including selective cyclooxygenase-2 inhibitors (COX-2 inhibitors). In some patients with

compromised renal function (e.g., elderly patients or patients who are volume-depleted including those on diuretic therapy) who are being treated with NSAIDS including selective COX-2 inhibitors, the co-administration of ACE inhibitors or angiotensin II receptor antagonists may result in further deterioration of renal function. Cases of acute renal failure, usually reversible, have also been reported. This combination should therefore be administered with caution in this patient population.

Dual Blockade of the Renin-Angiotensin System (RAS) with ACEIs, ARBs or aliskiren- containing drugs: Dual Blockade of the Renin-Angiotensin System (RAS) with ACEIs, ARBs or aliskiren-containing drugs is contraindicated in patients with diabetes and/or renal impairment, and is generally not recommended in other patients, since such treatment has been associated with an increased incidence of severe hypotension, renal failure, and hyperkalemia. Cardiovascular, Dual Blockade of the Renin-Angiotensin System (RAS) and Renal.

Gold: Nitritoid reactions (symptoms include facial flushing, nausea, vomiting and symptomatic hypotension) have been reported rarely in patients on therapy with injectable gold (sodium aurothiomalate) and concomitant ACE inhibitor therapy including enalapril.

Mammalian Target of Rapamycin (mTOR) Inhibitors: Patients taking concomitant mTOR inhibitor (e.g., temsirolimus, sirolimus, everolimus) therapy may be at increased risk for angioedema. Caution should be used when these drugs are used concomitantly.

Neprilysin Inhibitors

Patients taking a concomitant neprilysin inhibitor (e.g., sacubitril) may be at increased risk for angioedema.

Drug-Food Interactions

The absorption of enalapril is not influenced by the presence of food in the gastrointestinal tract.

4.5 Pregnancy and lactation

The use of FINAPRIL 10 during pregnancy and lactation is contra-indicated. Enalapril and enalaprilat are secreted into the breast milk.

4.7 Effects on ability to drive and use machines

Enalapril can cause blurred vision and can make some people feel dizzy or weak. Feeling dizzy is more likely to happen when you first start taking enalapril or after increasing

your dose. It's best to stop driving, cycling and using tools or machinery during these times.

4.8 Undesirable effects

Cases of severe hypotension and renal failure have been reported with therapy with FINAPRIL 10.

Commonly reported side-effects include dizziness and headache. Other side-effects occurred and include fatigue, asthenia, hypotension, orthostatic hypotension, syncope, nausea, diarrhoea, muscle cramps, rash, cough, renal dysfunction, renal failure, and oliguria.

Cardiovascular: Myocardial infarction or cerebro-vascular accident, possibly secondary to severe hypotension in high risk patients, chest pain, palpitations, rhythm disturbances, angina pectoris.

Gastrointestinal: Ileus, pancreatitis, hepatic failure, hepatitis –either hepatocellular or cholestatic jaundice, abdominal pain, vomiting, dyspepsia, constipation, anorexia, stomatitis.

Nervous system/Psychiatric: Depression, confusion, somnolence, insomnia, nervousness, paraesthesia, vertigo.

Respiratory: Pulmonary infiltrates, bronchospasm, asthma, dyspnoea, rhinorrhoea, sore throat and hoarseness.

Skin: Diaphoresis, erythema multiforme, exfoliative dermatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis, pemphigus, pruritus, urticaria, alopecia.

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

A symptom complex has been reported which may include fever, serositis, vasculitis, myalgia/myositis, arthralgia/arthritis, a positive ANA (Anti-Nuclear Antibody), elevated ESR (Erythrocyte Sedimentation Rate), eosinophilia, and leucocytosis. Rash, photosensitivity or other dermatological manifestations may occur.

4.9 Overdose

Limited data are available for overdosage in humans. The most prominent feature of overdosage reported to date is marked hypotension, beginning some six hours after ingestion of tablets, concomitant with blockade 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. FINAPRIL 10 may be removed from the general circulation by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Angiotensin converting enzyme inhibitors.

ATC Code: C09A A02

Enalapril maleate is the maleate salt of enalapril, a derivative of two amino-acids, L-alanine and L-proline. Angiotensin converting enzyme (ACE) is a peptidyl dipeptidase which catalyses the conversion of angiotensin I to the pressor substance angiotensin II.

After absorption, enalapril is hydrolysed to enalaprilat, which inhibits ACE. Inhibition of ACE results in decreased plasma angiotensin II, which leads to increased plasma renin activity (due to removal of negative feedback of renin release), and decreased aldosterone secretion. ACE is identical to kininase II. Thus, enalapril maleate may also block the degradation of bradykinin, a potent vasodepressor peptide. However, the role that this plays in the therapeutic effects of enalapril maleate remains to be elucidated.

Mechanism of action

While the mechanism through which enalapril maleate lowers blood pressure is believed to be primarily suppression of the renin-angiotensin-aldosterone system, enalapril maleate is antihypertensive even in patients with low-renin hypertension.

Pharmacodynamic effects

Administration of enalapril maleate to patients with hypertension results in a reduction of both supine and standing blood pressure without a significant increase in heart rate.

In hemodynamic studies in patients with essential hypertension, blood pressure reduction was accompanied by a reduction in peripheral arterial resistance with an increase in cardiac output and little or no change in heart rate. Following administration of enalapril, there was an increase in renal blood flow; glomerular filtration rate was usually unchanged. When enalapril is given together with thiazide-type diuretics, its blood pressure lowering effect is approximately additive. Administration of enalapril to patients with congestive heart failure reduces afterload and preload of the heart, resulting in an increase in cardiac output, without reflex tachycardia. When used in hypertensive, normolipidemic patients, enalapril had no effect on plasma lipoprotein fractions. Studies in dogs indicate that enalapril crosses the blood brain barrier poorly, if at all; enalaprilat does not enter the brain.

5.2 Pharmacokinetic properties

Table 3 - Summary of Enalaprilat's Pharmacokinetic Parameters in Healthy Volunteers Further to a 10 mg Oral Dose of Enalapril

	C_{max} ng/mL	**$t_{½}$ (h)***	**$AUC_{0-\infty}$** ng•h/mL
Single dose mean	32.3	11	423

*Effective half-life of accumulation.

Absorption: Enalapril maleate is rapidly absorbed with peak serum concentrations of enalapril occurring within one hour. Based on urinary recovery the extent of absorption of enalapril from enalapril tablets is approximately 60%. The absorption of enalapril is not influenced by the presence of food in the gastrointestinal tract.

Metabolism: Following absorption, enalapril is rapidly and extensively hydrolyzed to enalaprilat, a potent angiotensin converting enzyme inhibitor (which itself is poorly absorbed). Peak serum concentrations of enalaprilat occur 3 to 4 hours after an oral dose

of enalapril. Except for conversion to enalaprilat, there is no evidence of significant metabolism of enalapril.

Excretion: Excretion of enalapril is primarily renal. Approximately 94% of the dose is recovered in the urine and feces as enalaprilat or enalapril. The principal components in urine are enalaprilat, accounting for about 40% of the dose, and intact enalapril.

The serum concentration profile of enalaprilat exhibits a prolonged terminal phase, apparently associated with binding to ACE. The effective half-life for accumulation of enalaprilat following multiple doses of enalapril is 11 hours.
In hypertensive children aged 2 months to 15 years the kinetics of enalapril were approximately similar to adults.

Special Populations and Conditions
Pediatrics: In pediatric patients the antihypertensive effect of enalapril has been studied in hypertensive children aged 6 - 16 years.

Race: The antihypertensive effect of angiotensin converting enzyme inhibitors is generally lower in black than in non-black patients.

Renal Insufficiency: The disposition of enalapril and enalaprilat in patients with renal insufficiency is similar to that in patients with normal renal function until the glomerular filtration rate is 30 mL/min (0.50 mL/s) or less. With renal function ≤ 30 mL/min (≤ 0.50 mL/s), peak and trough enalaprilat levels increase, time to peak concentration increases and time to steady state may be delayed. The effective half-life of enalaprilat following multiple doses of enalapril is prolonged at this level of renal insufficiency. Enalaprilat is dialyzable at the rate of 62 mL/min (1.03 mL/s).

5.3 Preclinical Safety Data
Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential. Reproductive toxicity studies suggest that enalapril has no effects on fertility and reproductive performance in rats, and is not teratogenic. In a study in which female rats were dosed prior to mating through gestation, an increased incidence of rat pup deaths occurred during lactation. The compound has been shown to cross the placenta and is secreted in milk. Angiotensin converting enzyme inhibitors, as a class, have been shown to be foetotoxic (causing injury and/or death to the fetus) when given in the second or third trimester.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Maize Starch BP
Lactose BP
Colloidal Anhydrous Silica BP
Povidone BP
Purified Water BP
Magnesium Stearate BP
Purified Talc BP
Croscarmellose Sodium BP

6.2 Incompatibilities
Not Applicable

6.3 Shelf Life
36 Months

6.4 Special Precautions for Storage
Store below 30ºC in a cool and dry place. Protect from heat, light and moisture.
KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and Contents of Container
10 × 10 Alu-Alu Blister Pack.

6.6 Instructions for use and handling
No special requirements.

7. MARKETING AUTHORISATION HOLDER

SAGA
LIFESCIENCES LIMITED

Ahmedabad
Gujarat, India.
E-mail: info@sagalabs.com
URL: www.sagalabs.com

8. NUMBER(S) IN THE NATIONAL REGISTER OF FINISHED PHARMACEUTICAL PRODUCTS

06876/08818/NMR/2021

9. DATE OF FIRSHT AUTHORISATION/RENEWAL OF THE AUTHORISATION

28/11/2021

10. DATE OF REVISION OF THE TEXT

01 April 2026