APPROVED
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INSTRUCTION
for medical use of medicinal product
CEFOTAXIME

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 Cefotaxime 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 Cefotaxime, both drugs demonstrate synergic effect.
Cefotaxime 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.

Administration peculiarities.
It is administered with caution to patients with burdened allergic anamnesis.
Concurrent administration of Cefotaxime and nephrotoxic drugs requires monitoring of renal function; if the drug is used for more than 10 days, peripheral blood count should be monitored. Vitamin K should be administered to elderly patients and debilitated patients for hypocoagulation prevention. Cefotaxime 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).
Concurrent administration of cefotaxime and lidocaine is prohibited in the events specified below:
− at intravenous administration;
− to children to 30 months old (up to 2.5 years);
− to patients with established increased drug susceptible;
− to patients with heart block;
− to patients with severe cardiac failure.
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.
Skin tests for susceptibility to antibiotic and lidocaine should be carried out before administration of the drug.
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 Cefotaxime 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 Cefotaxime 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.
Cefotaxime 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).
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, 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.
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. Cefotaxime, powder for solution for injections – 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.
Cefotaxime 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 or 5, or 50 vials in the pack; 1 vial and 1 ampoule with solvent for parenteral administration (Water for injections, 10 ml in ampoule) in blister, 1 blister in the pack.

Prescription status. By prescription.

Manufacturer. JSC «Lekhim-Kharkov».

Location. 36, 17-go Partsyezda str., Kharkov, 61115, Ukraine.

Date of the last revision.