# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE MEDICINAL PRODUCT

Cefuroxime – Fresenius 750 mg Powder for Solution for Injection

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains 750 mg of cefuroxime (as 789 mg cefuroxime sodium).

Excipients with known effect:

Each vial contains 40.63 mg of sodium

For a full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Powder for solution for injection.
White to cream coloured powder.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Cefuroxime is a bactericidal cephalosporin antibiotic which is resistant to most beta-lactamases and is active against a wide range of Gram-positive and Gram-negative organisms. It is indicated for the treatment of infections before the infecting organism has been identified or when caused by sensitive bacteria.
In addition, it is an effective prophylactic against post-operative infection in a variety of operations. Usually Cefuroxime sodium 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), especially for prophylaxis in colonic or gynaecological surgery.

Indications include:

- Respiratory tract infections for example, acute and chronic bronchitis, infected bronchiectasis, bacterial pneumonia, lung abscess and post-operative chest infections.
- Ear, nose and throat infections for example, sinusitis, tonsillitis and pharyngitis.
- Urinary tract infections for example, acute and chronic pyelonephritis, cystitis and symptomatic bacteriuria.
- Soft-tissue infections for example cellulitis, erysipelas and wound infections.
- Bone and joint infections for example, osteomyelitis and septic arthritis.
- Obstetric and gynaecological infections, pelvic inflammatory diseases.
- Gonorrhoea particularly when penicillin is unsuitable.
- Other infections including septicaemia, meningitis and peritonitis.

Prophylaxis against infection in abdominal, pelvic, orthopaedic, cardiac, pulmonary oesophageal and vascular surgery where there is increased risk from infection.

Cefuroxime is available as the axetil ester 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. Where appropriate cefuroxime sodium is effective when used prior to oral therapy with cefuroxime axetil in the treatment of pneumonia and acute exacerbations of chronic bronchitis.

## 4.2 Posology and method of administration

Cefuroxime sodium injection for i.v. and/or i.m. administration.

**General Recommendations**
*Populations*
*Adults*
Many infections respond to 750 mg t.d.s. by i.m. or i.v. injection. For more severe infections, this dose should be increased to 1500 mg t.d.s. i.v. The frequency of i.m. or i.v. injections can be increased to six hourly if necessary, giving total doses of 3g to 6g daily. Where clinically indicated, some infections respond to 750 mg or 1500 mg twice daily (i.v. or i.m.) followed by oral therapy with cefuroxime axetil.

*Infants and Children*
Doses of 30 to 100 mg/kg/day given as three or four divided doses. A dose of 60 mg/kg/day is appropriate for most infections.

Preterm (born at <36 weeks of gestation) and term newborn infants (age 0-27 days).
Cefuroxime is not recommended for the use in these age groups due to insufficient data on safety and efficacy. In the first weeks of life the serum half-life of cefuroxime can be three to five times than in adults (see section 5.2).

**Gonorrhoea**
*Populations*
*Adults*
1500 mg should be given as a single dose. This may be given as 2 x 750 mg i.m. injections into different sites, e.g. each buttock.

**Meningitis**
Cefuroxime sodium is suitable for sole therapy of bacterial meningitis due to sensitive strains.
*Populations*
*Adults*
3 g given i.v. every 8 hours.

*Infants and Children*
150 to 250 mg/kg/day given i.v. in 3 or 4 divided doses.
(Note- Dosage of 200 to 240 mg/kg/day i.v. in 3 or 4 divided doses has also been reported. This dosage may be reduced to 100 mg/kg/day i.v. after three days or when clinical improvement occurs.

**Prophylaxis**
*Populations*
*Adults*
The usual dose is 1500 mg i.v. with induction of anaesthesia for abdominal, pelvic and orthopaedic operations. This may be supplemented with two 750 mg i.m. doses 8 and 16 hours later.
In cardiac, pulmonary, oesophageal and vascular operations, the usual dose is 1500 mg given i.v. with induction of anaesthesia, continuing with 750 mg given i.m. t.d.s. for further 24 to 48 hours.
In total joint replacements, 1500 mg cefuroxime powder may be mixed dry with each pack of methyl

methacrylate cement polymer before adding the liquid monomer.

**Sequential Therapy**

*Populations*
*Adults*
Duration of both parenteral and oral therapy is determined by the severity of the infection and the clinical status of the patient.

Pneumonia: 1500 mg Cefuroxime sodium three times daily or twice daily for 48 or 72 h, followed by 500 mg twice daily cefuroxime axetil oral therapy for 7 to 10 days.

Acute exacerbations of chronic bronchitis: 750 mg Cefuroxime sodium three times daily or twice daily for 48 to 72 h, followed by 500 mg twice daily cefuroxime axetil oral therapy for 5 to 10 days.

**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 sodium should be reduced to compensate for its slower excretion.

Dosage in impaired renal function for adolescents, adults and elderly:

It is not necessary to reduce the dose if creatinine clearance is more than 20 ml/min.

In patients with markedly impaired renal function the dosage of cefuroxime should be reduced as follows:

| Creatinine clearance (ml/min) | Recommended dosage of cefuroxime (mg) | Frequency of dosage (hours) |
|---|---|---|
| > 20 | normal dosage | |
| 10-20 | 750 | 12 |
| < 10 | 750 | 24 |
| Patients on continuous arteriovenous haemofiltration/haemodialysis | 750 | 12 |

Special precautions are required if creatinine clearance is <10 ml/minute and treatment should take place under appropriate expert supervision.
Serum concentration of cefuroxime should be monitored in patients with severe renal impairment.
For patients on haemodialysis a further 750 mg dose, by intravenous or intramuscular injection, should be given at the end of each session.
In addition to parenteral use, cefuroxime can be incorporated into the peritoneal dialysis fluid (usually 250 mg for every two litres of dialysis fluid).

For low-flux haemofilration follow the dosage recommended under impaired renal function.

Infants, toddlers (28 days to 23 months) and children (2 to 11 years) with impaird renal function:
There are insufficient data regarding the use of cefuroxime in pediatric renal insufficiency and therefore such use is not recommended.

**Route of Administration:**
Cefuroxime may be administered by intramuscular injection, intravenous injection
(within 3 - 5 minutes see section 6.6).
Intramuscular administration should be limited on special indication and/or exceptional clinical

situations after benefit-risk assessment. Intramuscular administration 3 times a day is not recommended. Doses above 750 mg of cefuroxime should not be administered intramuscularly.

## 4.3 Contraindications

Hypersensitivity to cefuroxime or to any of the excipients listed in section 6.1.

Patients with known hypersensitivity to cephalosporin antibiotics.

History of severe hypersensitivity (e.g. anaphylactic reaction) to any other type of beta-lactam antibacterial agent (penicillins, monobactams and carbapenems).

## 4.4 Special warning and 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 diarrhoea 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 40.63 mg sodium per vial, equivalent to 2 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Intracameral use and eye disorders

Cefuroxime is not formulated for intracameral use. Individual cases and clusters of serious ocular adverse reactions have been reported following unapproved intracameral use of cefuroxime sodium compounded from vials approved for intravenous/intramuscular administration. These reactions included macular oedema, retinal oedema, retinal detachment, retinal toxicity, visual impairment, visual acuity reduced, vision blurred, corneal opacity and corneal oedema.

## 4.5 Interaction with other medicinal products and other forms of interaction

Cefuroxime is excreted by glomerular filtration and tubular secretion. Concomitant use of probenecid is not recommended. Concurrent administration of probenecid prolongs the excretion of the antibiotic and produces an elevated peak serum level.

**Potential nephrotoxic drugs and loop diuretics**
High-dosage treatments with cephalosporins should be carried out with caution on patients who are taking strong-acting diuretics (such as furosemide) or potential nephrotoxic preparations (such as aminoglycoside antibiotics), since impairment of renal function through such combinations cannot be ruled out.

**Other Interactions**
Determination of blood/plasma glucose levels: refer to section 4.4.
Concomitant use with oral anticoagulants may give rise to increased international normalised ratio (INR).

## 4.6 Fertility, pregnancy and lactation

Pregnancy
There are limited amounts of data from the use of cefuroxime in pregnant women. Studies in animals have shown no reproductive toxicity (see section 5.3). 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.

Fertility
There are no data on the effects of cefuroxime sodium on fertility in humans. Reproductive studies in animals have shown no effects on fertility.

### 4.7 Effects on ability to drive and use machines

No studies on the effects of cefuroxime 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

The most common adverse reactions are neutropenia, eosinophilia, transient rise in liver enzymes or bilirubin, particularly in patients with pre-existing liver disease, but there is no evidence of harm to the liver and injection site reactions.

The frequency categories assigned to the adverse reactions below are estimates, as for most reactions suitable data for calculating incidence are not available. In addition the incidence of adverse reactions associated with cefuroxime sodium may vary according to the indication.

Data from clinical trials were used to determine the frequency of very common to rare adverse reactions. The frequencies assigned to all other adverse reactions (i.e. those occurring at <1/10,000) were mainly determined using post-marketing data, and refer to a reporting rate rather than a true frequency.

Treatment related adverse reactions, all grades, are listed below by MedDRA body system organ class, frequency and grade of severity. The following convention has been utilised for the classification of frequency: very common ≥ 1/10; common ≥ 1/100 to < 1/10, uncommon ≥ 1/1,000 to < 1/100; rare ≥ 1/10,000 to < 1/1,000; very rare < 1/10,000 and not known (cannot be estimated from the available data).

| System organ class | Common | Uncommon | Not known |
|---|---|---|---|
| Blood and lymphatic system disorders | Eosinophilia, Neutropenia, Decreased haemoglobin Concentration | Leucopenia, positive Coomb' s test | thrombocytopenia. haemolytic anaemia. |
| Gastrointestinal disorders | | Gastrointestinal disturbance | Pseudomonas colitis (see section 4.4) |
| Renal and urinary disoders | | | Elevations in serum creatinine . elevations in blood urea nitrogen and decreased creatinine clearance (see section 4.4) |
| Skin and subcutaneous tissue disorders | | Skin rashes, urticaria, pruritus | Erythema multiforme, toxic epidermal necrolysis and stevens -Johnson syndrome , angioneurotic oedema |

| | | | |
|---|---|---|---|
| **Infections and infestations** | | | Candida overgrowth. Overgrowth of Clostridium difficile |
| **General disorders and administration site conditions** | Injection site reactions which may include pain and thrombophlebitis | | |
| **Immune system disorders** | | | drug fever , interstitial nephritis, anaphylaxis,Cutaneous vasculitis |
| **Hepatobiliary disorders** | Transient rise in liver enzymes | Transient rise in bilirubin | |

*Description of selected adverse reactions*

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.

Transient rises in serum liver enzymes or bilirubin have been observed which are usually reversible.

Pain at the intramuscular injection site is more likely at higher doses. However it is unlikely to be a cause for discontinuation of treatment.

*Pediatric population*

The safety profile for cefuroxime sodium in children is consistent with the profile in adults.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form:https://sideeffects.health.gov.il and emailed to the Registration Holder's Patient Safety Unit at:drugsafety@neopharmgroup.com

### 4.9 Overdose

Overdose can lead to neurological sequelae including encephalopathy, convulsions and coma . Symptoms of overdose can occur if the dose is not reduced appropriately in patients with renal impairment (see sections 4.2 and 4.4).

Serum levels of cefuroxime can be reduced by haemodialysis or peritoneal dialysis.

## 5.0 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

**General properties:**
Pharmacotherapeutic group: antibacterials for systemic use, second-generation cephalosporines, ATC-code: J01D C02.

Mechanism of action

Cefuroxime inhibits bacterial cell wall synthesis following attachment to penicillin binding proteins (PBPs). This results in the interruption of cell wall (peptidoglycan) biosynthesis, which leads to bacterial cell lysis and death.

Mechanism of resistance

Bacterial resistance to cefuroxime may be due to one or more of the following mechanisms:

- hydrolysis by beta-lactamases including (but not limited to) extended-spectrum beta-lactamases (ESBLs) and Amp-C enzymes that may be induced or stably depressed in certain aerobic Gram-negative bacterial species
- reduced affinity of penicillin-binding proteins for cefuroxime
- outer membrane impermeability, which restricts access of cefuroxime to penicillin binding proteins in Gram-negative organisms
- bacterial efflux pumps

Organisms that have acquired resistance to other injectable cephalosporins are expected to be resistant to cefuroxime. Depending on the mechanism of resistance, organisms with acquired resistance to penicillins may demonstrate reduced susceptibility or resistance to cefuroxime.

Cefuroxime sodium breakpoints

Minimum inhibitory concentration (MIC) breakpoints established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) are as follows (Version 6.0, valid from 2016-01-01):

| **Microorganism** | **Breakpoints (mg/L)** | |
|---|---|---|
| | Susceptible | Resistant |
| *Enterobacteriaceae*[1] | ≤8[2] | >8[2] |
| *Staphylococcus* spp. | Note[3] | Note[3] |
| *Streptococcus* A, B, C and G | Note[4] | Note[4] |
| *Streptococcus pneumoniae* | ≤0.5 | >1 |
| *Viridans group streptococci* | ≤0.5 | >0.5 |
| *Haemophilus influenzae* | ≤1 | >2 |
| *Moraxella catarrhalis* | ≤4 | >8 |
| Non-species related breakpoints | ≤4 | >8 |

[1] The cephalosporin breakpoints for *Enterobacteriaceae* will detect all clinically important resistance mechanisms (including ESBL and plasmid mediated AmpC). Some isolates that produce beta-lactamases are susceptible or intermediate to 3rd or 4th generation cephalosporins with these breakpoints and should be reported as tested i.e. the presence or absence of an ESBL does not in itself influence the categorization of susceptibility. ESBL detection and characterization are recommended for public health and infection control purposes.

[2] Breakpoints are based to high dose therapy (1.5 g × 3) and relate to *E. coli, Klebsiella spp. and P. mirabilis* only

[3] Susceptibility of staphylococci to cephalosporins is inferred from the cefoxitin susceptibility except for cefixime, ceftazidime, ceftibuten and ceftolozane-tazobactam, which do not have breakpoints and should not be used for staphylococcal infections. Some methicillin-resistant S. aureus are susceptible to ceftaroline and ceftobiprole.

[4] The susceptibility of streptococcus groups A, B, C and G to cephalosporins is inferred from the benzylpenicillin susceptibility.

Microbiological susceptibility

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. As necessary, expert advice should be sought when the local prevalence of resistance is known and the utility of the agent in at least some types of infections is questionable.

Cefuroxime is usually active against the following microorganisms *in vitro.*

| **Commonly susceptible species** |
|---|
| Gram-positive aerobes:<br>*Staphylococcus aureus (methicillin-susceptible)* $<br>*Streptococcus pyogenes*<br>*Streptococcus agalactiae* |
| Gram-negative aerobes:<br>*Haemophilus parainfluenzae*<br>*Moraxella catarrhalis* |
| **Microorganisms for which acquired resistance may be a problem** |
| Gram-positive aerobes:<br>*Streptococcus pneumoniae*<br>*Streptococcus mitis* (viridans group) |
| Gram-negative aerobes:<br>*Citrobacter* spp. not including *C. freundii*<br>*Enterobacter* spp. not including *E. aerogenes* and *E. cloacae*<br>*Escherichia coli*<br>*Haemophilus influenzae*<br>*Klebsiella pneumoniae*<br>*Proteus mirabilis*<br>*Proteus* spp. not including *P. penneri* and *P. vulgaris*<br>*Providencia* spp.<br>*Salmonella* spp. |
| Gram-positive anaerobes:<br>*Peptostreptococcus* spp.<br>*Propionibacterium* spp. |
| Gram-negative anaerobes:<br>*Fusobacterium* spp.<br>*Bacteroides* spp. |
| **Inherently resistant microorganisms** |

| |
|---|
| Gram-positive aerobes:<br>*Enterococcus faecalis*<br>*Enterococcus faecium* |
| Gram-negative aerobes:<br>*Acinetobacter* spp.<br>*Burkholderia cepacia*<br>*Campylobacter* spp.<br>*Citrobacter freundii*<br>*Enterobacter aerogenes*<br>*Enterobacter cloacae*<br>*Morganella morganii*<br>*Proteus penneri*<br>*Proteus vulgaris*<br>*Pseudomonas aeruginosa*<br>*Serratia marcescens*<br>*Stenotrophomonas maltophilia* |
| Gram-positive anaerobes:<br>*Clostridium difficile* |
| Gram-negative anaerobes:<br>*Bacteroides fragilis* |
| Others:<br>*Chlamydia* spp.<br>*Mycoplasma* spp.<br>*Legionella* spp. |

$ All methicillin-resistant *S. aureus* are resistant to cefuroxime.

*In vitro* the activities of cefuroxime sodium and aminoglycoside antibiotics in combination have been shown to be at least additive with occasional evidence of synergy.

## 5.2 Pharmacokinetic properties

Absorption

After intramuscular (IM) injection of cefuroxime to normal volunteers, the mean peak serum concentrations ranged from 27 to 35 μg/mL for a 750 mg dose and from 33 to 40 μg/mL for a 1000 mg dose, and were achieved within 30 to 60 minutes after administration. Following intravenous (IV) doses of 750 and 1500 mg, serum concentrations were approximately 50 and 100 μg/mL, respectively, at 15 minutes.

AUC and $C_{max}$ appear to increase linearly with increase in dose over the single dose range of 250 to 1000 mg following IM and IV administration. There was no evidence of accumulation of cefuroxime in the serum from normal volunteers following repeat intravenous administration of 1500 mg doses every 8 hours.

Distribution

Protein binding has been stated as 33 to 50%, depending on the methodology used. The average volume of distribution ranges from 9.3 to 15.8 L/1.73 $m^2$ following IM or IV administration over the dosage range of 250 to 1000 mg. Concentrations of cefuroxime in excess of the minimum inhibitory levels for common pathogens can be achieved in the tonsilla, sinus tissues, bronchial mucosa, bone, pleural fluid, joint fluid, synovial fluid, interstitial fluid, bile, sputum and aqueous humour. Cefuroxime passes the blood-brain barrier when the meninges are inflamed.

Biotransformation

Cefuroxime is not metabolised.

Elimination

Cefuroxime is excreted unchanged by glomerular filtration and renal tubular secretion. The serum half-life after either intramuscular or intravenous injection is approximately 70 minutes. There is an almost complete recovery (85 to 90%) of unchanged cefuroxime in urine within 24 hours of administration. The majority of the cefuroxime is excreted within the first 6 hours. The average renal clearance ranges from 114 to 170 mL/min/1.73 $m^2$ following IM or IV administration over the dosage range of 250 to 1000 mg.

***Special patient populations***

Gender

No differences in the pharmacokinetics of cefuroxime were observed between males and females following a single IV bolus injection of 1000 mg of cefuroxime as the sodium salt.

Elderly

Following IM or IV administration, the absorption, distribution and excretion of cefuroxime in elderly patients are similar to younger patients with equivalent renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in cefuroxime dose selection, and it may be useful to monitor renal function (see section 4.2).

Paediatric population

The serum half-life of cefuroxime has been shown to be substantially prolonged in neonates according to gestational age. However, in older infants (aged >3 weeks) and in children, the serum half-life of 60 to 90 minutes is similar to that observed in adults.

Renal impairment

Cefuroxime is primarily excreted by the kidneys. As with all such antibiotics, in patients with markedly impaired renal function (i.e. $C1_{cr}$ <20 mL/minute) it is recommended that the dosage of cefuroxime should be reduced to compensate for its slower excretion (see section 4.2). Cefuroxime is effectively removed by haemodialysis and peritoneal dialysis.

Hepatic impairment

Since cefuroxime is primarily eliminated by the kidney, hepatic dysfunction is not expected to have an effect on the pharmacokinetics of cefuroxime.

PK/PD relationship

For cephalosporins, the most important pharmacokinetic-pharmacodynamic index correlating with *in vivo* efficacy has been shown to be the percentage of the dosing interval (%T) that the unbound concentration remains above the minimum inhibitory concentration (MIC) of cefuroxime for individual target species (i.e. %T>MIC).

## 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.

Gamma glutamyl transpeptidase activity in rat urine is inhibited by various cephalosporins, however the level of inhibition is less with cefuroxime. This may have significance in the interference in clinical laboratory tests in humans.

## 6.0 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

None.

### 6.2 Incompatibilities

This medicinal product must not be mixed with aminoglycoside antibiotics.

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

During intravenous administration cefuroxime should not be mixed with solutions containing other active substances.

### 6.3 Shelf life

*Unopened vials*: The expiry date of the product is indicated on the packaging materials.

*After reconstitution:* chemical and physical in-use stability has been demonstrated for 5 hours at 2ºC to 8ºC.

From a microbiological point of view, the product should be used immediately.
If not used immediately, in-use storage times and conditions are the responsibility of the user.

### 6.4 Special precautions for storage

Store below 25ºC.

Keep the vials in the outer carton in order to protect from light.

For storage conditions of the reconstituted medicinal product, see section 6.3.

### 6.5 Nature and contents of container

15 ml type II colourless glass vials closed with rubber stoppers covered with aluminium seals with plastic flip off caps.
Pack sizes:
1 vial
10 vials
50 vials

Not all the pack sizes may be marketed

### 6.6 Special precaution for disposal

**Compatibility with intravenous solutions**

Cefuroxime sodium is compatible with the following infusion fluids. It will remain potency for up to 5 hours at 2°C to 8°C in:

- water for injections
- 0.9 % sodium chloride solution

From a microbiological point of view, the product should be used immediately.

If not used immediately, in-use storage times and conditions are the responsibility of the user.

**Instructions for reconstitution**

Cefuroxime – Fresenius 750 mg powder for solution for injection as intravenous injection:
Dissolve Cefuroxime – Fresenius 750 mg powder for solution for injection, in 6 ml of water for injection or 0.9% sodium chloride solution.

Cefuroxime – Fresenius 750 mg powder for solution for injection as intramuscular injection:
Dissolve Cefuroxime – Fresenius 750 mg powder for solution for injection, in 3 ml of water for injection or 0.9% sodium chloride solution.

Shake gently to produce a clear solution.

The contents and concentrations of cefuroxime as solution are shown in the table below:

| mg cefuroxime per vial | Intravenous injection<br><br>addition of ml solvent | Intramuscular injection<br><br>addition of ml solvent | Final volume ml | Concentration mg/ml |
|---|---|---|---|---|
| 750<br>750 | -<br>6 | 3<br>- | 3.5<br>6.7 | 214<br>112 |

Note: Intravenous Cefuroxime injection should be given over 3-5 minutes.

The powder is white to cream coloured. The reconstituted solution is clear and colourless to yellowish.

The reconstituted solution is for single use only and is to be inspected visually for particulate matter and discoloration prior to administration.

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

**7.MARKETING AUTHORISATION HOLDER**

Neopharm (Israel) 1996 Ltd
Hashiloach 6, POB 7063 Petach Tiqva 4917001

**8. MANUFACTURER**

Labesfal - Laboratorios Almiro S.A Fresenius Kabi Group
Lagedo, 3465-157 Santiago De Besteiros, Portugal

**9. MARKETING AUTHORISATION NUMBER**

149 07 33467 00

10.Revised in sep 2022 according to the MOH guidelines.