SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

Cefuroxime Sodium for Injection 0.75 g

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains cefuroxime sodium corresponding to 0.75g cefuroxime.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for solution for injection or infusion

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Cefuroxime Sodium for Injection is indicated for the treatment of the infections listed below in adults and children, including neonates (from birth) (see sections 4.4 and 5.1).

Community acquired pneumonia

Acute exacerbation of chronic bronchitis

Complicated urinary tract infections, including pyelonephritis

Soft-tissue infections: cellulitis, erysipelas and wound infections

Intra-abdominal infections (see section 4.4)

Prophylaxis against infection in gastrointestinal (including oesophageal),orthopaedic, cardiovascular, and gynaecological surgery (including caesarean section).

In the treatment and prevention of infections in which it is very likely that anaerobic organisms will be encountered, cefuroxime should be administered with additional appropriate antibacterial agents. Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

[Posology and method of administration]

Adults

The usual dose is 0.75g to 1.5g every 8 hours, with a treatment course lasting 5 to 10 days. For the life-threatening infection or the infection induced by rare sensitive bacteria, a dose of 1.5 g should be used every 6 hours. For the bacterial meningitis, the used dose should not be greater than 3.0g every 8 hours. For the simple gonorrhea, a single dose of 1.5g should be administered through IM to either gluteal region, and at the same, patients should orally take 1g of probenecid.

Prophylaxis of surgical infection: at 0.5 to 1.5 hours before the operation, patients should receive the intravenous injection of this product 1.5g; in case of an excessively long surgery duration, patients should receive intravenous injection or intramuscular injection at the dose of 0.75g every 8 hours. In case of the need of sternotomy, the drug should be administered every 12 hours after the intravenous injection of 1.5g with the input of anesthetics until the total dose reaches 6 g.

Children

As for children aged over three months, the administration volume is calculated based on the ratio of 50 to 100 mg per kilogram of weight per day, and the administration is finished in three to four times per day. As for severe infection, the dose should not be less than 0.1g per kilogram of weight per day, but it should not exceed the maximal dose used by adults. As for bone and joint infections, the dose should be 0.15g per kilogram of weight per day (but it should not exceed the maximal dose used by adults), and the administration is finished in three times per day. As for meningitis patients, the administration volume is calculated based on the ratio of 0.2 to 0.24g per kilogram of weight per day, and the administration is finished in three to four times per day. The maximal dose for children per day is not more than 6 g.

For patients with renal insufficiency, the usage and dosage can be adjusted according to the degree of renal function impairment, and the recommended adjustment methods are shown in the following table.

As children with renal insufficiency, the adjustments can be made with reference to the following forms.

Creatinine clearance (ml / min)	Dose	Septum
>20	0.75-1.5g	Every 8 hours
10-20	0.75g	Every 12 hours
<10	0.75g	Every 24 hours

4.3 Contraindications

This product is contraindicated for the patients allergic to cephalosporin-like drugs.

4.4 Special warnings and special precautions for use

Hypersensitivity reactions

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.

Concurrent treatment with potent diuretics or aminoglycosides

Cephalosporin antibiotics at high dosage should be given with caution to patients receiving concurrent treatment with potent diuretics such as furosemide or aminoglycosides. Renal impairment has been reported during use of these combinations. Renal function should be monitored in the elderly and those with known pre-existing renal impairment (see section 4.2).

Overgrowth of non-susceptible microorganisms

Use of cefuroxime may result in the overgrowth of *Candida*. Prolonged use may also result in the overgrowth of other non-susceptible microorganisms (e.g. enterococci and *Clostridium difficile*), which may require interruption of treatment (see section 4.8).

Antibacterial agent-associated pseudomembranous colitis has been reported with use of cefuroxime and may range in severity from mild to life threatening. This diagnosis should be

considered in patients with diarrhea during or subsequent to the administration of cefuroxime (see section 4.8). Discontinuation of therapy with cefuroxime and the administration of specific treatment for *Clostridium difficile* should be considered. Medicinal products

that inhibit peristalsis should not be given.

Intra-abdominal infections

Due to its spectrum of activity, cefuroxime is not suitable for the treatment of infections caused by Gram-negative non-fermenting bacteria (see section 5.1).

Interference with diagnostic tests

The development of a positive Coomb's Test associated with the use of cefuroxime may interfere with cross matching of blood (see section 4.8).

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.

As a false negative result may occur in the ferricyanide test, it is recommended that either the glucose oxidase or hexokinase methods are used to determine blood/plasma glucose levels in patients receiving cefuroxime sodium.

Important information about excipients

This medicinal product contains sodium. This should be considered for patients who are on a controlled sodium diet.

4.5. Interaction with other FPPs and other forms of interaction

As is reported, the combined therapy between aminoglycoside antibiotics and cephalosporin can result in nephrotoxicity.

False positive reactions may sometimes occur in case of the urine sugar test using the benedict's reagent and Fehling test or Clintest Tablets test strip when cephalosporin is clinically applicable to patients, but the false positive reaction will not occur when the enzyme method is used. During the blood glucose examination, false negative results may occur when the ferricyanic acid method is used; cefuroxime sodium will not interfere with the urine and blood creatinine levels measured using the alkaline picric acid method.

Cefuroxime is incompatible with the following drugs: ascorbic acid, gentamicin, kanamycin, tobramycin, neomycin, chlortetracycline hydrochloride, tetracycline hydrochloride, oxytetracycline hydrochloride, colistin sodium methanesulfonate, polymyxin b sulfate, erythromycin gluconate, erythromycin lactobionate, lincomycin, sulfafurazole, aminophylline, soluble barbiturates, calcium chloride, calcium gluconate, diphenhydramine hydrochloride and other antihistamines, lidocaine, norepinephrine, metaradrine, methylphenidate, succinylcholine and the like. Occasionally, it may be compatible with the following drugs: penicillin, methicillin, hydrocortisone sodium succinate, phenytoin, propranolazine, vitamin B and vitamin C, hydrolyzed proteins.

The combined therapy of intense diuretics such as frusemide, ethacrynic acid and bumetanide, anti-tumor drugs such as carmustinum and streptozicin and aminoglycoside antibiotics may increase the nephrotoxicity.

Clavulanic acid can enhance the anti-bacterial activity of cefuroxime against Gram negative bacilli which are resistant to it due to the generation of lactamase.

4.6. Pregnancy and lactation

Pregnant

There are limited amounts of data from the use of cefuroxime in pregnant women. Cefuroxime should be prescribed to pregnant women only if the benefit outweighs the risk.

Cefuroxime has been shown to cross the placenta and attain therapeutic levels in amniotic fluid and cord blood after intramuscular or intravenous dose to the mother.

Breastfeeding

Cefuroxime is excreted in human milk in small quantities. Adverse reactions at therapeutic doses are not expected, although a risk of diarrhoea and fungus infection of the mucous membranes cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from cefuroxime therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

4.7. Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, based on known adverse reactions, cefuroxime is unlikely to have an effect on the ability to drive and use machines.

4.8. Undesirable effects

Patients often have a good tolerance to this product, and the common adverse reactions are as follows:

Local reactions

Such as thrombophlebitis.

Gastrointestinal reactions

Such as diarrhea, nausea and pseudomembranous colitis.

Allergic reactions

The common reactions are rash, pruritus, urticaria etc. Occasional allergies, drug fever, erythema multiforme, interstitial nephritis, toxic epidermal exfoliative dermatitis, Stevens-Johnson syndrome.

Blood

Decrease in hemoglobin and hematocrit, temporary eosinophilia, temporary neutropenia and leukopenia, and occasional thrombopenia.

Liver function

Transient increase in ALT, AST, alkaline phosphatase, lactate dehydrogenase and serum bilirubin.

Others

vomiting, abdominal pain, conjunctivitis, vaginitis (including vaginal candidiasis), abnormal liver function (including cholestasis), aplastic anemia, hemolytic anemia, bleeding, triggered epilepsy, prolonged prothrombin time, deficiency of various kinds of cells, and agranulemia etc.

4.9. Overdose

Overdose will stimulate brain to have convulsion, and hemolialysis or peritoneal dialysis can lower the serum concentration of this product.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacological effects

As a second generation broad-spectrum cephalosporin, it takes effect by binding with bacterial protein to inhibit the synthesis of bacterial wall. Cefuroxime has a wide antibacterial activity to pathogenic bacteria, and is stable to many β-lactamases, especially the plasmid-mediated enzymes common in Enterobacteriaceae.

As is verified in in vitro tests on animals and clinical infection treatment, cefuroxime has an antibacterial activity to most of the following bacteria.

Aerobic gram positive bacteria: Staphylococcus aureus (including β-lactamase-producing bacteria), Streptococcus pneumoniae, Streptococcus pyogenes.

Aerobic gram negative bacteria: Escherichia coli, Hemophilus influenzae (including β-lactamase producing bacteria), Haemophilus parainfluenzae, Klebsiella pneumoniae, Moraxelle catarrhalis (including β-lactamase producing bacteria), Neisseria gonorrhoeae (β-lactamase producing bacteria).

In vitro tests show that, Enterococcus faecalis, methicillin-resistant Staphylococcus aureus, Clostridium difficile and Bacteroides fragilis are resistant to cefuroxime.

Toxicology study

Genotoxicity: although no animal lifelong study has been carried out to evaluate the cancerigenic potential of this product, no mutagenic action has been found in this product in the micronucleus test and bacterial test.

Reproductive toxicity: The administration of this product to rats at the dose of 1,000 mg/kg/day has no obvious impact on animal's fertility. The administration of this product to mice and rats at the dose of 32,000 mg/kg/day has no impairment on the fetal development. However, no correlation between animals and human has not been supported by clinical studies.

5.2. Pharmacokinetic properties

According to Physicians' Desk Reference, in case of the intramuscular injection of cefuroxime at the dose of 0.75 g to normal subjects, the mean plasma concentration reaches 27 ug/ml, and the time to peak is 45 minutes (ranging from 15 to 60 minutes). After the intravenous administration at the doses of 0.75 g and 1.5 g, the plasma concentration at 15 minutes reaches about 50 ug/ml and 100 ug/ml, respectively; plasma concentration can be maintained for 5.3 and 8 hours, respectively, or for longer time, and the concentration can be maintained more effective. The intravenous injection at the dose of 1.5 g to normal subjects every 8 hours does not produce accumulation effects of cefuroxime in blood. The half life of intravenous administration or intramuscular administration is about 80 minutes.

About 89% of the drug is excreted through kidneys at 8 hours after the administration, so the drug concentration in urine is relatively high.

At 8 hours after the intramuscular injection of cefuroxime at the single dose of 0.75 g, the mean drug concentration in urine can reach 1,300 ug/ml. At 8 hours after the intravenous injection of cefuroxime at the single doses of 0.75 g and 1.5 g, the mean drug concentration in urine can reach 1,150 ug/ml and 2,500 ug/ml.

The simultaneous administration of probenecid can prolong the renal tubular excretion time of cefuroxime, lower the renal clearance rate by about 40%, improve the plasma concentration by about 30%, and prolong the plasma half-life by about 30%. Cefuroxime reaches treatment concentration in pleural fluid, synovial fluid, bile, sputum, bone and ocular humor.

Studies have indicated that, cefuroxime can reach the treatment concentration in the cerebrospinal fluid of adult and pediatric meningitis patients. Cefuroxime is detectable in the cerebrospinal fluid of meningitis patients who take the drug for multiple times.

Cefuroxime has a serum protein binding rate of about 50%.

5.3. Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and toxicity to reproduction and development. No carcinogenicity studies have been performed; however, there is no evidence to suggest carcinogenic potential.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

None

6.2. Incompatibilities

This product may not be preserved in the same container together with aminoglycoside antibiotics for the administration; precipitation may occur after the mixing with vancomycin.

6.3. Shelf life

3 years

6.4. Special precautions for storage

Store below 30°C and protect from light.

6.5. Nature and contents of container

Cefuroxime sodium powders for injection or infusion is packaged in a 10 mL Injection vials made of low borosilicate glass tubing with a halogenated butyl rubber stopper and an aluminum-plastic cap.

6.6. Instructions for use and handling

Compatibility with intravenous liquids

The following solvents are suitable for preparation of the solution:

- Water for injections

- 5% glucose solution

- Physiological sodium chloride solution.

As for all parenteral medicinal products, inspect the reconstituted solution visually for particulate matter and discoloration prior to administration. The solution should only be used if the solution is clear and practically free from particles.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Shandong Luoxin Pharmaceutical Group Stock Co., Ltd.

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8. NUMBER(S) IN THE NATIONAL REGISTER OF FINISHED PHARMACEUTICAL PRODUCTS

07430/08026/NMR/2019

9. DATE OF FIRST AUTHORISATION/RENEWALOF THE AUTHORISATION

May 28, 2022

10. DATE OF REVISION OF THE TEXT