INSTRUCTION
for medical use
of medicinal product
LEKTAXIME®

Composition:
active ingredient: cefotaxime;
1 vial contains cefotaxime (as cefotaxime sodium) − 1.0 g.

Pharmaceutical form. Powder for solution for injections.
Basic physical and chemical properties: crystalline powder from near-white to light yellow color.

Pharmacotherapeutic group. Antibacterial agents for system usage.
Beta-lactam antibiotics. Third generation cephalosporins. ATC code: J01D D01.

Pharmacological properties.
Pharmacodynamics. Cefotaxime is a semisynthetic cephalosporin antibiotic of III generation for parenteral administration. It has broad spectrum of action. Species susceptible to the drug: *Streptococcii* (except group D), including *Streptococcus pneumoniae*; *Staphylococcus aureus*, including penicillin-producing and penicillin non-producing strains; *Bacillus subtilis* and *Mycoides*; *Neisseria gonorrhoeae* (penicillin-producing and penicillin non-producing strains), *Neisseria meningitidis*, other species of *Neisseria*, *Escherichia coli*, *Klebsiella spp*., including *Klebsiella pneumoniae*, *Enterobacter spp.* (some resistant strains), *Serratia spp.*, *Proteus* (indol-positive and indol-negative species), *Salmonella*, *Citrobacter spp.*, *Providencia*, *Shigella*, *Yersinia*, *Haemophilus influenzae* and *parainfluenzae* (penicillin-producing and penicillin non-producing strains, including resistant to ampicillin), *Bordetella pertussis*, *Moraxella*, *Aeromonas hydrophilia*, *Veillonella*, *Clostridium perfringens*, *Eubacterium*, *Propionibacterium*, *Fusobacterium*, *Bacteroides spp*. and *Morganella*. The following species are inconstantly susceptible to the drug: *Pseudomonas aeruginosa*, *Acinetobacter*, *Helicobacter pylori*, *Bacteroides fragilis* and *Clostridium difficile*. Drug resistant species: *Streptococcus* of group D, *Listeria* and methicillin-resistant staphylococci.
Pharmacokinetics.
Absorption. Blood serum cefotaxime concentration will make up 100 mcg/mL in 5 minutes after single intravenous administration of the drug in dose 1 g. Maximum blood cefotaxime concentration is achieved in 0.5 hours after intramuscular administration of the drug in the same dose and it makes up 24 mcg/mL. Blood bactericidal concentration is achieved within 12 hours.
Distribution. Blood protein binding is 25-40%, in average. Cefotaxime penetrates well into tissues and biological fluids of the organism. It is found in effective concentrations in pleural, peritoneal and synovial fluids. It penetrates through the blood-brain barrier. It is biotransformed with creation of the active metabolite.
Excretion. Approx. 60-70% of administered drug dose is excreted unchanged with urine, and the rest – in the form of metabolites. It is excreted partially with bile. Drug elimination half-life makes up 1 hour at intravenous administration and 1-1.5 hours – at intramuscular administration. Drug elimination half-life is increased approx. 2 folds in patients with renal failure and elderly patients. Drug elimination half-life in newborns makes up 0.75 to 1.5 hours, and in premature newborns – 1.4 to 6.4 hours.

Clinical particulars.
Indications.
Infections caused by the drug susceptible microorganisms:
− infections of ENT-organs (tonsillitis, otitis);
− respiratory tract infections (bronchitis, pneumonia, pleuritis, abscess);
− urinary tract infections;
− septemia, bacteriemia;

− intra-abdominal infections (including peritonitis);
− skin and soft tissue infections;
− bone and joint infections;
− meningitis (except listeric) and other CNS-related infections.
Infection prevention after surgical interventions to digestive tracts, urological and obstetric-gynecologic surgeries.

Contraindications.
Hypersensitivity to cephalosporins, lidocaine (if lidocaine is used as a solvent), and to other β-lactam antibiotics in anamnesis; haemorrhage, enterocolitis in anamnesis (in particular, nonspecific ulcerative colitis), AV-block without integrated cardiac pacemaker, severe cardiac failure.

Interaction with other medicinal products and other forms of interaction.
Concurrent administration of Lektaxime® and antibiotics-aminoglycosides increases nephrotoxicity. The same is related to diuretics – ethacrynic acid derivatives and other diuretics (furosemide). At concurrent administration of indirect anticoagulant and Lektaxime®, both drugs demonstrate synergic effect.
Lektaxime® solution is incompatible with solutions of other antibiotics, so they have to be administered separately.
Concurrent administration with nifedipine elevates cefotaxime bioavailability by 70%.
Probenicid blocks tubular secretion of cefotaxime and elongates its elimination half-life.
In the course of the treatment with Lektaxime® the effectiveness of oral contraceptives can be reduced. In this period additional contraception should be used.
Lektaxime® should not be used together with bacteriostatic antibiotics (for example, tetracyclines, erythromycin and chloramphenicol) as antagonistic effect is possible.
At concomitant therapy the Lektaxime® solution should not be mixed with aminoglycoside solutions; they should be introduced separately.
Lektaxime® shall not be used together with lidocain:
– if administrated by the intravenous route;
– in children aged less than 30 months of age;
– in patients with a history of hypersensitivity to lidocain;
– in patients with heart block;
– in patients with severe heart failure.

Administration peculiarities.
Concurrent administration of Lektaxime® and nephrotoxic drugs requires monitoring of renal function; if the drug is used for more than 10 days, peripheral blood count should be monitored. Caution should be exercised when the drug is administered in patients with renal or hepatic impairment, with a history of hypersensitivity to penicillin. The dosage should be reduced in patients with renal impairment according to the severity of renal disease and sensitivity of the causative organism. At prolonged administration of the drug, renal function should be monitored and preventive measures for dysbacteriosis should be taken.
Vitamin K should be administered to elderly patients and debilitated patients for hypocoagulation prevention. Lektaxime® treatment is discontinued, if the symptoms of pseudomembranous colitis are observed.
Blood count should be monitored in the process of long-term treatment as well as laboratory parameters of hepatic and renal function. Positive direct Coombs' test reaction and pseudo-positive urine reaction to glucose are possible in the course of drug administration.
Erroneous positive results may be obtained at determination of urine glucose level with recovery method. Enzymatic test should be used to avoid such erroneous results. Alcohol is prohibited to consume during the treatment, because it may cause effects like disulfiram effect (hyperaemia of face, abdominal and stomach spasm, nausea, vomiting, headache, arterial pressure decrease, tachycardia, difficulty in breathing).

As with other antibiotics of broad spectrum, prolonged use may result in overgrowth of non susceptible microorganisms, and the treatment should be stopped. If in the course of the treatment the superinfection occurs, the antimicrobial therapy should be administrated.
Anaphylactic reactions. Preliminary enquiry about history of allergies (allergic diathesis, hypersensitivity to β-Lactam antibiotics) is necessary before prescribing cephalosporins. If a hypersensitivity reaction in a patient occurs, the treatment must be stopped. The use of Lektaxime® is strictly contra-indicated in patients with a previous history of immediate-type hypersensitivity to cephalosporins. In case of any doubts, the doctor must obligatory be present at the fist introduction of the drug, as the development of anaphylactic reactions is possible. The cross allergy is known between penicillins and cephalosporins that occurs in 5–10% of cases. Extreme caution should be undertaken when administered in patients with indications of the allergy for penicillin.
Pseudomembranous colitis. Pseudomembranous colitis may occur in the first weeks of treatment presented by severe persistent diarrhea. The diagnosis can be confirmed by endoscopy and/or histology. These side effects should be considered as serious: introduction of the drug should be stopped immediately and appropriate therapy including oral administration of vancomycin or metronidazole should be prescribed.
Administration during pregnancy or breast-feeding.
Drug administration during pregnancy is prohibited.
Breast feeding should be stopped temporary in case of drug administration during lactation.
Effects on ability to drive and use machines.
Driving of motor vehicles or using of machines should be avoided during treatment due to possibility of adverse reactions development related to central nervous system.

Posology and method of administration.
The drug is used for intravenous bolus injection, intravenous infusion and intramuscular administration.
Intravenous bolus injection: 1 g of powder is diluted in 8 ml of sterile water for injection. Injection is administered slowly during 3-5 minutes.
Intravenous infusion: 1 g of powder is diluted in 50 ml of 0.9% sodium chloride solution or 5% glucose solution. Intravenous infusion duration is 50-60 minutes.
Intramuscular administration: 1 g of is diluted in 4 ml of sterile water for injection or 1% lidocaine solution and injected deeply into gluteus.
Treatment course duration is set individually.
Adults and children with body weight 50 kg and over are administered Lektaxime® in dose 1 g every 12 hours. The drug in dose 1 g 3-4 time/day is administered in severe occurrences. Maximum daily dose is 12 g.
The drug is administered intramuscular or intravenous in dose 1 g every 12 hours for uncomplicated infections and urinary tract infection; for uncomplicated acute gonorrhoea – the drug is administered intramuscular or intravenous in dose 1 g once daily; for moderately severe infections – the drug is administered in dose 1-2 g every 12 hours; for severe infections (meningitis) – the drug is administered intravenous in dose 2 g every 6-8 hours.
Children with body weight up to 50 kg is administered the drug in dose 50-100 mg/kg of body weight per day; the dose is divided into 3-4 intramuscular or intravenous injections. For severe infections, including meningitis, daily dose is recommended to increase up to 100-200 mg/kg of body weight and to administer for 4-6 intravenous or intramuscular injections.
Daily dose for premature newborns and children aged to 1 week makes up 50 mg/kg of body weight; the dose is divided into 2 equal doses and administered intravenous only.
Daily dose for children aged 1-4 weeks makes up 50-100 mg/kg of body weight; the dose is divided into 3 equal doses and administered intravenous only.
Single dose 1 g of Lektaxime® is administered before surgical intervention in the process of anaesthetic management to prevent infection development. If necessary, the dose is administered repeatedly in 6-12 hours.
Drug dose must be decreased for patients with impaired renal function. If creatinine clearance is 10 ml/min and less, daily dose should be decreased twice.

Children.
Lektaxime® is administered to children in the appropriate dose (see section «Posology and method of administration»).
Intramuscular administration is contraindicated to children aged up to 2.5 years.

Overdose.
Symptoms: fever, leukopenia, thrombocytopenia, acute haemolytic anaemia, skin, gastrointestinal and hepatic reactions, short breath, stomatitis, anorexia, temporary hearing loop, loss of balance, renal failure, encephalopathy (especially, at renal failure). In individual cases cramps are observed as well increase of side effects.
Treatment: haemodialysis/peritoneal dialysis, symptomatic therapy. Drug administration should be discontinued at signs of hypersensitivity (cutaneous eruption, urticaria, headache, nausea, loss of consciousness). In the event of severe hypersensitivity reaction/anaphylactic reaction, administration of epinephrine and/or glucocorticoids should be initiated. Additional measures could be required for other clinical conditions: artificial ventilation, use of histamine receptor antagonists. In the event of circulatory collapse, resuscitation procedure should be started. No specific antidote is available.

Adverse reactions.
Digestive tract disorders: nausea, vomiting, diarrhoea, abdominal pain, dysbacteriosis, flatulence, stomatitis, glossitis; rare – pseudomembranous colitis.
Hepatobiliary system disorders: hepatitis, acute hepatic failure, hepatic function impairment, jaundice, cholestasis.
Allergic reactions: rash, hyperaemia, polymorphic exudative erythema, Stevens-Johnson syndrome, fever, eosinophilia, anaphylactic reactions, itch, urticaria, bronchospasm, toxic epidermal necrolysis (Lyell's disease), Quincke's edema; rare – anaphylactic shock.
Urinary tract disorders: renal function impairment, oliguria, interstitial nephritis.
Laboratory parameters: elevation of hepatic transaminases, lactic dehydrogenase, alkaline phosphatase and bilirubin, urea nitrogen and creatinine concentration, hypocoagulation.
Blood and lymphatic system disorders: neutropenia, transient leukopenia, thrombocytopenia, agranulocytosis, hypoprotrombinemia, haemolytic anaemia, granulocytopaenia, anisocytosis, eosinophilia, hypocoagulation.
CNS disorders: headache, reversible encephalopathy, dizziness, convulsions, increased fatigue, weakness.
Local reactions: pain, tissue inflammation, phlebitis, infiltrate in the administration site.
Effects conditioned by biological effect: possible development of superinfection (e.g. Candida vaginitis).
Other: haemorrhage and bleeding, autoimmune haemolytic anaemia, interstitial nephritis, acute hepatic failure, arrhythmia (at rapid bolus administration), positive Coombs' test.
Complications similar to Herxheimer's reaction may develop at treatment of infections caused by Spirochaeta. This may result in fever, rigor, headache and joint pain.

Shelf life. Lektaxime®, powder for solution for injections, 1.0 g – 2 years.
Water for injections, solvent for parenteral administration, 10 ml in ampoule – 4 years.

Storage. Store in original package at temperature not exceeding 25 °C. Keep away from children.

Incompatibilities.
Lektaxime® solution is incompatible with other antibiotic solutions in the same syringe or in infusion solution; they have to be administered separately.

Package. 1.0 g of powder in vial; 1 vial in the pack; 1 vial and 1 ampoule with a solvent for parenteral administration (Water for injections, 10 ml in ampoule) in blister, 1 blister in the pack.

Prescription status. By prescription.

Manufacturer. Joint Stock Company «Lekhim-Kharkiv».

Location. Ukraine, 61115, Kharkiv region, Kharkiv, Severyna Pototskoho street, building 36.

Date of the last revision.