**APPROVED**
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# INSTRUCTION
## for medical use of medicinal product
## CEFUROXIME

***Composition:***
*active ingredient:* cefuroxime;
1 vial contains cefuroxime (as cefuroxime sodium) 0.75 g or 1.5 g.

**Pharmaceutical form.** Powder for solution for injections.
*Basic physical and chemical properties:* a white to off-white powder.

**Pharmacotherapeutic group.** Antibacterials for systemic use. Second-generation cephalosporins.
ATC code: J01D C02.

***Pharmacological properties.***
*Pharmacodynamics.*
Cefuroxime is a bactericidal cephalosporin antibiotic with high activity against a wide range of Gram-positive and Gram-negative bacteria, including β-lactamase producing strains. Cefuroxime has good stability to bacterial β-lactamase, and consequently is active against many ampicillin-resistant or amoxycillin-resistant strains. The major bactericidal action of cefuroxime results from inhibition of cell wall synthesis.
The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections.
The drug is active against *Staphylococcus aureus* (methicillin-susceptible strains) and *Coagulase negative staphylococcus* (methicillin susceptible strains), *Haemophilus influenzae, Klebsiella spp., Enterobacter spp., Streptococcus pyogenes, Escherichia coli, Streptococcus mitis (viridians group), Clostridium spp., Proteus mirabilis, Proteus rettgeri, Salmonella typhi, Salmonella typhimurium* and other strains of *Salmonella, Shigella spp., Neisseria spp.* (including *N. gonorrhoea*, which produce beta-lactamase), *Bordetella pertussis*. The drug is moderately susceptible to *Proteus vulgaris, Morganella morganii (Proteus morganii)* and *Bacteroides fragilis*.
The following organisms are not susceptible to Cefuroxime: *Clostridium difficile, Pseudomonas spp., Campylobacter spp., Acinetobacter calcoaceticus, Legionella spp.*, methicillin resistant strains of *Staphylococcus aureus, Staphylococcus epidermidis* and coagulase negative staphylococcus.
Some strains of the following genera are not susceptible to Cefuroxime: *Streptococcus faecalis, Morganella morganii, Proteus vulgaris, Enterobacter spp., Citrobacter spp., Serratia spp.* and *Bacteroides fragilis.*
*In vitro* the activities of cefuroxime and aminoglycoside antibiotics in combination have been shown to be at least additive with occasional evidence of synergy.
*Pharmacokinetics.*
Peak levels of cefuroxime are achieved within 30 to 45 minutes after intramuscular administration.
The serum half-life after either intramuscular or intravenous injection is approximately 70 minutes.
Concurrent administration of probenecid prolongs the excretion of cefuroxime and produces an elevated peak serum level.
Protein binding has been variously stated as 33-50%.
There is an almost complete recovery (85-90%) of unchanged cefuroxime in urine within 24 hours of administration. The major part is excreted in the first six hours.
Cefuroxime is not metabolised and is excreted by glomerular filtration and tubular secretion.

Serum levels of cefuroxime are reduced by dialysis.
Concentrations of cefuroxime in excess of MIC (the minimum inhibitory concentration) for common pathogens can be achieved in bone, synovial fluid and aqueous humour. Cefuroxime passes the blood-brain barrier when the meninges are inflamed.

**Clinical particulars.**

***Indications.***

Treatment of infections caused by cefuroxime sensitive bacteria, or treatment of infections before the infecting organism has been identified.
*Respiratory tract infections:* acute and chronic bronchitis, infected bronchiectasis, bacterial pneumonia, lung abscess and post-operative chest infections;
*Ear, nose and throat infections:* sinusitis, tonsillitis, pharyngitis;
*Urinary tract infections:* acute and chronic pyelonephritis, cystitis and asymptomatic bacteriuria;
*Soft-tissue infections:* cellulitis, erysipelas and wound infections;
*Bone and joint infections:* osteomyelitis and septic arthritis;
*Obstetric and gynaecological infections:* pelvic inflammatory diseases;
*Gonorrhoea* particularly when penicillin is unsuitable.
*Other infections* including septicaemia and meningitis.
Prophylaxis against post-operative chest, abdominal, pelvic infections, after vascular, cardiac and orthopaedic infection.
Usually Cefuroxime will be effective alone, but when appropriate it may be used in combination with an aminoglycoside antibiotic, or in conjunction with metronidazole (orally or by suppository or injection).
In situations where mixed aerobic and anaerobic infections are encountered or suspected (e.g. peritonitis, aspiration pneumonia, abscesses in the lung, pelvis and brain), or are likely to occur (e.g. in association with colorectal or gynaecological surgery) it is appropriate to administer Cefuroxime in combination with metronidazole.
Where appropriate cefuroxime is effective when used prior to oral therapy with cefuroxime axetil in the treatment of pneumonia and acute exacerbations of chronic bronchitis.

***Contraindications.***

Hypersensitivity to cefuroxime.
Hypersensitivity to cephalosporin antibiotics.
A history of severe hypersensitivity (e.g. anaphylactic reactions) to other beta-lactam antibiotics (penicillins, monobactams and carbapenems).

***Interactions with other medicinal products and other forms of interaction.***

In common with other antibiotics Cefuroxime may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral contraceptives.
It is recommended that either the glucose oxidase or hexokinase methods are used to determine blood/plasma glucose levels in patients receiving Cefuroxime.
Cefuroxime does not interfere in enzyme-based tests for glycosuria.
Slight interference with copper reduction methods (Benedict's, Fehling's, Clinitest) may be observed. However, this should not lead to false-positive results, as may be experienced with some other cephalosporins.
Cefuroxime does not interfere in the alkaline picrate assay for creatinine.

***Special warnings and precautions for use.***

As with all beta-lactam antibacterial agents, serious and occasionally fatal hypersensitivity reactions have been reported. In case of severe hypersensitivity reactions, treatment with cefuroxime must be discontinued immediately and adequate emergency measures must be initiated.
Before beginning treatment, it should be established whether the patient has a history of severe hypersensitivity reactions to cefuroxime, to other cephalosporins or to any other type of beta-lactam agent. Caution should be used if cefuroxime is given to patients with a history of non-severe hypersensitivity to other beta-lactam agents.

Cephalosporin antibiotics at high dosage should be given with caution to patients receiving concurrent treatment with potent diuretics such as furosemide and aminoglycosides, as these combinations are suspected of adversely affecting renal function. Renal function should be monitored in these patients, the elderly, and those with pre-existing renal impairment (see section "Posology and method of administration").
As with other therapeutic regimens used in the treatment of meningitis, mild-to-moderate hearing loss has been reported in a few paediatric patients treated with cefuroxime sodium. Persistence of positive CSF cultures of *Haemophilus influenzae* at 18-36 hours has also been noted with cefuroxime injection, as well as with other antibiotic therapies; however, the clinical relevance of this is unknown.
As with other antibiotics, prolonged use of cefuroxime may result in the overgrowth of nonsusceptible organisms (e.g. *Candida, Enterococci, Clostridium difficile*), which may require interruption of treatment.
Antibacterial agent-associated pseudomembranous colitis have been reported with antibacterial agents and may range in severity from mild to life threatening. This diagnosis should be considered in patients with diarrhoea during or subsequent to the administration of the antibacterial agent. In the event that the patient develops prolonged and severe diarrhoea or abdominal cramps, treatment should be discontinued and further examination instituted.
With a sequential therapy regime the timing of change to oral therapy is determined by severity of the infection, clinical status of the patient and susceptibility of the pathogens involved. If there has been no clinical improvement after 72 hours of parenteral treatment, then the patient's treatment should be reviewed. Please refer to the relevant prescribing information for cefuroxime before initiating sequential therapy.
*Use during pregnancy and in nursing women.*
There is no experimental evidence of embryopathic or teratogenic effects attributable to Cefuroxime but, as with all drugs, it should be administered with caution during the early months of pregnancy.
Cefuroxime is excreted in human milk, and consequently caution should be exercised when Cefuroxime is administered to a nursing mother.
*Effects on ability to drive and use machines*.
There are no reports on the effect of cefuroxime on ability to drive and use machines.
***Posology and method of administration.***
Susceptibility to cefuroxime may vary geographically and with time. If necessary, refer to local antibiotic sensitivity data.
Cefuroxime Injection is used for intravenous or intramuscular administration only.
Cefuroxime is also available as cefuroxime axetil for oral administration. This permits the use of sequential therapy with the same antibiotic, when a change from parenteral to oral therapy is clinically indicated.
Intramuscular injection should not exceed 0.75 g per site.
*General recommendations.*
Adults.
Many infections will respond to 0.75 g three times daily by intravenous or intramuscular injection. For more severe infections, this dose should be increased to 1.5 g three times daily intravenously. The frequency of injection can be increased to 4 times daily (six-hourly) if necessary, giving total doses of 3 g to 6 g daily. Where clinically indicated, some infections respond to 0.75 g or 1.5 g twice daily (intravenously or intramuscularly) followed by oral therapy with cefuroxime.
Children (incl. Infants).
30-100 mg/kg/day given as 3 or 4 divided doses. A dose of 60 mg/kg/day is appropriate for most infections.
Neonates.
30-100 mg/kg/day given as 2 or 3 divided doses. In the first weeks of life the serum half-life of cefuroxime can be three to five times that in adults.
*Gonorrhea.*
1.5 g should be given as a single dose. This may be given as 2 x 0.75 g injections into each buttock.
*Meningitis.*
Cefuroxime is suitable for sole therapy of bacterial meningitis due to sensitive strains.

Adults: 3 g every eight hours.
Children (incl. Infants): 200 to 240 mg/kg/day intravenously in three or four divided doses. This dosage may be reduced to 100 mg/kg/day intravenously after three days or when clinical improvement occurs.
Neonates: The initial dosage should be 100 mg/kg/day intravenously. A reduction to 50 mg/kg/day intravenously may be made when clinically indicated.
*Prophylaxis.*
The usual dose is 1.5 g given intravenously with induction of anaesthesia for abdominal, pelvic and orthopaedic operations. This may be supplemented with two 0.75 g intramuscular doses eight and sixteen hours later.
In cardiac, pulmonary, oesophageal and vascular operations, the usual dose is 1.5 g given intravenously with induction of anaesthesia, continuing with 0.75 g given intramuscularly three times daily for a further 24 to 48 hours.
In total joint replacement, 1.5 g cefuroxime powder may be mixed dry with each pack of methyl methacrylate cement polymer before adding the liquid monomer.
*Sequential therapy*
*Pneumonia:* 1.5 g 2-3 times daily (intravenously or intramuscularly) for 48-72 hours, followed by 500 mg 2 times daily cefuroxime oral therapy for 7-10 days.
*Exacerbation of chronic bronchitis:* 0.75 g 2-3 times daily (intravenously or intramuscularly) for 48-72 hours, followed by 500 mg 2 times daily cefuroxime oral therapy for 7 days.
Duration of both parenteral and oral therapy is determined by the severity of the infection and the clinical status of the patient.
*Renal impairment.*
Cefuroxime is excreted by the kidneys. Therefore, as with all such antibiotics, in patients with markedly impaired renal function it is recommended that the dosage of Cefuroxime should be reduced to compensate for its slower excretion. However, it is not necessary to reduce the standard dose (0.75-1.5 g 3 times daily) until the creatinine clearance falls below 20 ml/min. In adults with marked impairment (creatinine clearance 10-20 ml/min) 0.75 g 2 times daily is recommended and with severe impairment (creatinine clearance <10 ml/min) 0.75 g once daily is adequate.
For patients on haemodialysis a further 0.75 g dose should be given intravenously or intramusculary at the end of each dialysis. In addition to parenteral use, cefuroxime can be incorporated into the peritoneal dialysis fluid (usually 250 mg for every 2 litres of dialysis fluid). For patients on continuous arteriovenous haemodialysis or high-flux haemofiltration in intensive therapy units a suitable dosage is 0.75 g twice daily. For low-flux haemofiltration follow the dosage recommended under impaired renal function.
*Instructions for use.*
For intramuscular administration add 3 mL Water for Injections to 0.75 g of Cefuroxime. Shake gently to produce an opaque solution.
For intravenous administration dissolve Cefuroxime in Water for Injections using at least 6 mL for 0.75 g, or at least 15 mL for 1.5 g. For intravenous infusion which last not more than 30 min dissolve 1.5 g of cefuroxime in 50 or 100 ml of Water for Injections. These solutions may be given directly into the vein or introduced into the tubing of the giving set.
Some increase in the colour of prepared solutions of Cefuroxime may occur on storage.
*Paediatric patients.*
The drug can be used from the first days of life.

***Overdose.***
Overdosage of cephalosporins can cause cerebral irritation leading to convulsions. Serum levels of cefuroxime can be reduced by haemodialysis or peritoneal dialysis.

***Undesirable effects.***
*Infection and infestations:* overgrowth of non-susceptible organisms, e.g. *Candida.*
*Blood and lymphatic system disorders:* Neutropenia, eosinophilia; leukopenia, decreased haemoglobin concentration, positive Coomb's test, thrombocytopenia, haemolytic anaemia. Cephalosporins as a class tend to be absorbed onto the surface of red cell membranes and react with

antibodies directed against the drug to produce a positive Coomb's Test (which can interfere with cross matching of blood) and very rarely haemolytic anaemia.
*Immune system disorders:* Hypersensitivity reactions including skin rash, urticaria and pruritus; drug fever; interstitial nephritis, anaphylaxis, cutaneous vasculitis.
*Gastrointestinal system disorders:* Gastrointestinal disturbance; pseudomembranous colitis (see "Special warnings and precautions for use").
*Hepatobiliary disorders:* transient rise in liver enzymes, transient rise in bilirubin.
Transient rises in serum liver enzymes or bilirubin occur, particularly in patients with pre-existing liver disease, but there is no evidence of harm to the liver.
*Skin and subcutaneous tissue disorders:* Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis.
*Urinary system disorders:* elevations in serum creatinine, elevations in blood urea nitrogen and decreased creatinine clearance.
*General disorders and administration site conditions:* Injection site reactions which may include pain and thrombophlebitis.
Pain at the intramuscular injection site is more likely at higher doses. However it is unlikely to be a cause for discontinuation of treatment.

***Shelf life.*** 2 years.

**Storage.** Store in original package at temperature not exceeding 25 °C. Keep out of reach of children.
The reconstituted solution should be stored at 2-8 °C for no longer than 48 hours if refrigerated and for five hours if kept below 25 °C.

***Incompatibilities.***
Cefuroxime should not be mixed in the syringe with aminoglycoside antibiotics.
The pH of 2.74% sodium bicarbonate injection considerably affects the colour of solutions and therefore this solution is not recommended for the dilution of Cefuroxime. However, if required, for patients receiving sodium bicarbonate injection by infusion the Cefuroxime may be introduced into the tube of the giving set.
1.5 g cefuroxime injection constituted with 15 mL Water for Injections may be added to metronidazole injection (500 mg/100 mL) and both retain their activity for up to 24 hours below 25 °C.
1.5 g cefuroxime injection is compatible with azlocillin 1g (in 15 mL solvent) or 5 g (in 50 mL solvent) for up to 24 hours at 4 °C or 6 hours below 25 °C.
Cefuroxime injection (5 mg/mL) in 5% or 10% xylitol injection may be stored for up to 24 hours at 25 °C.
Cefuroxime injection is compatible with aqueous solutions containing up to 1% lignocaine hydrochloride.
Cefuroxime injection is compatible with the more commonly used intravenous infusion fluids. It will retain potency for up to 24 hours at room temperature in: Sodium Chloride Injection 0.9%; Glucose Injection 5%; Sodium Chloride 0.18% plus Glucose Injection 4%; Glucose 5% and Sodium Chloride Injection 0.9%; Glucose 5% and Sodium Chloride Injection 0.45%; Glucose 5% and Sodium Chloride Injection 0.225%; Glucose Injection 10%; Invert Sugar 10% in Water for Injection; Ringer's Injection; Lactated Ringer's Injection; M/6 Sodium Lactate Injection; Hartmann's Solution.
The stability of cefuroxime in Sodium Chloride Injection 0.9% and in Glucose Injection 5% is not affected by the presence of hydrocortisone sodium phosphate.
Cefuroxime injection has also been found compatible for 24 hours at room temperature when admixed in intravenous infusion with:
– Heparin (10 and 50 units/mL) in Sodium Chloride Injection 0.9%;
– Potassium Chloride (10 and 40 mEqL) in Sodium Chloride Injection 0.9%.

**Package.** 0.75 g of powder in a vial; 1 or 5, or 50 vials in a pack; 1 vial and 1 ampoule with a solvent (Water for Injection, 10 ml in an ampoule) in a pack.

1.5 g of powder in a vial; 1 or 5, or 50 vials in a pack.

**Prescription status.** By prescription.

**Manufacturer.** Joint Stock Company «Lekhim-Kharkov».

**Location.** Ukraine, 61115, Kharkov region, Kharkov, Severyna Pototskoho street, building 36.

**Date of the last revision.**