ENAHEXAL® 5MG / 20MG

Each **Enahexal® 5mg** tablet and **Enahexal® 20mg** tablet contains enalapril maleate 5mg and 20mg respectively.

DESCRIPTION
Enahexal® 5mg: Oval, convex, white snap tab tablets, one side scored with marking of EN 5.
Enahexal® 20mg: Oval, convex, orange snap tab tablets, one side scored with marking of EN 20.

MECHANISM(S) OF ACTION
Enalapril maleate is a prodrug of enalaprilat and has little pharmacologic activity until hydrolysed in vivo to enalaprilat. The mechanism(s) of action of enalaprilat and enalapril maleate have not been fully elucidated. The drugs appear to reduce blood pressure in normotensive individuals and hypertensive patients and to produce beneficial hemodynamic effects in patients with congestive heart failure mainly by suppressing the renin-angiotensin-aldosterone system. Following oral administration, enalapril is rapidly absorbed and then hydrolysed to the active metabolite enalaprilat. Enalaprilat exerts its effect on the renin angiotensin-aldosterone system by inhibiting the angiotensin-converting enzyme (ACE). It reduces peripheral arterial resistance. In heart failure, it reduces both preload and afterload and the cardiac output may be increased without significant change in heart rate.
ACE catalyses the conversion of angiotensin I to the vasoconstrictor substance, angiotensin II. Angiotensin II also stimulates aldosterone secretion by the adrenal cortex. The beneficial effects of enalapril in hypertension and heart failure appear to result primarily from suppression of the renin-angiotensin-aldosterone system. Inhibition of ACE results in decreased plasma angiotensin II, which leads to decreased vasopressor activity and to decreased aldosterone secretion. Although the latter decrease is small, it results in small increases of serum potassium.
ACE is identical to kininase, an enzyme that degrades bradykinin. Whether increased levels of bradykinin, a potent vasodepressor peptide, play a role in the therapeutic effects of enalapril remains to be elucidated.

Pharmacology
Enalapril is structurally and pharmacologically similar to captopril, but contains a disubstituted nitrogen rather than a sulfhydryl group at position 3 of 2-methyl-1-oxopropyl-1-proline. The lack of the sulfhydryl group in enalapril may result in decreased risk of certain adverse effects (e.g. cutaneous reactions, taste disturbances, proteinuria).

Pharmacodynamics
1. *Hypertension:* Administration of enalapril to patients with hypertension of severity ranging from mild to severe results in a reduction of both supine and standing blood pressure usually with no orthostatic component. Symptomatic postural hypotension is therefore infrequent, although it might be anticipated in volume-depleted patients. In most patients, after oral administration of a single dose of enalapril, onset of antihypertensive activity begins at one hour with peak reduction of blood pressure achieved by 4 to 6 hours. At recommended doses, antihypertensive effects have been maintained for at least 24 hours. In some patients, achievements of optimal blood pressure reduction may require several weeks of therapy. The antihypertensive effects of enalapril have continued during long-term therapy. Abrupt withdrawal of enalapril has not been associated with rapid increase in blood pressure.

2. *Heart failure:* In patients with congestive heart failure, enalapril, usually in conjunction with digitalis and diuretics, decreases systemic vascular resistance, blood pressure, pulmonary capillary wedge pressure and heart size and increases cardiac output and exercise tolerance. Heart rate remains unchanged or decreases slightly, and mean ejection remains unchanged or increases slightly in these patients. Enalapril causes an increase in renal blood flow, however, glomerular filtration rate is usually unchanged. These effects appear to be similar in patients with renovascular hypertension.

Pharmacokinetics
Following oral administration of enalapril, peak serum concentrations of enalapril occur within about one hour. Approximately 60% of an oral dose is absorbed. Enalapril absorption is not influenced by the presence of food in the GI tract. Following absorption, enalapril is hydrolysed to enalaprilat, which is a more potent angiotensin converting enzyme (ACE) inhibitor than enalapril. Enalaprilat is poorly absorbed when administered orally. Peak serum concentrations of enalaprilat occur 3 to 4 hours after an oral dose of enalapril maleate. Distribution of enalapril into human body tissues and fluid has not been fully characterised. Approximately, 50 – 60% of enalaprilat is bound to plasma protein. 2 binding sites have been identified, a low affinity, high capacity site and a high affinity, low capacity site. Drug bound to the latter site may represent enalaprilat bound to circulating serum ACE, possibly accounting for the prolonged terminal elimination of the drug. The half-life of unchanged enalapril appears to be less than 2 hours in healthy individuals and in patients with normal hepatic and renal functions, but may be increased in patients with congestive heart failure. Excretion of enalapril is primarily renal. Approximately 94% of the dose is recovered in the urine and faeces as enalaprilat or enalapril.

INDICATIONS
- All grades of essential hypertension.
- Cardiac failure: As an adjuvant therapy in addition to diuretics and especially in case of severe cardiac failure in addition to digitalis.

CONTRAINDICATIONS
- Hypersensitivity to enalapril, to any of the excipients or any other ACE inhibitor
- History of angioedema associated with previous ACE inhibitor therapy
- Hereditary or idiopathic angioedema
- Pregnancy (see *Pregnancy and lactation*)
- With aliskiren in patients with diabetes.

PREGNANCY AND LACTATION
Pregnancy
Enalapril is contraindicated during pregnancy (see *Contraindications*). ACE INHIBITOR CAN CAUSE INCREASED RISK OF BIRTH DEFECTS, FOETAL AND NEONATAL MORBIDITY AND DEATH WHEN USED THROUGHOUT PREGNANCY

Use of ACE inhibitors during the second and third trimesters of pregnancy has been associated with fetal and neonatal damage, including hypotension, neonatal skull hypoplasia, anuria, reversible or irreversible renal failure, and death. Oligohydramnios, presumably due to impaired fetal renal function, has also been reported; oligohydramnios in this setting has been associated with fetal limb contractures, craniofacial deformation, and hypoplastic lung development. Prematurity, intrauterine growth retardation, and patent ductus arteriosus have also been reported, although it is not clear whether these were due to ACE inhibitor exposure.

Lactation
Limited pharmacokinetic data demonstrate very low concentrations in breast milk. Although these concentrations seem to be clinically irrelevant the use of enalapril in breast-feeding 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. In case of an older infant the use of enalapril in breast-feeding mother may be considered if this treatment is necessary for the mother and the child is observed for any adverse effect.

SIDE EFFECTS / ADVERSE REACTIONS
Nervous system and psychiatric disorders
- Ataxia
- Confusion
- Depression
- Dizziness
- Dream abnormality
- Fatigue
- Headache
- Insomnia
- Malaise
- Nervousness
- Peripheral neuropathy (e.g. paraesthesia, dysesthesia, asthenia and somnolence)
- Vertigo

Gastrointestinal disorders
- Abdominal pain
- Anorexia
- Constipation
- Dyspepsia
- Glossitis
- Hepatic failure
- Hepatitis - either hepatocellular or cholestatic
- Ileus
- Jaundice
- Loss of appetite
- Melena
- Pancreatitis
- Stomatitis
- Vomiting
- Diarrhea
- Nausea
- Taste alteration

Cardiac and vascular disorders
- Hypotension (including postural hypotension and orthostatic effects)
- Myocardial infarction or cerebrovascular accident possibly secondary to excessive hypotension in high risk patients
- Rhythm disturbances (including atrial tachycardia and bradycardia)
- Angina pectoris
- Atrial fibrillation
- Cardiac arrest
- Chest pain
- Palpitations
- Pulmonary embolism
- Pulmonary oedema
- Raynaud phenomenon
- Dizziness
- Syncope

Renal Effects
- Rare incidences reported include renal dysfunction
- Acute reversible renal failure
- Flank pain
- Oliguria
- Uraemia
- Glycosuria
- Proteinuria
- Dysuria/Burning urination

Hypersensitivity Reactions
- Symptom complex (may include a positive ANA titer, increased erythrocytes sedimentation rate)
- Anaphylactoid reactions (associated with initiation of haemodialysis with ACE inhibitor)
- Angiodema of the face
- Arthralgias / arthritis
- Eosinophilia
- Extremities
- Fever
- Glottis and/or larynx
- Intestinal angioderma (associated with ACE inhibitors enalapril)
- Leukocytosis
- Lips
- Myalgias
- Photosensitivity
- Rash and other dermatologic manifestations
- Serositis
- Tongue
- Vasculitis
- Vulvovaginal pruritus

Skin and subcutaneous tissue disorders
- Alopecia
- Diaphoresis
- Erythema multiforme
- Erythema/eosinophilia
- Exfoliative dermatitis
- Herpes zoster
- Pemphigus
- Pruritus
- Rash accompanied by pruritus
- Stevens-Johnson syndrome
- Toxic epidermal necrolysis
- Uticaria
- Flushing

Blood and lymphatic system disorders
- Decrease in haemoglobin and haemotocrit values
- Anaemia (including aplastic and haemolytic)
- Agranulocytosis
- Autoimmune diseases
- Bone marrow depression
- Lymphadenopathy
- Myeloid hypoplasia thrombocytopenia
- Neutropenia (less than 1000 neutrophils/mm3)
- Pancytopenia
- Thrombocytopenia

Clinical Laboratory Alterations
- Elevation of certain liver enzyme values and / or of the serum bilirubin level, hyperkalaemia and hyponatraemia may occur, as well as elevation of the serum creatinine and blood urea nitrogen (BUN) level (reversible).
- Decreases in haemoglobin and haematocrit
- Neutropenia
- Thrombocytopenia
- Bone marrow depression
- Agranulocytosis

Respiratory Effects
- Angioedema
- Upper respiratory infection
- Asthma
- Bronchitis
- Bronchospasm
- Cough
- Dyspnoea
- Hoarseness
- Nasal congestion
- Pneumonia
- Pulmonary infiltrates
- Rhinorrhoea
- Sore throat
- Wheezing

Endocrine disorders
- Syndrome of inappropriate antidiuretic hormone secretion (SIADH)

Eye disorders
- Blurred vision
- Dry eyes
- Tearing eyes
- Conjunctivitis

Hepatobiliary disorders
- Hepatic failure
- Hepatitis - either hepatocellular or cholestatic
- Hepatitis including necrosis
- Cholestasis (including jaundice)

Reproductive system and breast disorders
- Impotence
- Gynecomastia
- Decreased libido

Metabolism and nutrition disorders
- Hypoglycaemia in diabetes patients on oral antidiabetic agent or insulin.

Other Adverse Effects
- Tinnitus
- Hearing loss
- Disturbance of equilibrium
- Muscle cramps
- Perspiration

PRECAUTIONS / WARNINGS

ACE INHIBITOR CAN CAUSE INCREASED RISK OF BIRTH DEFECTS, FOETAL AND NEONATAL MORBIDITY AND DEATH WHEN USED THROUGHOUT PREGNANCY

Initiation of ACE inhibitors therapy is recommended in hospital, particularly for patients with mild to moderate heart failure: receiving multiple or high-dose diuretic therapy; with hypovolaemia; with hyponatraemia; with pre-existing hypotension; with unstable heart failure; with renal impairment; receiving high-dose vasodilator therapy; aged 70 years or more.

Symptomatic hypotension

Symptomatic hypotension is rarely seen in uncomplicated hypertensive patients. In hypertensive patients receiving enalapril, symptomatic hypotension is more likely to occur if the patient has been volume-depleted, e.g., by diuretic therapy, dietary salt restriction, dialysis, diarrhea or vomiting (see *Interaction with other medicaments* and *Side effects*). In patients with heart failure, with or without associated renal insufficiency, symptomatic hypotension has been observed. This is most likely to occur in those patients with more severe degrees 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 the patients should be followed closely whenever the dose of enalapril, 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 a myocardial infarction or cerebrovascular accident.

If hypotension occurs, the patient should be placed in the supine position and, if necessary, should receive an intravenous infusion of normal saline. A transient hypotensive response is not a contraindication to further doses, which can be given usually without difficulty once the 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 enalapril. 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 the diuretic and/or enalapril may be necessary.

Aortic or mitral valve stenosis/hypertrophic cardiomyopathy

As with all vasodilators, ACE inhibitors should be given with caution in patients with left ventricular valvular and outflow tract obstruction and avoided in cases of cardiogenic shock and hemodynamically significant obstruction.

Renal function impairment

In cases of renal impairment (creatinine clearance < 80 ml/min) the initial enalapril dosage should be adjusted according to the patient's creatinine clearance (see *Recommanded Dosage*) and then as a function of the patient's response to treatment. Routine monitoring of potassium and creatinine are part of normal medical practice for these patients.

Renal failure has been reported in association with enalapril and has been mainly in patients with severe heart failure or underlying renal disease, including renal artery stenosis. If recognized promptly and treated appropriately, renal failure when associated with therapy with enalapril is usually reversible.

Some hypertensive patients, with no apparent pre-existing renal disease have developed increases in blood urea and creatinine when enalapril has been given concurrently with a diuretic. Dosage reduction of enalapril and/or discontinuation of the diuretic may be required. This situation should raise the possibility of underlying renal artery stenosis (see under renovascular hypertension).

Renovascular hypertension

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. Loss of renal function may occur with only mild changes in serum creatinine. In these patients, therapy should be initiated under close medical supervision with low doses, careful titration, and monitoring of renal function.

Kidney transplantation

There is no experience regarding the administration of enalapril in patients with recent kidney transplantation. Treatment with enalapril is therefore not recommended.

Hepatic failure

Rarely, ACE inhibitors have been associated with a syndrome that starts with cholestatic jaundice or hepatitis and progresses to fulminant hepatic necrosis and (sometimes) death. The mechanism of this syndrome is not understood. Patients receiving ACE inhibitors who develop jaundice or marked elevations of hepatic enzymes should discontinue the ACE inhibitor and receive appropriate medical follow-up.

Neutropenia/agranulocytosis

Neutropenia/agranulocytosis, thrombocytopenia and anemia have been reported in patients receiving ACE inhibitors. In patients with normal renal function and no other complicating factors, neutropenia occurs rarely. Enalapril should be used with extreme caution in patients with collagen vascular disease, immunosuppressant therapy, treatment with allopurinol or procainamide, or a combination of these complicating factors, especially if there is pre-existing impaired renal function. Some of these patients developed serious infections which in a few instances did not respond to intensive antibiotic therapy. If enalapril is used in such patients, periodic monitoring of white blood cell counts is advised and patients should be instructed to report any sign of infection.

Hypersensitivity/angioneurotic edema

Angioneurotic edema of the face, extremities, lips, tongue, glottis and/or larynx has been reported in patients treated with angiotensin converting enzyme inhibitors, including enalapril. This may occur at any time during treatment. In such cases, enalapril should be discontinued promptly and appropriate monitoring should be instituted to ensure complete resolution of symptoms prior to dismissing the patient. Even in those instances where swelling of only the tongue is involved, without respiratory distress, patients may require prolonged observation since treatment with antihistamines and corticosteroids may not be sufficient.

Very rarely, fatalities have been reported due to angioedema associated with laryngeal edema or tongue edema. Patients with involvement of the tongue, glottis or larynx are likely to experience airway obstruction, especially those with a history of airway surgery. Where there is involvement of the tongue, glottis or larynx, likely to cause airway obstruction, appropriate therapy, which may include subcutaneous epinephrine solution 1:1000 (0.3 ml to 0.5 ml) and/or measures to ensure a patent airway, should be administered promptly.

Black patients receiving ACE inhibitors have been reported to have a higher incidence of angioedema compared to non-blacks.

Patients with a history of angioedema unrelated to ACE inhibitor therapy may be at increased risk of angioedema while receiving an ACE inhibitor (see *Contraindications*).

Anaphylactoid reactions during hymenoptera desensitization

Rarely, patients receiving ACE inhibitors during desensitization with hymenoptera venom have experienced life-threatening anaphylactoid reactions. These reactions were avoided by temporarily withholding ACE-inhibitor therapy prior to each desensitization.

Anaphylactoid reactions during LDL apheresis

Rarely, patients receiving ACE inhibitors during low density lipoprotein (LDL)-apheresis with dextran sulfate have experienced life-threatening anaphylactoid reactions. These reactions were avoided by temporarily withholding ACE-inhibitor therapy prior to each apheresis.

Hemodialysis patients

Anaphylactoid reactions have been reported in patients dialyzed with high-flux membranes (e.g., AN 69®) and treated concomitantly with an ACE inhibitor. In these patients consideration should be given to using a different type of dialysis membrane or a different class of antihypertensive agent.

Hypoglycemia

Diabetic patients treated with oral antidiabetic agents or insulin starting an ACE inhibitor, should be told to closely monitor for

hypoglycemia, especially during the first month of combined use (see *Interaction with other medicaments*).

Cough
Cough has been reported with the use of ACE inhibitors. Characteristically, the cough is nonproductive, persistent and resolves after discontinuation of therapy. ACE inhibitor-induced cough should be considered as part of the differential diagnosis of cough.

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.

Hyperkalemia
Elevations in serum potassium have been observed in some patients treated with ACE inhibitors, including enalapril. Risk factors for the development of hyperkalemia include those with renal insufficiency, worsening of renal function, age (> 70 years), diabetes mellitus, intercurrent events, in particular dehydration, acute cardiac decompensation, metabolic acidosis and concomitant use of potassium-sparing diuretics (e.g., spironolactone, eplerenone, triamterene, or amiloride), potassium supplements or potassium-containing salt substitutes; or those patients taking other drugs associated with increases in serum potassium (e.g. heparin). The use of potassium supplements, potassium-sparing diuretics, or potassium-containing salt substitutes particularly in patients with impaired renal function may lead to a significant increase in serum potassium.

Hyperkalemia can cause serious, sometimes fatal arrhythmias. If concomitant use of enalapril and any of the above-mentioned agents is deemed appropriate, they should be used with caution and with frequent monitoring of serum potassium (see *Interactions with other medicament*).

Lithium
The combination of lithium and enalapril is generally not recommended (see *Interaction with other medicaments*).

Ethnic differences
As with other angiotensin converting enzyme inhibitors, enalapril is apparently less effective in lowering blood pressure in black people than in non-blacks, possibly because of a higher prevalence of low-renin states in the black hypertensive population.

Lactose
This medicinal product contains lactose and therefore should not be used by patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption. Contains less than 200 mg of lactose per tablet.

WARNING
ACE inhibitors have been shown to be strongly foetotoxic in animal studies. Recently available data indicate that ACE inhibitors can cause foetal and neonatal morbidity and mortality when administered to pregnant women. The use of these agents during pregnancy is not recommended.

Effects on ability to drive and use machines
When driving vehicles or operating machines it should be taken into account that occasionally dizziness or weariness may occur.

DRUG INTERACTIONS
Potassium sparing diuretics or potassium supplements
ACE inhibitors attenuate diuretic induced potassium loss. Potassium sparing diuretics (e.g. spironolactone, eplerenone, triamterene or amiloride), potassium supplements, or potassium-containing salt substitutes may lead to significant increases in serum potassium. If concomitant use is indicated because of demonstrated hypokalemia they should be used with caution and with frequent monitoring of serum potassium (see *Warning and Precautions*).

Diuretics (thiazide or loop diuretics)
Prior treatment with high dose diuretics may result in volume depletion and a risk of hypotension when initiating therapy with enalapril (see *Warning and Precautions*). The hypotensive effects can be reduced by discontinuation of the diuretic, by increasing volume or salt intake or by initiating therapy with a low dose of enalapril.

Other antihypertensive agents
Concomitant use of these agents may increase the hypotensive effects of enalapril. Concomitant use with nitroglycerine and other nitrates, or other vasodilators, may further reduce blood pressure.

Lithium
Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with ACE inhibitors. Concomitant use of thiazide diuretics may further increase lithium levels and enhance the risk of lithium toxicity with ACE inhibitors. Use of enalapril with lithium is not recommended, but if the combination proves necessary, careful monitoring of serum lithium levels should be performed (see *Warning and Precautions*).

Tricyclic antidepressants/antipsychotics/anesthetics/narcotics
Concomitant use of certain anesthetic medicinal products, tricyclic antidepressants and antipsychotics with ACE inhibitors may result in further reduction of blood pressure (see *Warning and Precautions*).

Non-steroidal anti-inflammatory drugs (NSAIDs)
Chronic administration of NSAIDs may reduce the antihypertensive effect of an ACE inhibitor. NSAIDs (including COX-2 inhibitors) and ACE inhibitors exert an additive effect on the increase in serum potassium, and may result in a deterioration of renal function. These effects are usually reversible. Rarely, acute renal failure may occur, especially in patients with compromised renal function (such as the elderly or patients who are volume-depleted, including those on diuretic therapy). Patients should be adequately hydrated and consideration should be given to monitoring renal function after initiation of concomitant therapy, and periodically thereafter.

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

Sympathomimetics
Sympathomimetics may reduce the antihypertensive effects of ACE inhibitors.

Antidiabetics
Epidemiological studies have suggested that concomitant administration of ACE inhibitors and antidiabetic medicines (insulins, oral hypoglycemic agents) may cause an increased blood-glucose-lowering effect with risk of hypoglycemia. This phenomenon appeared to be more likely to occur during the first weeks of combined treatment and in patients with renal impairment (see *Warning and Precautions* and *Side effects*).

Alcohol
Alcohol enhances the hypotensive effect of ACE inhibitors.

Acetylsalicylic acid, thrombolytics and β-blockers
Enalapril can be safely administered concomitantly with acetylsalicylic acid (at cardiologic doses), thrombolytics and β-blockers.

Concomitant therapy with ACE inhibitor and angiotensin – receptor blocker.
It has been reported in the literature that in patients with established atherosclerotic disease, heart failure, or with diabetes with end organ damage, concomitant therapy with ACE inhibitor and angiotensin–receptor blocker, is associated with a higher frequency of hypotension, syncope, hyperkalaemia, and worsening renal function (including acute renal failure) as compared to use of a single renin-angiotensin-aldosterone system agent. Dual blockade (e.g, by combining an ACE-inhibitor with an angiotensin II receptor antagonist) should be limited to individually defined cases with close monitoring of renal function, potassium levels and blood pressure. Avoid use in patients with renal impairment (GFR <60ml/min/1.73m^2).

ROUTE OF ADMINISTRATION
For oral administration

RECOMMENDED DOSAGE
Since absorption of **Enahexal®** tablets is not affected by food, the tablets may be administered before, during or after meals.

Hypertension:
The usual initial dose is 5mg enalapril maleate in the morning. Unless normalization of the blood pressure is achieved by administration of this dose, the dosage can be increased to 10mg enalapril maleate per day. The time interval between the dosage increase should not be less than 3 weeks. The maintenance dose is 10mg enalapril maleate per day. The maximum dose is 2 X 20mg enalapril maleate per day.
In patients who are being treated with diuretics, it is recommended to discontinue the diuretics therapy prior to administration of **Enahexal®**. If this is not possible, then the initial dose of 2.5mg tablet of enalapril maleate should be administered under medical supervision.

Heart failure
The initial dose is 2.5mg tablet of enalapril maleate in the morning. The physician may increase the dosage only gradually depending on the patient's individual responsiveness to the therapy. The maintenance dose is 5 – 10mg enalapril maleate per day. The maximum dose of 20mg enalapril maleate per day should not be exceeded.
In patients treated with diuretics, the dosage should be reduced if possible before initiating treatment with **Enahexal®**.

Dosage for patients with moderately impaired renal function (creatinine clearance 30-60ml/min) and elderly patients (of more than 65 years of age)
The initial dose is 2.5mg enalapril maleate in the morning. The maintenance dose is 5 – 10mg of enalapril maleate per day. The maximum dose of 20mg enalapril maleate should not be exceeded.
Dosage in patients with severe renal function disorders (creatinine clearance less than 30ml/min) and dialysis
The initial dose is 2.5mg enalapril maleate per day. Haemodialysis patients take this dose after dialysis. The maintenance dose is 5mg of enalapril maleate per day. The maximum dose of 10mg enalapril maleate per day should not be exceeded.

SYMPTOMS & TREATMENT FOR 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 blockade of the renin-angiotensin system, and stupor. Symptoms associated with overdosage of ACE inhibitors may include circulatory shock, electrolyte disturbances, renal failure, hyperventilation, tachycardia, palpitations, bradycardia, dizziness, anxiety, and cough.
Serum enalaprilat levels 100- and 200-fold higher than usually seen after therapeutic doses have been reported after ingestion of 300 mg and 440 mg of enalapril, respectively.
The recommended treatment of overdosage is intravenous infusion of normal saline solution. If hypotension occurs, the patient should be placed in the shock position. If available, treatment with angiotensin II infusion and/or intravenous catecholamines may also be considered. If ingestion is recent, take measures aimed at eliminating enalapril maleate (e.g., emesis, gastric lavage, administration of absorbents, and sodium sulphate). Enalaprilat may be removed from the general circulation by hemodialysis (see Warning *and Precautions*). Pacemaker therapy is indicated for therapy-resistant bradycardia. Vital signs, serum electrolytes and creatinine concentrations should be monitored continuously.

PACKING / PACK SIZE
Enahexal® 5mg and **Enahexal® 20mg** tablets are packed in blister pack of 30, 50 & 100 tablets in a box.

STORAGE CONDITION, USER INSTRUCTION & PHARMACEUTICAL PRECAUTIONS
Do not store above 30 °C.
Keep out of the reach of children.
(Jauhi daripada kanak-kanak)

Shelf life: Please refer to the outer box label.

Revision date: May 2016

Manufactured by:
Salutas Pharma GmbH
Otto-von-Guericke-Allee 1, 39179 Barleben, Germany.

For:
HEXAL AG
Industriestraβe 25, 83607 Holzkirchen, Germany.
