APPROVED
Order of Ministry of
Health of Ukraine
13.07.2018 № 1309
Registration certificate
№ UA/8765/01/01
№ UA/8765/01/02
№ UA/8765/01/03

INSTRUCTION
for medical use

KLOSART®

Composition:
active substance: losartan;
1 tablet contains 25 mg, 50 mg, or 100 mg of losartan potassium;
excipients: microcrystalline cellulose, croscarmellose sodium, magnesium stearate, silica colloidal anhydrous, Opadry O3B 52014 yellow*.
*Opadry O3B 52014 yellow: yellow iron oxide (E 172), quinoline yellow (E 104), hydroxypropyl methylcellulose, polyethylene glycol, titanium dioxide (E 171).

Pharmaceutical form. Film-coated tablets.
Basic physico-chemical properties: round biconvex yellow film-coated tablets.

Pharmacotherapeutic group. Angiotensin II antagonists, plain.
ATC code C09C A01.

Pharmacological properties.
Pharmacodynamics.
Losartan is a synthetic oral angiotensin-II receptor (type AT_1) antagonist. Angiotensin II, a potent vasoconstrictor, is the primary active hormone of the renin-angiotensin system and an important determinant of the pathophysiology of hypertension. Angiotensin II binds to the AT_1 receptor found in many tissues (e.g., vascular smooth muscle, adrenal glands, kidneys, and the heart) and elicits several important biological effects, including vasoconstriction and the release of aldosterone. Angiotensin II also stimulates proliferation of smooth muscle cells.
Losartan selectively blocks the AT_1 receptor. *In vitro* and *in vivo* losartan and its pharmacologically active carboxylic acid metabolite E-3174 block all physiologically relevant effects of angiotensin II regardless of the source or route of its synthesis.
Losartan does not have an agonist effect nor does it block other hormone receptors or ion channels important in cardiovascular regulation. Furthermore, losartan does not inhibit ACE (kininase II), the enzyme that degrades bradykinin. Consequently, there is no potentiation of undesirable bradykinin-mediated effects.
During administration of losartan, removal of the angiotensin II negative feedback on renin secretion leads to increased plasma renin activity. Such increase in the activity leads to an increase in angiotensin II in plasma. Despite these increases, antihypertensive activity and suppression of plasma aldosterone concentrations are maintained, indicating effective angiotensin II receptor blockade. After discontinuation of losartan, plasma renin activity and angiotensin II values returned within 3 days to the baseline values.
Both losartan and its principal metabolite have a far greater affinity for the AT_1 receptor than for the AT_2 receptor. The active metabolite is 10–40 times more active than losartan (on a weight for weight basis).
Pharmacokinetics.

Absorption.
Following oral administration, losartan is well absorbed and undergoes first-pass metabolism, forming an active carboxylic acid metabolite and inactive metabolites. The systemic bioavailability of losartan tablets is approximately 33 %. Mean peak concentrations of losartan and its active metabolite are reached in 1 hour and in 3–4 hours, respectively.
Distribution.
Both losartan and its active metabolite are ≥ 99 % bound to plasma proteins, primarily to albumin. The volume of distribution of losartan is 34 litres.
Biotransformation.
Approximately 14 % of intravenously- or orally-administered losartan is converted to its active metabolite. Following intravenous and oral administration of ^{14}C-labelled losartan potassium, circulating plasma radioactivity is primarily attributed to losartan and its active metabolite. Minimal conversion of losartan to its active metabolite was seen in about 1 % of cases. In addition to the active metabolite, inactive metabolites are also formed.
Elimination.
Plasma clearance of losartan and its active metabolite is 600 ml/min and 50 ml/min, respectively. Renal clearance of losartan and its active metabolite is about 74 ml/min and 26 ml/min, respectively. When losartan is administered orally, about 4 % of the dose is excreted unchanged in the urine, and about 6 % of the dose is excreted in the urine as the active metabolite. The pharmacokinetics of losartan and its active metabolite are linear with oral losartan potassium doses up to 200 mg.
Following oral administration, plasma concentrations of losartan and its active metabolite decline polyexponentially with a terminal half-life of about 2 hours and 6–9 hours, respectively. During once-daily dosing with 100 mg, neither losartan nor its active metabolite accumulates significantly in plasma. Losartan and its metabolites are excreted both in bile and in urine. Following an oral dose/intravenous administration of ^{14}C-labelled losartan, about 35 %/43 % of the radiolabeled medicinal product was recovered in the urine and 58 %/50 % in the feces.
Special patient groups.
Elderly patients.
In elderly hypertensive patients the plasma concentrations of losartan and its active metabolite do not differ significantly from those found in young hypertensive patients.
Gender.
In female hypertensive patients the plasma levels of losartan were up to 2 times as high as in male hypertensive patients, while the plasma levels of the active metabolite did not differ between men and women.
Hepatic and renal impairment.
In patients with mild to moderate alcohol-induced hepatic cirrhosis, the plasma levels of losartan and its active metabolite following oral administration were respectively 5 and 1.7 times higher than in young male volunteers (see sections “Dosage and administration” and “Administration details”).
Plasma concentrations of losartan in patients with a creatinine clearance above 10 ml/min did not differ from those in patients with unchanged renal function. In patients with normal renal function, the area under the curve “concentration – time” (AUC) for losartan was about 2 times higher than in hemodialysis patients. The plasma concentrations of the active metabolite are not altered in patients with renal impairment or in hemodialysis patients. Neither losartan nor its active metabolite can be removed by hemodialysis.
Pharmacokinetics in children.
The active metabolite of losartan is formed in patients of all age groups. The pharmacokinetic parameters of losartan following oral administration in infants, preschool children, and school-age children were similar.
The pharmacokinetic parameters for the metabolite differed to a greater extent between the age groups. When comparing preschool children with adolescents, these differences were statistically significant. Exposure in infants and children under 2 years of age was comparatively high.

Clinical characteristics.
Indications.
- Treatment of essential hypertension in adults and in children over 6 years of age.

- Treatment of renal disease in adult patients with hypertension and type 2 diabetes mellitus with proteinuria ≥ 0.5 g/day as part of antihypertensive treatment (see sections "Pharmacological properties", "Contraindications" and "Administration details").
- Treatment of chronic heart failure in adult patients when treatment with angiotensin-converting enzyme (ACE) inhibitors is not considered suitable due to incompatibility, especially in case of cough, or is contraindicated. Patients with heart failure who have been stabilized with an ACE inhibitor should not be switched to treatment with losartan. The patients should have a left ventricular ejection fraction of ≤ 40 %, and should be clinically stable. Patients should also be on an established treatment regimen for chronic heart failure.
- Reduction in the risk of stroke in adult hypertensive patients with left ventricular hypertrophy documented by ECG.

Contraindications.
- Hypersensitivity to losartan or to any of the excipients of the medicinal product.
- 2nd and 3rd trimester of pregnancy (see sections "Administration details" and "Use during pregnancy or breastfeeding").
- Severe hepatic impairment.
- The concomitant use of losartan with aliskiren-containing medicinal products is contraindicated in patients with diabetes mellitus or renal impairment (GFR < 60 ml/min/1.73 m^2 [see section "Interaction with other medicinal products and other forms of interaction"]).

Interaction with other medicinal products and other forms of interaction.
Other antihypertensive agents may potentiate the hypotensive action of losartan. Concomitant use with other medicinal products which may induce hypotension as an adverse reaction (like tricyclic antidepressants, antipsychotics, baclofen, and amifostine) may increase the risk of hypotension.
Losartan is predominantly metabolized by cytochrome P450 (CYP) 2C9 to the active carboxy-acid metabolite. Fluconazole (CYP2C9 inhibitor) decreases the exposure to the active metabolite by approximately 50 %. It was found that concomitant treatment of losartan with rifampicin (inducer of metabolism enzymes) gave a 40 % reduction in plasma concentrations of the active metabolite. The clinical relevance of this effect is unknown. No difference in exposure was found with concomitant treatment with losartan together with fluvastatin (weak inhibitor of CYP2C9).
As with other medicinal products that block angiotensin II or its effects, concomitant use of other medicinal products which retain potassium (e.g. potassium-sparing diuretics: spironolactone, triamterene, amiloride) or may increase potassium levels (e.g. heparin, trimethoprim-containing medicinal products), potassium supplements or salt substitutes containing potassium may lead to increases in serum potassium. Co-administration of such drugs is not recommended.
Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with ACE inhibitors. Very rare cases of such interaction have also been reported with angiotensin II receptor blockers. Co-administration of lithium and losartan should be undertaken with caution. If this combination proves essential, monitoring of serum lithium levels is recommended during concomitant use of these medicinal products.
When angiotensin II antagonists are administered simultaneously with non-steroidal anti-inflammatory drugs (NSAIDs; e.g. selective cyclooxygenase-2 (COX-2) inhibitors, acetylsalicylic acid at anti-inflammatory doses, non-selective NSAIDs), attenuation of the antihypertensive effect may occur. Concomitant use of angiotensin II antagonists or diuretics with NSAIDs may lead to an increased risk of deterioration of renal function, including possible acute renal failure, as well as to an increase in serum potassium, especially in patients with pre-existing impaired renal function. This combination should be administered with caution, especially in elderly patients. Patients should be adequately hydrated and consideration should be given to monitoring renal function after initiation of concomitant therapy, as well as periodically during treatment.
There are data indicating that dual blockade of the renin-angiotensin-aldosterone system (RAAS) through the combined use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren is associated with a higher frequency of adverse events such as hypotension, hyperkalemia, and decreased renal function (including

acute renal failure) compared to the use of a single RAAS-acting agent (see sections “Contraindications” and “Administration details”).
Grapefruit juice contains components that inhibit CYP450 enzymes and may lower the concentration of the active metabolite of losartan which may reduce the therapeutic effect. Consumption of grapefruit juice should be avoided while taking tablets that contain losartan.

Administration details.
Hypersensitivity.
Angioedema.
Patients with a history of angioedema (swelling of the face, lips, throat, and/or tongue) should be closely monitored (see section “Adverse reactions”.
Hypotension/fluid-electrolyte imbalance.
Symptomatic hypotension, especially after the first dose of the medicinal product and after increasing its dose, may occur in patients who are volume- and/or sodium-depleted by vigorous diuretic therapy, dietary salt restriction, diarrhea or vomiting. Such conditions should be corrected prior to administration of losartan, or a lower starting dose of the medicinal product should be used (see section “Dosage and administration”). These recommendations also apply to children 6 to 18 years of age.
Electrolyte imbalance.
Electrolyte imbalances are common in patients with renal impairment (with or without diabetes mellitus), and should be addressed. In a clinical study conducted in type 2 diabetic patients with nephropathy, the incidence of hyperkalemia was higher in patients treated with losartan as compared to those treated with placebo (see section “Adverse reactions”). Therefore, plasma potassium concentrations as well as creatinine clearance values should be closely monitored, especially in patients with heart failure and a creatinine clearance between 30–50 ml/min.
Concomitant use of potassium-sparing diuretics, potassium supplements, potassium-containing salt substitutes, or other medicinal products that may increase serum potassium concentrations (e.g., trimethoprim-containing medicinal products) with losartan is not recommended (see section “Interaction with other medicinal products and other forms of interaction”).
Hepatic impairment.
Since pharmacokinetic data demonstrate significantly increased plasma concentrations of losartan in cirrhotic patients, dose reduction should be considered in patients with a history of hepatic impairment. There is no therapeutic experience with losartan in patients with severe hepatic impairment, therefore losartan must not be administered in such patients (see sections “Dosage and administration”, “Contraindications” and “Pharmacological properties”).
Losartan is not recommended for use in children with hepatic impairment (see section “Administration details”).
Renal impairment.
Changes in renal function including renal failure have been reported and were associated with the inhibition of the renin-angiotensin system (in particular, in patients whose renal function is dependent on the RAAS, such as those with severe cardiac insufficiency or pre-existing renal dysfunction).
Medicinal products that affect the RAAS may cause an increase in blood urea and serum creatinine in patients with bilateral renal artery stenosis or stenosis of the artery to a solitary kidney. These changes in renal function may be reversible upon discontinuation of therapy. Losartan should be used with caution in patients with bilateral renal artery stenosis or stenosis of the artery to a solitary kidney.
Use in children with renal impairment
Losartan is not recommended in children with GFR < 30 ml/min/1.73 m^2 as no respective data regarding use are available (see section “Dosage and administration”).
Renal function should be regularly monitored during treatment with losartan as it may deteriorate. This applies particularly when losartan is given in the presence of other conditions (fever, dehydration) likely to impair renal function.
Concomitant use of losartan and ACE-inhibitors impairs renal function, therefore, the use of this combination is not recommended (see section “Interaction with other medicinal products and other forms of interaction”).
Renal transplantation.

There is no experience regarding the safety of using losartan in patients with recent kidney transplantation.
Primary hyperaldosteronism.
Patients with primary hyperaldosteronism generally will not respond to medicinal products acting through inhibition of the renin-angiotensin system. Therefore, the use of losartan is not recommended in this group of patients.
Coronary heart disease and cerebrovascular disease.
As with any antihypertensive medicinal products, excessive decrease of blood pressure in patients with ischemic cardiovascular and cerebrovascular disease could result in myocardial infarction or stroke.
Heart failure.
As with other medicinal products affecting the RAAS, there is a risk of severe arterial hypotension, and (often acute) renal impairment in patients with heart failure, with or without renal impairment.
There is insufficient therapeutic experience with losartan in patients with heart failure and concomitant severe renal impairment, in patients with severe heart failure (NYHA class IV) as well as in patients with heart failure and symptomatic life-threatening cardiac arrhythmias. Therefore, losartan should be used with caution in these patient groups. The combination of losartan with β-blockers should be used with caution.
Aortic and mitral valve stenosis, obstructive hypertrophic cardiomyopathy.
As with other vasodilators, special caution should be exercised when prescribing losartan in patients suffering from aortic or mitral valve stenosis, or obstructive hypertrophic cardiomyopathy.
Pregnancy.
Losartan should not be initiated during pregnancy. Unless continued losartan therapy is considered essential, patients planning pregnancy should be changed to alternative anti-hypertensive treatments which have an established safety profile for use in pregnancy. When pregnancy is diagnosed, treatment with losartan should be stopped immediately, and, if appropriate, alternative therapy should be initiated (see sections “Contraindications” and “Use during pregnancy or breastfeeding”).
Other precautions.
As observed for ACE inhibitors, losartan and other angiotensin antagonists are apparently less effective in black patients than in non-black patients, possibly because of higher prevalence of low-renin states in the black hypertensive population.
Dual blockade of the renin-angiotensin-aldosterone system (RAAS).
There is evidence that the concomitant use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren increases the risk of hypotension, hyperkalemia, and decreases renal function (including acute renal failure). Dual blockade of RAAS through the combined use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren is therefore not recommended (see section “Interaction with other medicinal products and other forms of interaction”).
If dual blockade of RAAS is considered absolutely necessary, this should only occur under specialist supervision and subject to close monitoring of renal function, electrolytes and blood pressure.
ACE-inhibitors and angiotensin II receptor blockers should not be used concomitantly in patients with diabetic nephropathy.
Intestinal angioedema.
Intestinal angioedema has been reported in patients treated with angiotensin II receptor antagonists, including losartan (see section “Adverse reactions”). These patients presented with abdominal pain, nausea, vomiting and diarrhoea. Symptoms resolved after discontinuation of angiotensin II receptor antagonists. If intestinal angioedema is diagnosed, losartan should be discontinued and appropriate monitoring should be initiated until complete resolution of symptoms has occurred.
Excipients.
This medicinal product contains less than 1 mmol (23 mg) of sodium/dose of the drug, i.e., is essentially sodium-free.

Use during pregnancy or breastfeeding.
Pregnancy.
The use of losartan is not recommended during the first trimester of pregnancy (see section “Administration details”). The use of losartan is contraindicated during the 2nd and 3rd trimester of pregnancy (see sections “Contraindications” and “Administration details”).

Epidemiological evidence regarding the risk of teratogenicity following exposure to ACE inhibitors during the first trimester of pregnancy has not been conclusive; however, a small increase in risk cannot be excluded. As there is no controlled epidemiological data regarding the risk associated with the use of angiotensin II receptor antagonists (AIIRAs), similar risks may exist for this class of medicinal products. Unless continued AIIRA therapy is considered essential, patients planning pregnancy should be changed to alternative anti-hypertensive treatments which have an established safety profile for use in pregnancy. When pregnancy is diagnosed, treatment with losartan should be stopped immediately and, if appropriate, alternative therapy should be started.
The use of AIIRA therapy during the 2nd and 3d trimesters of pregnancy is known to induce fetotoxicity (decreased renal function, oligohydramnios, skull ossification retardation) and neonatal toxicity (renal failure, hypotension, hyperkalemia).
Should exposure to losartan have occurred from the 2nd trimester of pregnancy, ultrasound examination of the child's renal function and skull is recommended.
Infants whose mothers have taken losartan during pregnancy should be closely observed for hypotension (see sections "Contraindications" and "Administration details").
Breastfeeding.
Because no information is available regarding the use of losartan during breastfeeding, it is not recommended to prescribe this medicinal product. Alternative treatments with medicinal products with better established safety profiles during breastfeeding are preferable, especially while nursing a newborn or preterm infant.

Effect on reaction rate when driving motor transport or using other mechanisms.
There is no data regarding the effects on the ability to drive motor transport or use other mechanisms. However, it must be borne in mind that such adverse reactions as dizziness or drowsiness may occur, in particular during initiation of treatment or when the dose of the medicinal product is increased.

Dosage and administration.
Tablets may be administered with or without food, with 1 glass of water.
Arterial hypertension.
The usual starting and maintenance dose is 50 mg of the medicinal product once daily for most patients. The maximum antihypertensive effect is attained 3–6 weeks after initiation of the medicinal product. Some patients may receive an additional benefit by increasing the dose of the medicinal product to 100 mg once daily (in the morning).
Losartan may be administered with other antihypertensive medicinal products, especially with diuretics (e.g. hydrochlorothiazide) (see section "Interaction with other medicinal products and other forms of interaction").
Patients with hypertension and type II diabetes mellitus (proteinuria ≥ 0.5 g/day).
The usual starting dose is 50 mg once daily. The dose may be increased to 100 mg once daily based on blood pressure response from one month onwards after initiation of therapy. Losartan may be administered with other antihypertensive medicinal products (e.g. diuretics, calcium channel blockers, α- or β-blockers, and centrally acting medicinal products) (see section "Administration details") as well as with insulin and with other commonly used hypoglycemic agents (e.g. sulfonylureas, glitazones and glucosidase inhibitors).
Heart failure.
The usual starting dose of losartan in patients with heart failure is 12.5 mg once daily. The dose should generally be titrated at weekly intervals (i.e. 12.5 mg daily, 25 mg daily, 50 mg daily, 100 mg daily, up to a maximum dose of 150 mg once daily) as tolerated by the patient.
Reduction of the risk of stroke in hypertensive patients with left ventricular hypertrophy documented by ECG.
The usual starting dose is 50 mg of losartan once daily. A low dose of hydrochlorothiazide should be added and/or the dose of losartan should be increased to 100 mg once daily based on changes in the blood pressure.
Special patient groups.
Use in patients with intravascular volume depletion.
For patients with intravascular volume depletion (e.g. those treated with high-dose diuretics), the feasibility of using the medicinal product at a starting dose of 25 mg once daily should be considered.

Use in patients with renal impairment and hemodialysis patients.
No initial dose adjustment is necessary in patients with renal impairment and in hemodialysis patients.
Use in patients with hepatic impairment.
A lower dose of the medicinal product should be considered for patients with a history of hepatic impairment. There is no therapeutic experience in patients with severe hepatic impairment, therefore, losartan is contraindicated in this group of patients (see sections "Contraindications", "Administration details").

Children.
Use in children from 6 months to 6 years of age.
The safety and efficacy of the medicinal product in children from 6 months to 6 years of age have not been established. Currently available data are described in section "Pharmacological properties", but no recommendations regarding the posology of the medicinal product can be made.
Use in children from 6 to 18 years of age.
For patients who can swallow tablets, and with a body weight over 20 kg and under 50 kg, the recommended dose is 25 mg once daily. In exceptional cases the dose can be increased to a maximum of 50 mg once daily. The dosage should be adjusted according to the blood pressure response.
In patients with a body weight over 50 kg, the usual single dose is 50 mg once daily. In exceptional cases the dose can be adjusted to a maximum of 100 mg once daily. Doses above 1.4 mg/kg (or in excess of 100 mg) daily have not been studied in children.
Losartan is not recommended for use in children under 6 years of age, as data regarding the use of the medicinal product in this patient group is insufficient.
Losartan is not recommended in children with glomerular filtration rate < 30 ml/min/1.73 m^2, as no respective data are available regarding its use (see section "Administration details").
Losartan is also not recommended in children with hepatic impairment.
Use in elderly patients.
Although consideration should be given to prescribing the medicinal product at a starting dose of 25 mg in patients over 75 years of age, starting dose adjustment is not usually necessary for elderly patients.

Children.
Losartan is not recommended in children under 6 years of age as data regarding this group of patients is limited.

Overdose.
Symptoms.
Limited data are available regarding losartan overdose. The most likely manifestations of overdose are hypotension and tachycardia; bradycardia could occur as a result of parasympathetic (vagal) stimulation.
Treatment.
If symptomatic hypotension should occur, supportive treatment should be used.
Treatment depends on the time since the intake of the medicinal product as well as the nature and severity of symptoms.
Stabilization of the cardiovascular system should be given priority. After oral intake of the medicinal product, administration of a sufficient dose of activated charcoal is indicated. Afterwards, vital parameters should be frequently monitored closely and corrected if necessary. Neither losartan nor the active metabolites can be removed by hemodialysis.

Adverse reactions.
The most commonly reported adverse reaction was dizziness.
The frequency of adverse reactions listed below is established as follows: very common: ≥ 1/10; common: from ≥ 1/100 to < 1/10; uncommon: from ≥ 1/1000 to ≤ 1/100; rare: from ≥ 1/10000 to ≤ 1/1000; very rare: ≤ 1/10000; unknown (cannot be established from the available data).

Table.
The frequency of adverse reactions identified from placebo-controlled clinical studies and post-marketing experience with losartan

Adverse reaction	Frequency of adverse reactions by indication				Other
	Hypertension	Hypertensive patients with left-ventricular hypertrophy	Chronic heart failure	Hypertension and type 2 diabetes mellitus with renal disease	Post-marketing experience with the drug
Blood and lymphatic system disorders					
anemia			common		frequency unknown
thrombocytopenia					frequency unknown
Immune system disorders					
hypersensitivity reactions, anaphylactic reactions, angioedema*, and vasculitis**					rare
Psychiatric disorders					
depression					frequency unknown
Nervous system disorders					
dizziness	common	common	common	common	
somnolence	uncommon				
headache	uncommon		uncommon		
sleep disorders	uncommon				
paresthesia			rare		
migraine					frequency unknown
dysgeusia					frequency unknown
Ear and labyrinth disorders					
vertigo	common	common			
tinnitus/sonitus					frequency unknown
Cardiac disorders					
palpitations	uncommon				
angina pectoris	uncommon				
syncope			rare		
atrial fibrillation			rare		
cerebrovascular accident			rare		
Vascular disorders					
(orthostatic) hypotension (including dose-dependent orthostatic effects) ‖	uncommon		common	common	
Respiratory, thoracic and mediastinal disorders					
dyspnea			uncommon		
cough			uncommon		frequency unknown
Gastrointestinal disorders					
abdominal pain	uncommon				

constipation	uncommon				
diarrhea			uncommon		frequency unknown
nausea			uncommon		
vomiting			uncommon		
intestinal angioedema					rare
Hepatobiliary disorders					
pancreatitis					frequency unknown
hepatitis					rare
liver function abnormalities					frequency unknown
Skin and subcutaneous tissue disorders					
urticaria			uncommon		frequency unknown
pruritus			uncommon		frequency unknown
rash	uncommon		uncommon		frequency unknown
photosensitivity					frequency unknown
Musculoskeletal and connective tissue disorders					
myalgia					frequency unknown
arthralgia					frequency unknown
rhabdomyolysis					frequency unknown
Renal and urinary disorders					
renal impairment			common		
renal failure			common		
Reproductive system and breast disorders					
erectile dysfunction / impotence					frequency unknown
General disorders and administration site conditions					
asthenia	uncommon	common	uncommon	common	
increased fatigability	uncommon	common	uncommon	common	
edema	uncommon				
malaise					frequency unknown
Investigations					
hyperkalemia	common		uncommon †	common ‡	
increased alanine aminotransferase (ALT)§	rare				
increase in blood urea, serum creatinine, and serum potassium			common		

hyponatremia					frequency unknown
hypoglycemia				common	

***** Including swelling of the larynx, glottis, face, lips, pharynx, and/or tongue (causing airway obstruction); in some of these patients angioedema had been reported in the past in connection with the administration of other medicinal products, including ACE inhibitors.
****** Including Henoch–Schonlein purpura.
‖ Especially in patients with intravascular hypovolemia, e.g. patients with severe heart failure or patients undergoing treatment with high dose diuretics.
†This adverse reaction was common in patients who received 150 mg losartan instead of 50 mg.
‡In a clinical study conducted in type 2 diabetic patients with nephropathy, hyperkalemia (> 5.5 mmol/l) was observed in 9.9 % of patients treated with losartan tablets and in 3.4 % of patients treated with placebo.
§ This adverse reaction usually resolved upon discontinuation of losartan.

The following additional adverse reactions occurred more frequently in patients who received losartan than those receiving placebo (frequency unknown): back pain, urinary tract infection, and flu-like symptoms.
Renal and urinary disorders.
As a consequence of RAAS inhibition, changes in renal function including renal failure have been reported in patients at an increased risk; these changes in renal function may be reversible upon discontinuation of the medicinal product (see section "Administration details").
Children.
The adverse reaction profile for children appears to be similar to that seen in adult patients. Data regarding adverse reactions in children are limited.
Reporting of suspected adverse reactions
Reporting adverse reactions after the registration of the medicinal product is of great importance. It allows to monitor the correlation of the benefits and risks related to the use of the medicinal product. Healthcare and pharmaceutical professionals, as well as patients or their legal representatives are asked to report any suspected adverse reactions and lack of efficacy of the medicinal product through the Automated pharmacovigilance information system available at: https://aisf.dec.gov.ua.

Shelf life.
3 years.

Storage conditions.
Store in the original package at a temperature not more than 25 °C.
Keep out of reach of children.

Package.
25 mg, 50 mg tablets.
14 tablets are in a blister; 1, 2 or 6 blisters are in a carton box.
100 mg tablets.
14 tablets are in a blister; 1, 2 or 6 blisters are in a carton box.
10 tablets are in a blister; 3, 9 or 10 blisters are in a carton box.

Conditions of supply.
By prescription.

Manufacturer.
LLC "KUSUM PHARM" (for 25 mg, 50 mg, 100 mg dosages).

Address of manufacturer and manufacturing site.
40020, Ukraine, Sumy region, Sumy, Skryabina Str. 54.

or

Manufacturer.
KUSUM HEALTHCARE PVT LTD (for 50 mg, 100 mg dosages).

Address of manufacturer and manufacturing site.
SP-289 (A), RIICO Industrial area, Chopanki, Bhiwadi, Dist. Alwar (Rajasthan), India.

or

Manufacturer.
LLC “GLADPHARM LLC” (for 50 mg, 100 mg dosages).

Address of manufacturer and manufacturing site.
40020, Ukraine, Sumy region, Sumy, Davydovskoho Hryhoriia Str., 54.

Last revision date. 12.06.2025