SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Cefuroxime 750 mg powder for solution for injection/infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

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

Sodium content per vial: 40.6 mg (equivalent to 1.8 mmol)

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder for solution for injection/infusion.

White or almost white powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Cefuroxime 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 exacerbations 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

Table 1. Adults and children ≥ 40 kg

Indication	Dosage
Community acquired pneumonia and acute exacerbations of chronic bronchitis	750 mg every 8 hours (intravenously or intramuscularly)
Soft-tissue infections: cellulitis, erysipelas and wound infections.	
Intra-abdominal infections	
Complicated urinary tract infections, including pyelonephritis	1500 mg every 8 hours (intravenously or intramuscularly)
Severe infections	750 mg every 6 hours (intravenously) 1500 mg every 8 hours (intravenously)
Surgical prophylaxis for gastrointestinal, gynaecological surgery (including caesarean section) and orthopaedic operations	1500 mg with the induction of anaesthesia. This may be supplemented with two 750 mg doses (intramuscularly) after 8 hours and 16 hours
Surgical prophylaxis for cardiovascular and oesophageal operations	1500 mg with induction of anaesthesia followed by 750 mg (intramuscularly) every 8 hours for a further 24 hours

Table 2. Children < 40 kg

	Infants and toddlers > 3 weeks and children < 40 kg	**Infants (birth to 3 weeks)**
Community acquired	30 to 100 mg/kg/day (intravenously) given	30 to 100 mg/kg/day (intravenously) given

pneumonia	as 3 or 4 divided doses; a dose of 60 mg/kg/day is appropriate for most infections	as 2 or 3 divided doses (see section 5.2)
Complicated urinary tract infections, including pyelonephritis		
Soft-tissue infections: cellulitis, erysipelas and wound infections		
Intra-abdominal infections		

Patients with renal impairment

Cefuroxime is primarily 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.

Table 3. Recommended doses for Cefuroxime in renal impairment

Creatinine clearance	**$T_{1/2}$ (hours)**	**Dose (mg)**
> 20 ml/min/1.73 m^2	1.7-2.6	It is not necessary to reduce the standard dose (750 mg to 1500 mg three times daily)
10-20 ml/min/1.73 m^2	4.3-6.5	750 mg twice daily
< 10 ml/min/1.73 m^2	14.8-22.3	750 mg once daily
Patients on haemodialysis	3.75	A further 750 mg dose should be given intravenously or intramuscularly at the end of each dialysis; in addition to parenteral use, cefuroxime sodium can be incorporated into the peritoneal dialysis fluid (usually 250 mg for every 2 litres of dialysis fluid)
Patients in renal failure on continuous arteriovenous haemodialysis (CAVH) or high-flux haemofiltration (HF) in intensive therapy units	7.9-12.6 (CAVH) 1.6 (HF)	750 mg twice daily; for low-flux haemofiltration follow the dosage recommended under impaired renal function.

Patients with hepatic impairment

Cefuroxime is primarily eliminated by the kidney. In patients with hepatic dysfunction this is not expected to affect the pharmacokinetics of cefuroxime.

Method of administration

Cefuroxime should be administered by intravenous injection over a period of 3 to 5 minutes directly into a vein or via a drip tube or infusion over 30 to 60 minutes, or by deep intramuscular injection.

Intramuscular injections should be injected well within the bulk of a relatively large muscle and not more than 750 mg should be injected at one site.

Caution is required when 1500 mg as a unit dose is administered by intramuscular injection: 2 doses of 750 mg should be injected, each one in a separate site.

For doses greater than 1500 mg intravenous administration should be used.

If the solvent used for reconstitution of cefuroxime for intramuscular injection is lidocaine, the reconstituted medicinal product should never be administered intravenously (see section 4.3). The information in the Summary of Product Characteristics of lidocaine should be considered.

After addition of the specified amount of diluent for intramuscular injection, a suspension is formed. The colour of suspension is almost white to yellowish-white.

After addition of the specified amount of diluent for intravenous injection or infusion, a clear yellowish solution is formed. The intensity of colour of the solution after reconstitution/dilution may vary, depending on the duration of storage and concentration, but this does not affect the efficacy of the medicinal product (see section 6.6).

For instructions on reconstitution/dilution of the medicinal product before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to cefuroxime.

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).

Contraindications to lidocaine must be excluded before intramuscular injection of cefuroxime when lidocaine solution is used as a solvent (see section 4.4). See information in the Summary of Product Characteristics of lidocaine, especially contraindications. Lidocaine should never be administered intravenously.

4.4 Special warnings and precautions for use

Hypersensitivity reactions

As with all beta-lactam antibacterial agents, serious and occasionally fatal hypersensitivity reactions have been reported. There have been reports of hypersensitivity reactions which progressed to Kounis syndrome (acute allergic coronary arteriospasm that can result in myocardial infarction, see section 4.8). 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.

Severe cutaneous adverse reactions (SCARS)

Severe cutaneous adverse reactions including: Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and drug reaction with eosinophilia and systemic symptoms (DRESS), which can be life-threatening or fatal, have been reported in association with cefuroxime treatment (see section 4.8).

At the time of prescription patients should be advised of the signs and symptoms and monitored closely for skin reactions. If signs and symptoms suggestive of these reactions appear, cefuroxime should be withdrawn immediately and an alternative treatment considered. If the patient has developed a serious reaction such as SJS, TEN or DRESS with the use of cefuroxime, treatment with cefuroxime must not be restarted in this patient at any time.

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 *Clostridioides 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 *Clostridioides difficile* should be considered. Medicinal products that inhibit peristalsis should not be given.

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.

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 Coombs 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.

Use of lidocaine

In case a lidocaine solution is used as a solvent, reconstituted medicinal product must only be used for intramuscular injection. Contraindications to lidocaine, warnings and other relevant information as detailed in the Summary of Product Characteristics of lidocaine must be considered before use (see section 4.3). Lidocaine should never be administered intravenously.

Sodium

This medicinal product contains 40.6 mg sodium per vial, equivalent to 2 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

4.5 Interaction with other medicinal products and other forms of interaction

Cefuroxime may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral contraceptives.

Cefuroxime is excreted by glomerular filtration and tubular secretion. Concomitant use of probenicid 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.

Breast-feeding

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), not known (cannot be estimated from the available data).

Table 4. Tabulated list of adverse reactions

System organ class	Common	Uncommon	Not known
Infections and infestations			*Candida* overgrowth *Clostridioides difficile* overgrowth
Blood and lymphatic system disorders	Neutropenia Eosinophilia Decreased haemoglobin concentration	Leukopenia Positive Coombs test	Thrombocytopenia Haemolytic anaemia

Immune system disorders			Drug fever Interstitial nephritis Anaphylaxis Cutaneous vasculitis
Cardiac disorders			Kounis syndrome
Gastrointestinal disorders		Gastrointestinal disturbance	Pseudomembranous colitis (see section 4.4)
Hepatobiliary disorders	Transient rise in liver enzymes	Transient rise in bilirubin	
Skin and subcutaneous tissue disorders		Skin rash Urticaria Pruritus	Erythema multiforme Toxic epidermal necrolysis Stevens-Johnson syndrome Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) Angioneurotic oedema
Renal and urinary disorders			Elevations in serum creatinine Elevations in blood urea nitrogen Decreased creatinine clearance (see section 4.4)
General disorders and administration site conditions	Injection site reactions which may include pain and thrombophlebitis		

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 Coombs 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.

Paediatric 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. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antibacterials for systemic use, second-generation cephalosporins, ATC code: J01DC02

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 derepressed 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 bacteria;
- 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.

Susceptibility testing breakpoints
Minimum inhibitory concentration (MIC) breakpoints established by EUCAST (The European Committee on Antimicrobial Susceptibility Testing) are listed on the EMA (European Medicines Agency) website:

https://www.ema.europa.eu/en/evaluation-medicinal-products-indicated-treatment-bacterial-infections-scientific-guideline#minimum-inhibitory-concentration-(mic)-breakpoints-section.

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
Staphylococcus aureus (methicillin-susceptible)[£]
Streptococcus pyogenes
Streptococcus agalactiae

Gram-negative aerobes
Haemophilus parainfluenzae
Moraxella catarrhalis

Species for which acquired resistance may be a problem
Gram-positive aerobes
Streptococcus pneumoniae
Streptococcus mitis (viridans group)

Gram-negative aerobes
Citrobacter spp. not including *C. freundii*
Enterobacter spp. not including *E. aerogenes* and *E. cloacae*
Escherichia coli
Haemophilus influenzae
Klebsiella pneumoniae
Proteus mirabilis
Proteus spp. not including *P. penneri and P. vulgaris*
Providencia spp.
Salmonella spp.

Gram-positive anaerobes
Peptostreptococcus spp.
Propionibacterium spp.

Gram-negative anaerobes
Fusobacterium spp.
Bacteroides spp.

Inherently resistant organisms
Gram-positive aerobes
Enterococcus faecalis
Enterococcus faecium

Gram-negative aerobes

Acinetobacter spp.
Burkholderia cepacia
Campylobacter spp.
Citrobacter freundii
Enterobacter aerogenes
Enterobacter cloacae
Morganella morganii
Proteus penneri
Proteus vulgaris
Pseudomonas aeruginosa
Serratia marcescens
Stenotrophomonas maltophilia

Gram-positive anaerobes
Clostridioides difficile

Gram-negative anaerobes
Bacteroides fragilis

Others
Chlamydia spp.
Mycoplasma spp.
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 healthy volunteers, the mean peak serum concentrations ranged from 27 to 35 micrograms/ml for a 750 mg dose and from 33 to 40 micrograms/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 micrograms/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 healthy 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 by glomerular filtration and 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 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.

Patients with renal impairment

Cefuroxime is primarily excreted by the kidneys. As with all such antibiotics, in patients with markedly impaired renal function (i.e. Cl_{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.

Patients with hepatic impairment

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

Pharmacokinetic/pharmacodynamic 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 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

None.

6.2 Incompatibilities

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

6.3 Shelf life

18 months.

Intravenous or intramuscular injection

Shelf life after reconstitution in vial:

Chemical and physical in-use stability has been demonstrated for 6 hours at 25 °C and 72 hours at 2 to 8 °C, when reconstituted with water for injection (see section 6.6).

From a microbiological point of view, the reconstituted product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 °C, unless reconstitution has taken place in controlled and validated aseptic conditions.

Intravenous infusion

The reconstituted solution should be diluted immediately after reconstitution.

Shelf life after reconstitution and dilution:

Chemical and physical in-use stability of the diluted reconstituted solution has been demonstrated for 6 hours at 25 °C and 72 hours at 2 to 8 °C, when using one of the compatible solvents for further dilution (see section 6.6).

From a microbiological point of view, the diluted product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 °C, unless reconstitution/dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Do not store above 25 °C.

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

For storage conditions after reconstitution/dilution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

10 ml colourless glass vial with bromobutyl rubber stopper sealed with aluminium seal and blue plastic flip-off cap.

The vials are placed into outer cartons.

Pack sizes: 1 or 10 vials

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

For single use only.

Instructions for reconstitution

Table 5. Additional volumes and concentrations, which may be useful when fractional doses are required.

	Additional volumes and concentrations, which may be useful when fractional doses are required			
Vial size	Routes of administration	Physical state	Amount of water for injections to be added (ml)	Approximate cefuroxime concentration (mg/ml)**
750 mg	intramuscular intravenous bolus intravenous infusion	suspension solution solution	3 ml at least 6 ml at least 6 ml*	234 122 122
1500 mg	intravenous bolus intravenous infusion intramuscular could also be given if necessary ***	solution solution suspension	at least 15 ml 15 ml* 6 ml	99 99 238

* *Reconstituted solution to be added to 50 or 100 ml of compatible infusion solution (see information on compatibility, below).*
** *The resulting volume of the solution of cefuroxime in reconstitution medium is increased due the displacement factor of the drug substance resulting in the listed concentrations in mg/ml.*
*** *The method of preparation of both doses of 750 mg to be administered at a same period of time should be in accordance with standard quality requirements (see section 4.2).*

Compatibility
1500 mg cefuroxime sodium constituted with 15 ml water for injection may be added to metronidazole injection (500 mg/100 ml).
1500 mg cefuroxime sodium is compatible with azlocillin 1 g (in 15 ml) or 5 g (in 50 ml).
Cefuroxime sodium (5 mg/ml) in 5 % or 10 % xylitol injection may be used.

Cefuroxime sodium is compatible with aqueous solutions containing up to 1 % lidocaine hydrochloride (for intramuscular injection only). Lidocaine should never be administered intravenously.

Cefuroxime sodium is compatible with the following infusion fluids:
- 9 mg/ml (0.9 %) sodium chloride solution
- 50 mg/ml (5 %) glucose solution
- 40 mg/ml (4 %) glucose solution and 1.8 mg/ml (0.18 %) sodium chloride solution
- 50 mg/ml (5 %) glucose solution and 9 mg/ml (0.9 %) sodium chloride solution
- 50 mg/ml (5 %) glucose solution and 4.5 mg/ml (0.45 %) sodium chloride solution
- 50 mg/ml (5 %) glucose solution and 2.25 mg/ml (0.225 %) sodium chloride solution
- 100 mg/ml (10 %) glucose solution
- lactated Ringer's solution (Hartmann’s solution)

The stability of cefuroxime sodium in 9 mg/ml (0.9 %) sodium chloride solution and in 50 mg/ml (5 %) glucose solution is not affected by the presence of hydrocortisone sodium phosphate.

Cefuroxime sodium has also been found compatible when admixed in IV infusion with:
- heparin (10 and 50 units/ml) in 9 mg/ml (0.9 %) sodium chloride solution for infusion
- potassium chloride (10 and 40 mEq/l) in 9 mg/ml (0.9 %) sodium chloride solution for infusion

After addition of the specified amount of diluent for intramuscular injection, a suspension is formed. The colour of suspension is almost white to yellowish-white.

After addition of the specified amount of diluent for intravenous injection or infusion, a clear yellowish solution is formed. The intensity of colour of the solution after reconstitution/dilution may vary, depending on the duration of storage and concentration, but this does not affect the efficacy of the medicinal product. The solution should be visually inspected prior to use. Only clear, yellowish solutions free from particles should be used.

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

7 MARKETING AUTHORISATION HOLDER

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