APPROVED
The Order of Ministry
of Health of Ukraine
10.12.2020 № 2854
Registration certificate
№ UA/18487/01/01
№ UA/18487/01/02
№ UA/18487/01/03

AMENDED
The Order of Ministry of
Health of Ukraine
03.08.2023 № 1399

INSTRUCTION
for medical use

TIUREX®

Composition:
active substance: hydrochlorothiazide;
1 tablet contains: 12.5 mg or 25 mg, or 50 mg of hydrochlorothiazide;
excipients: lactose monohydrate, microcrystalline cellulose, hydroxypropyl cellulose, iron oxide red (E 172), iron oxide yellow (E 172), magnesium stearate.

Pharmaceutical form. Tablets.
Main physical and chemical properties:
tablets of 12.5 mg; 25 mg: beige or light beige tablets, round, flat, with possible red speckles, with a score line on one side and smooth on the other side;
tablets of 50 mg: beige or light beige tablets, round, biconvex, with possible red speckles, smooth on both sides.

Pharmacotherapeutic group. Low-ceiling diuretics, thiazide group. Plain thiazide diuretics. Hydrochlorothiazide. ATC code C03A A03.

Pharmacological properties.
Pharmacodynamics.
Hydrochlorothiazide (HCTZ), an active ingredient of the medicinal product Tiurex®, belongs to the group of benzothiadiazine (thiazide) diuretics that increase urination by enhancing the excretion of electrolytes and water osmotically associated with them. HCTZ inhibits the reabsorption of Na^+ ions mainly in the distal tubules of nephrons, due to which up to 15% of sodium filtered by the kidneys can be excreted. The amounts of excreted Cl^- and Na^+ ions are approximately equivalent. HCTZ increases the excretion of K^+ ions by increasing their secretion in the distal tubules and collecting ducts of the nephrons as well.
High doses of HCTZ can enhance the excretion of bicarbonates by suppressing the activity of carbonic anhydrase, which is accompanied with urine alkalinization. Changes in urine pH do not significantly affect the diuretic and natriuretic effect of HCTZ. Initially, the glomerular filtration rate decreases slightly. With prolonged therapy with HCTZ, hypercalcemia may occur due to a decrease in renal excretion of Ca^{2+} ions.
Hypertension

In hypertensive patients, HCTZ exhibits an antihypertensive effect, the mechanism of which is not yet sufficiently clarified. There is an assumption that the effect of thiazide diuretics on reducing vascular tone is due to a decrease in sodium concentrations in the vessel wall and, consequently, a decrease in the response to norepinephrine. HCTZ is almost ineffective in patients with chronic renal failure (creatinine clearance below 30 ml/min and/or serum creatinine above 1.8 mg/100 ml). HCTZ has an antidiuretic effect in patients with renal and ADH-sensitive diabetes insipidus. Depending on the dose taken, the diuretic effect of HCTZ can persist for 10–12 hours, the antihypertensive effect – up to 24 hours.

Non-melanoma skin cancer (NMSC)

The results in two pharmacoepidemiological studies based on the data of the Danish National Cancer Registry, have shown a cumulative dose-dependent association between HCTZ and basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). One study included a population of 71 533 patients with BCC and 8 629 patients with SCC, who were compared with 1 430 833 and 172 462 patients from the control population, respectively. The use of high HCTZ doses (≥50,000 mg cumulative) was associated with an adjusted odds ratio (OR) of 1.29 (95% confidence interval (CI): 1.23-1.35) for BCC and 3.98 (95 % CI: 3.68-4.31) for SCC. A clear cumulative dose-dependent association was observed for both BCC and SCC. Another study showed a possible association between lip cancer (SCC) and exposure to HCTZ: 633 cases of lip-cancer (SCC) were matched with 63 067 patients from the control population, using a risk-set sampling strategy. A cumulative dose-dependent association was demonstrated with an adjusted OR 2.1 (95% CI: 1.7-2.6) increasing to an OR of 3.9 (3.0-4.9) for high doses (~25,000 mg) and an OR of 7.7 (5.7-10.5) for the highest cumulative dose (~100,000 mg) (see section “Administration details”).

Pharmacokinetics.

Absorption

After oral administration, approximately 80 % of HCTZ is absorbed from the gastrointestinal tract (GIT). The absolute bioavailability is approximately 70 %. The maximum plasma concentration is reached after 2–5 hours.

Distribution

The plasma protein binding of HCTZ is 64 %, the relative volume of distribution is 0.5-1.1 l/kg.

Elimination

More than 95% of HCTZ is eliminated by the kidneys unchanged in healthy volunteers. The elimination half-life with normal renal function is 6–8 hours. In case of impaired renal function, it is prolonged (up to 20 hours in patients with end-stage renal disease).

The diuretic effect develops within 1–2 hours.

Clinical particulars.

Indications.

- Hypertension.
- Cardiogenic, hepatogenic, nephrogenic edema.
- Hepatogenic edema, most often in combination with potassium-sparing diuretics.

Contraindications.

- Hypersensitivity to HCTZ, other thiazides, sulfonamides or any other drug component.
- Severe renal impairment (creatinine clearance less than 30 ml/min and/or serum creatinine greater than 1.8 mg/100ml).
- Anuria.
- Acute glomerulonephritis.
- Hepatic coma or precoma.
- Refractory hypokalemia, hyponatremia, or hypercalcemia.
- Hypovolemia.
- Symptomatic hyperuricemia/gout.

- Gestational hypertension.

Interaction with other medicinal products and other types of interaction.

Other drugs that enhance the antihypertensive effect of HCTZ

The antihypertensive effect of HCTZ may be enhanced by other diuretics, antihypertensive drugs, guanethidine, methyldopa, calcium antagonists, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), direct renin inhibitors, β-blockers, nitrates, barbiturates, phenothiazine derivatives, tricyclic antidepressants, vasodilators and alcohol.

ACE inhibitors

In patients who take HCTZ concurrently with ACE inhibitors (e.g. captopril), at the beginning of therapy there is a risk of a sudden drop in blood pressure and impaired renal function. To prevent the possibility of hypotension at the beginning of therapy, diuretics should be discontinued 2–3 days before the start of therapy with ACE inhibitors.

Acetylsalicylic acid and other non-steroidal anti-inflammatory drugs (NSAIDs)

Salicylates and other NSAIDs (e.g. indomethacin) may reduce the antihypertensive and diuretic effect of HCTZ. In case of administration of high doses of salicylates, their toxic effect on the central nervous system may be increased. Concomitant use of NSAIDs can cause acute renal failure in patients who developed hypovolemia during treatment with HCTZ.

Allopurinol

Co-administration of thiazides (including HCTZ) and allopurinol may increase the incidence of hypersensitivity reactions to allopurinol.

Amantadine

The co-administration of thiazides and amantadine may increase the risk of adverse reactions, associated with amantadine.

β-blockers

There is an increased risk of developing hyperglycemia when HCTZ is co-administered with β-blockers.

Catecholamines, hypoglycemic and hyperuricemic drugs

HCTZ can weaken the effect of noradrenaline, adrenaline, insulin, oral hypoglycemic and hyperuricemic drugs. Therefore, dosage adjustment of insulin or oral hypoglycemic drugs may be required.

Cardiac glycosides

Myocardial sensitivity to cardiac glycosides and, respectively, the risk of adverse reactions associated with them increases in case of the development of hypokalemia and/or hypomagnesemia associated with their concomitant use with HCTZ.

Other drugs that lower plasma potassium levels

Concomitant administration of HCTZ and loop diuretics (for example, furosemide), glucocorticoids, adrenocorticotropic hormone (ACTH), carbenoxolone, penicillin G, salicylates, amphotericin B, antiarrhythmic drugs or laxatives can cause increased potassium losses.

Antidepressants, antipsychotic and antiepileptic drugs

Concomitant administration of HCTZ with antidepressants, antipsychotic or antiepileptic drugs can cause hyponatremia due to increased sodium loss. Caution should be exercised in case of long-term concomitant use of these drugs.

Cytostatics

Concomitant use of thiazide diuretics and cytostatics (e.g cyclophosphamide, fluorouracil, methotrexate) may reduce renal excretion of cytostatics and, respectively, increase their toxic effect on the bone marrow (especially the risk of granulocytopenia increases).

Drugs affecting gastrointestinal motility

Anticholinergic agents (e.g. atropine, biperiden) may increase the bioavailability of thiazide-type diuretics by decreasing gastrointestinal motility and gastric emptying rate. Conversely, prokinetic agents (e.g, cisapride) may reduce the bioavailability of thiazide diuretics.

Lithium

Since diuretics increase plasma lithium levels (as a result of its decreased renal clearance), the concomitant administration of HCTZ with lithium preparations may increase their cardio- and neurotoxicity. Plasma lithium levels should be controlled if it is required to use this combination. Diuretics may have a paradoxical antidiuretic effect in patients with lithium-induced polyuria.

Curariform muscle relaxants

HCTZ can potentiate or prolong the effect of curariform muscle relaxants. The anesthesiologist should be informed about HCTZ administration if it cannot be discontinued before the use of curariform muscle relaxants.

Bile acid sequestrants

HCTZ absorption is decreased when it is co-administered with cholestyramine or colestipol. HCTZ should be administered at least 4 hours before or 4-6 hours after the administration of drugs of this group.

Vitamin D

Concomitant administration of HCTZ with vitamin D may decrease urinary calcium excretion and lead to hypercalcemia, respectively.

Calcium salts

Concomitant administration of HCTZ with calcium salts may result in hypercalcemia associated with increased calcium reuptake in the renal tubules.

Ciclosporin

Concomitant administration of HCTZ and ciclosporin can increase the risk of hyperuricemia (gout) and associated complications.

Diazoxide

Thiazides can potentiate the hyperglycemic action of diazoxide.

Methyldopa

There is a reported case of red blood cell hemolysis associated with the effect of HCTZ antibodies that were formed as a result of its co-administration with methyldopa.

Adrenergic amines

HCTZ can decrease the effect of adrenergic amines (e.g. noradrenaline). However, clinical significance of this effect does not preclude its use.

Administration details.

Pseudo-Bartter's syndrome

Chronic HCTZ abuse can cause Pseudo-Bartter's syndrome accompanied by edemas that result from increased renin concentrations associated with secondary hyperaldosteronism.

Fluid and electrolyte balance

Thiazide diuretics may cause or aggravate hypokalemia. They should be administered with caution in patients with diseases associated with significant potassium loss (e.g. salt-losing nephropathy or renal failure of prerenal (cardiogenic) genesis). It is recommended to correct hypokalemia and possible hypomagnesemia prior to the initiation of treatment with thiazide diuretics. Serum potassium and magnesium levels should be regularly checked. All patients receiving thiazide diuretics should be monitored for the electrolyte balance, in particular serum potassium levels.

Potassium excretion during treatment with thiazide diuretics including HCTZ is dose-dependent. In case of long-term treatment, serum potassium levels should be checked prior to and 3 – 4 weeks following the initiation of treatment. Later on, serum potassium levels should be checked regularly, excluding cases with the presence of other factors that influence this indicator (e.g. vomiting, diarrhea, changes in renal function).

Oral administration of potassium supplements (e.g. KCl) in individually adjusted doses can be applied in patients who receive cardiac glycosides (see section "Interaction with other medicinal products and other types of interaction"), have signs of ischemic heart disease (if they are not additionally receiving ACE inhibitors), receive high doses of β-agonists, and all patients with serum potassium concentrations under 3,0 mmol/l. HCTZ may be combined with potassium-sparing diuretics in case of intolerance to oral potassium supplements

In any case, the potassium balance should be supported or normalized during combined therapy with potassium supplements. HCTZ should be discontinued in case of hypokalemia symptoms (e.g. muscle weakness, pareses or ECG changes).
Patients receiving additional treatment with ACE inhibitors, ARBs or direct renin inhibitors should avoid concomitant treatment with HCTZ and potassium supplements or potassium-sparing diuretics.
Thiazide diuretics may cause or aggravate existing hyponatremia. In rare cases, patients with significantly lowered serum sodium levels and/or dehydration (e.g. in individuals following high doses of diuretics) develop symptomatic hypotension following HCTZ treatment. There have been isolated reports of hyponatremia with neurological symptoms (nausea, progressive disorientation, apathy). Thiazide diuretics should only be administered after correcting serum sodium levels and/or dehydration. Otherwise, treatment should only be initiated under close medical supervision. Regular serum sodium monitoring is advised.
Serum electrolyte monitoring is particularly indicated in patients with ascites associated with hepatic cirrhosis or edemas associated with nephrotic syndrome. In case of nephrotic syndrome, HCTZ should be administered under strict supervision and only in patients with normal serum potassium levels and no signs of hypovolemia or pronounced hypoalbuminemia.
Like other diuretics, HCTZ can increase serum uric acid concentrations due to its reduced urinary excretion and, consequently, cause or aggravate existing hyperuricemia that may provoke gout attacks in predisposed patients.
Metabolic effects
Thiazide diuretics, including HCTZ, may affect glucose tolerance as well as increase serum cholesterol and triglyceride concentrations.
Thiazide diuretics decrease urinary calcium excretion and may cause a slight elevation of calcium levels in the absence of known disorders of calcium metabolism. HCTZ should be used with caution in patients with hypercalcemia since it may increase serum calcium levels. Pronounced hypercalcemia ≥12 mg/dl or hypercalcemia which is not resolved by discontinuation of thiazides may indicate the presence of a hypercalcemia process not associated with thiazides.
In a few patients on prolonged thiazide therapy, pathological changes in the parathyroid gland associated with hypercalcemia and hypophosphatemia have been observed. Further examination is required in case of hypercalcemia.
During HCTZ therapy, patients should have an adequate water intake and consume more potassium-rich products (i.e. bananas, vegetables, nuts).
Patients with renal impairment
HCTZ is contraindicated in patients with severe renal impairment (creatinine clearance less than 30 ml/min or serum creatinine concentrations more than 1,8 mg/100 ml) since it does not produce a diuretic effect and can lead to further deterioration of renal function. HCTZ can cause thiazide azotemia in patients with moderate renal impairment (creatinine clearance of 30-60 ml/min or serum creatinine concentrations more than 1.0-1.8 mg/100 ml). This category of patients should be regularly monitored for serum potassium, creatinine and uric acid concentrations. There is no experience of using HCTZ in patients following kidney transplantation.
Patients with hepatic impairment
Patients with mild and moderate hepatic impairment do not require initial HCTZ dose adjustment (see section “Pharmacological properties” and “Dosage and administration”). Using thiazides, like other diuretics, to treat ascites associated with hepatic cirrhosis may cause electrolyte imbalance, hepatic encephalopathy and hepatorenal syndrome. HCTZ should be used with extreme caution in patients with severe hepatic impairment.
Acute respiratory toxicity
Very rare severe cases of acute respiratory toxicity, including acute respiratory distress syndrome (ARDS), have been reported after HCTZ administration. Pulmonary edema typically develops within minutes to hours after HCTZ intake. At the onset, symptoms include dyspnea, fever, pulmonary deterioration and hypotension. If diagnosis of ARDS is suspected, the drug Tiurex® should be

withdrawn and appropriate treatment given. The drug Tiurex® should not be administered to patients who previously experienced ARDS following HCTZ intake.

Choroidal effusion, acute myopia and secondary angle-closure glaucoma.

HCTZ can cause an idiosyncratic reaction resulting in choroidal effusion with visual field defect, acute transient myopia and acute angle-closure glaucoma. Symptoms are characterized by acute onset of decreased visual acuity and/or ocular pain and typically occur within hours to weeks following the initiation of HCTZ treatment.

Untreated acute angle-closure glaucoma can lead to permanent vision loss. The primary treatment is to discontinue HCTZ as rapidly as possible. Prompt medical or surgical treatments may need to be considered if intraocular pressure remains uncontrolled. Risk factors for developing acute angle-closure glaucoma may include a history of sulfonamide or penicillin allergy.

Non-melanoma skin cancer (NMSC)

An increased risk of NMSC has been observed with an increasing cumulative dose of HCTZ in two pharmacoepidemiological studies (see section "Pharmacological properties"). The photosensitizing action of HCTZ could act as a possible mechanism for this condition.

Patients taking HCTZ alone or combined with other medicinal products should be informed of the risk of NMSC (especially in case of long-term administration) and advised to regularly check their skin and promptly report any new or changed skin lesions/moles as well as any suspicious lesions to the physician. The need for preventive measures such as limited exposure to sunlight and UV rays and, in case of exposure, adequate protection of skin, should be advised to the patients in order to minimize the risk of skin cancer. Suspicious skin lesions should be promptly examined, including histological examinations of biopsies. The use of HCTZ may also need to be reconsidered in patients with a history of NMSC (see section "Adverse reactions").

Particularly close monitoring is required in patients with:

- hypotension;
- cerebrovascular disease;
- ischemic heart disease.

Cerebrovascular insufficiency and ischemic heart disease

In patients with cerebrovascular insufficiency and ischemic heart disease HCTZ should be used only under close supervision.

Combination with antihypertensive drugs

The antihypertensive effect of ACE inhibitors, ARBs or direct renin inhibitors is potentiated by drugs that increase plasma renin activity (diuretics in particular).

Caution should be exercised when combining ACE inhibitors, ARBs or direct renin inhibitors with HCTZ, especially in patients with pronounced hyponatremia or dehydration.

Systemic lupus erythematosus

Thiazide diuretics have been associated with reports of activation of latent systemic lupus erythematosus.

Hypersensitivity reactions to HCTZ are more common in patients with allergy and asthma.

Professional sports

HCTZ administration can cause a positive reaction to tests carried out during doping control in athletes.

Elderly patients (over 65 years of age)

Patients over 65 years of age should be aware of the possibility of renal impairment.

Excipients.

The drug contains lactose monohydrate. In case of identified intolerance to some sugars, a healthcare professional should be consulted before taking the drug.

Use during pregnancy or breastfeeding.

Pregnancy.

There is limited data as to the use of HCTZ during pregnancy, especially in the first trimester. Data received from animal studies is insufficient. HCTZ crosses the placental barrier. Based on the

pharmacological effects of HCTZ, its use during the second and third trimester may compromise fetoplacental perfusion and may cause fetal and neonatal effects like jaundice, electrolyte imbalance and thrombocytopenia.
HCTZ should not be used for gestational edema or preeclampsia due to the risk of decreased plasma volume and placental hypoperfusion, without a beneficial effect on the course of the disease.
Breastfeeding.
HCTZ is excreted in breast milk in small amounts. Thiazide diuretics in high doses causing intense diuresis can inhibit lactation. Using the drug during breastfeeding is not recommended. If its use is absolutely necessary, breastfeeding should be stopped.
Fertility.
There is no data on the effect of HCTZ on human fertility. During animal studies, the drug did not affect fertility or ability to conceive.

Effect on reaction rate when driving motor transport or using other mechanisms.
Treatment of high blood pressure with HCTZ should be conducted under regular medical supervision. The ability to drive and use other machines may be impaired in case of individual reactions. In particular, this applies to the initial stage of treatment, increasing the dose of HCTZ, replacing it, as well as alcohol consumption.

Dosage and administration.
The dose of the drug is titrated and adjusted by the physician individually. The tablets are to be taken orally, with water, after the meal. The daily dose of the drug can be administered at once or split into two.
Arterial hypertension
The initial dose is 12.5 or 25 mg once daily. The maintenance dose is 12.5 mg once daily.
Hyponatremia or dehydration should be corrected before using the drug combined with ACE inhibitors, ARBs or direct renin inhibitors. Otherwise, the treatment should be initiated under close medical supervision.
Cardiogenic, hepatogenic, nephrogenic edema.
The initial dose is 25 or 50 mg daily. The maintenance dose is 25, 50 or 100 mg daily.
In case of hepatic or renal impairment the drug should be dosed according to the restriction. Patients with decompensated heart failure may have a significantly reduced absorption of the drug.
The duration of HCTZ therapy is not limited and depends on the type and severity of the disease. In case of long-term use, the drug should be discontinued gradually.
Special patient groups
Renal impairment
Initial dose adjustment is not required in patients with mild and moderate renal impairment (see sections “Pharmacological properties” and “Administration details”). The drug is contraindicated in patients with severe renal impairment (creatinine clearance <30 ml/min) and anuria (see sections “Contraindications” and “Administration details”).
Hepatic impairment
Initial dose adjustment is not required in patients with mild and moderate hepatic impairment (see sections “Pharmacokinetics” and “Administration details”). Using thiazides, like other diuretics, to treat ascites associated with hepatic cirrhosis may cause electrolyte imbalance, hepatic encephalopathy and hepatorenal syndrome. The drug should be used with special caution in patients with severe hepatic impairment (see section “Administration details”).

Children.
The drug is not recommended for use in children.

Overdose.
Symptoms.

The clinical manifestation of acute or chronic HCTZ overdose depends on the degree of dehydration and electrolyte loss. In case of significant fluid and sodium loss, overdose may manifest as thirst, weakness, dizziness, vomiting, muscle pain and muscle spasms (e.g. calf muscle cramps), headache, tachycardia, orthostatic hypotension caused by dehydration and hypovolemia, which leads to hemoconcentration, cramps, drowsiness, lethargy, confusion, circulatory collapse and acute renal failure. Electrolyte imbalance can cause cardiac arrhythmias.
Hypokalemia may manifest as fatigue, muscle weakness, paresthesias, pareses, apathy, flatulence, constipation or cause cardiac arrhythmias. Severe hypokalemia can cause paralytic ileus and impairment of consciousness up to hypokalemic coma.
Treatment.
The drug should be discontinued immediately if overdose symptoms develop. In all cases of drug overdose, general supportive measures should be taken. Treatment measures include restoration of the water and electrolyte balance and, in case of circulatory collapse, transfer to the intensive care unit, if necessary - anti-shock therapy.

Adverse reactions.
The following classification is used to assess the frequency of adverse reactions: very common (≥ 1/10), common (≥ 1/100 and < 1/10), uncommon (≥ 1/1000 and < 1/100), rare (≥ 1/10000 and < 1/1000), very rare (< 1/10000), including isolated cases, unknown (cannot be estimated from the available data).
Metabolic disorders:
Very common: hypokalemia, hyperlipidemia (especially in case of high doses).
Common: hyperuricemia, hypomagnesemia, hyponatremia, loss of appetite.
Rare: hypercalcemia, hyperglycemia, glycosuria, exacerbation of metabolic syndrome.
Very rare: hypochloremic alkalosis.
Skin and subcutaneous tissue disorders:
Common: skin rash, including urticaria.
Rare: photosensitization.
Very rare: systemic lupus erythematosus, lupus-like syndrome, reactivation of systemic lupus erythematosus, toxic epidermal necrolysis.
Gastrointestinal disorders:
Common: nausea, vomiting.
Rare: diarrhea, abdominal discomfort, constipation.
Very rare: pancreatitis.
Hepatobiliary disorders:
Rare: intrahepatic cholestasis, jaundice.
Cardiovascular disorders:
Common: orthostatic hypotension which may be potentiated by the use of alcohol, analgesic and sedative drugs.
Rare: cardiac arrhythmia.
Respiratory, thoracic and mediastinal disorders:
Very rare: acute respiratory distress-syndrom (see section “Administration details”).
Nervous system disorders:
Rare: headache, dizziness, depression, paresthesias.
Psychiatric disorders:
Rare: sleep disturbances.
Eye disorders:
Rare: visual impairment, especially during the first weeks of therapy.
Frequency unknown: choroidal effusion, acute angle-closure glaucoma (see section “Administration details”).
Blood and lymphatic system disorders:
Rare: thrombocytopenia, thrombocytopenic purpura.

Very rare: hemolytic anemia, leucopenia, agranulocytosis, depression of bone marrow hematopoiesis.
Reproductive system and breast disorders:
Often: erectile dysfunction.
Immune system disorders:
Very rare: necrotizing vasculitis, hypersensitivity reactions – respiratory distress syndrome, including pneumonitis and pulmonary edema.
Neoplasms benign, malignant and unspecified (including cysts and polyps):
Frequency unknown: non-melanoma skin cancer (basal cell carcinoma and squamous cell carcinoma, see sections "Pharmacodynamics" and "Administration details").
During the postmarketing period there have been reports of the following adverse reactions after administration of medicinal products that contain HCTZ: aplastic anemia, angle-closure glaucoma, choroidal effusion, erythema multiforme, muscle cramps, acute renal failure, renal impairment, fever, asthenia, NMSC (BCC and SCC).
Description of selected adverse reactions
Cases of choroidal effusion with visual field defect have been observed following the administration of thiazide and thiazide-like diuretics.
Non-melanoma skin cancer. Based on available data from epidemiological studies, cumulative dose-dependent association between hydrochlorothiazide use and non-melanoma skin cancer has been observed (see sections "Administration details" and "Pharmacological properties").
Reporting of suspected adverse reactions
Reporting of suspected adverse reactions after authorization of the medicinal product by the licensing authority is an important procedure. It allows continued monitoring of the "benefit/risk" balance of the use of the medicinal product. Healthcare professionals are asked to report all suspected adverse reactions through national reporting systems.

Shelf life.
3 years.

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

Package.
10 tablets are in a blister. 3, 6 or 9 blisters are in a carton package.

Conditions of supply.
Prescription only.

Manufacturer.
LLC "KUSUM PHARM".

Address of manufacturer and manufacturing site.
40020, Ukraine, Sumy Oblast, Sumy, Skryabina str., 54.

Last revision date.
03.08.2023 № 1399