Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Cefotaxime 2 g Powder for Solution for Injection.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 2 g vial contains 2 g cefotaxime (as cefotaxime sodium).

Sodium content: 96 mg/vial.

3 PHARMACEUTICAL FORM

Powder for solution for injection or infusion.

Description: Sterile, crystalline, white to slightly yellow powder for solution for injection or infusion.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Cefotaxime is indicated for the treatment of the following severe infections when known or thought very likely to be due to bacteria that are susceptible to cefotaxime (see section 5.1):

- Bacterial pneumonia
- Complicated infections of the kidneys and upper urinary tract
- Severe infections of the skin and soft tissue
- Genital infections including Gonorrhea
- Intra-abdominal infections (such as peritonitis) (see section 4.2)
- Acute bacterial meningitis
- Treatment of patients with bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Cefotaxime may be administered by intravenous bolus injection, by intravenous infusion, or by intramuscular injection, after reconstitution of the solution according to the directions given below. Dosage and mode of administration should be determined by the severity of the infection, susceptibility of the causative organism and the patient's condition. Therapy may be started before the result of sensitivity tests are known.
Cefotaxime has synergistic effects with aminoglycosides.

Adults and children over 12 years:

The usual dose in adults is 2 to 6 g daily. The daily dosage should be divided. However, dosage may be varied according to the severity of the infection, sensitivity of causative organisms and condition of the patient.
Guidelines for dosage

Typical infection in presence (or suspicion) of a sensible micro-organism: 1 g every 12 hours corresponding to a total daily dosage of 2 g intramuscularly or intravenously.

Infection in presence (or suspicion) of sensible or moderately sensible multiple micro-organisms: *1* -2 g every 12 hours corresponding to a total daily dosage of 2 - 4 g.

Severe infection by unidentified micro-organisms or for infections that can not be localised*:* 2-3 g as a single dose every 6 to 8 hours up to a maximum daily dosage of
12 g.

A combination of Cefotaxime and other antibiotics is indicated in severe infections.

Infants and children (1 month to 12 years of age):

The usual dosage for infants and children is < 50kg is 50 - 150 mg/kg/day in 2 to 4 divided doses. In very severe infections up to 200 mg/kg/day in divided doses may be required. In infants and children >50kg the usual dose in adults, without exceeding the maximum daily dose of 12 g should be given.

New born infants and premature infants:

The recommended dosage is 50 mg/kg/day in 2 to 4 divided doses.
In case of life-threatening situations it may be necessary to increase the daily dose. In severe infections 150 – 200 mg/kg/day have been given: In those situations the following table may serve as a guide, since there are differences in kidney maturation.

Age	Daily dose of Cefotaxime
0-7 days	50 mg/kg every 12 h
8 days-1 month	50 mg/kg every 8 h

Elderly:

No dosage adjustment is required, provided that renal and hepatic function are normal.

Other recommendations:

Gonorrhoea:
For gonorrhoea, a single injection (intramuscularly or intravenously) of 0.5 g to 1 g Cefotaxime. For complicated infections consideration should be given to available official guidance. Syphilis should be excluded before initiating the treatment.

Urinary tract infections:
In uncomplicated UTI 1 g every 12 hours.

Bacterial meningitis:
In adults daily doses of 6 to 12 g and in children daily doses of 150 to 200 mg/kg divided in equal doses every 6 to 8 hours are recommended. For the new-born, 50mg/kg of cefotaxime can be given every 12 h to infants 0-7 of age and every 8 h to those 7-28 days of age.

Intraabdominal infections:
Intraabdominal infection should be treated with Cefotaxime in combination with other appropriate antibiotics that are active against anaerobic bacteria.

Duration of therapy:

The duration of therapy with Cefotaxime depends on the clinical condition of the patient and varies according to the course of the disease. Administration of Cefotaxime should be continued until symptoms have subsided or evidence of bacterial eradication has been obtained. Treatment over at least 10 days is necessary in infections caused by Streptococcus pyogenes (Parenteral therapy may be switched to an adequate oral therapy before the end of the 10 days period).

Dosage in renal functional impairment:

In adult patients with a creatinine clearance of ≤ 5 ml/min, the initial dose is similar to the recommended usual dose but the maintenance dose should be halved without change in the frequency of dosing.

Dosage in dialysis or peritoneal dialysis:

In patients on hemodialysis and peritoneal dialysis an i.v. injection of 0.5 g- 2 g, given at the end of each dialysis session and repeated every 24 hours, is sufficient to treat most infections efficaciously.

Method of administration:

In order to prevent any risk of infection, the preparation of the infusion should be done in close aseptic conditions. Do not delay the infusion after the preparation of the solution.

Cefotaxime and aminoglycosides should not be mixed in the same syringe or perfusion fluid.

- Intravenous infusion:

  For *short intravenous infusion* 1 g or 2 g Cefotaxime should be dissolved in 40-50 ml Water for Injections or in another compatible fluid (e.g. glucose 10%). After preparation the solution should be given as a 20 minute intravenous infusion.

  For *long lasting intravenous infusion* 2g Cefotaxime should be dissolved in 100 ml of a suitable fluid e.g. 0.9 % sodium chloride or isotonic glucose solution or other compatible fluids for infusions. After preparation, the solution may be given as a 50-60 minute intravenous infusion.

- Intravenous injection:

  For intravenous injection Cefotaxime 0.5g should be dissolved in 2 ml Water for Injections, Cefotaxime 1g should be dissolved in 4 ml Water for Injections, Cefotaxime 2g should dissolved in 10 ml Water for Injections and should be injected over a period of 3-5 minutes. During post-marketing surveillance, potentially life-threatening arrhythmia has been reported in a very few patients who received rapid intravenous administration of cefotaxime through a central venous catheter.

- Intramuscular injection:

  Cefotaxime 0.5g is dissolved in the 2 ml Water for Injections or Cefotaxime 1.0g is dissolved in the 4 ml Water for Injections. The solution should be administered by deep intramuscular injection. In order to prevent pain from injection Cefotaxime 0.5g may be dissolved in the 2 ml 1 % Lidocaine Hydrochloride or Cefotaxime 1.0g may be dissolved in the 4 ml 1 % Lidocaine Hydrochloride (only for adults). Solutions with lidocaine must *not* be administered intravenously. If the total daily dose is more than 2 g, the intravenous administration should be chosen. In the case of severe infections, intramuscular injection is not recommended. The product information of the chosen lidocain-containing medicinal product must be regarded.

The following table shows the volume of dilution for each vial size

	Method of administration			
Vial size	Short intravenous Infusion	Long lasting intravenous infusion	Intravenous injection	Intramuscular injection
0.5 g	-	-	2ml	2ml
1 g	40-50ml	-	4ml	4ml
2 g	40-50ml	100ml	10ml	-

4.3 Contraindications

- Hypersensitivity to the active substance cefotaxime or to any of the excipients listed in section 6.1
- Hypersensitivity to cephalosporins.
- Previous immediate and/or severe hypersensitivity reaction to a penicillin or to any other type of beta-lactam drug (see also section 4.4).

4.4 Special warnings and precautions for use

As with other broad-spectrum antibiotics, prolonged use may result in the overgrowth of non-susceptible organisms. Repeated evaluation of the patient's condition is essential.. If super-infection occurs during treatment, specific anti-microbial therapy should be instituted if considered clinically necessary.

* Anaphylactic 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 cefotaxime 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 cefotaxime, to other cephalosporins or to any other type of beta-lactam agent. Caution should be used if cefotaxime is given to patients with a history of non-severe hypersensitivity to other beta-lactam agents.

* Serious bullous reactions

Cases of serious bullous skin reactions like Stevens-Johnson syndrome or toxic epidermal necrolysis have been reported with cefotaxime (see section 4.8). Patients should be advised to contact their doctor immediately prior to continuing treatment if skin and/or mucosal reactions occur.

- Clostridium difficile associated disease (e.g. pseudomembranous colitis)

Diarrhea, particularly if severe and/or persistent, occurring during treatment or in the initial weeks following treatment, may be symptomatic of *Clostridium difficile* associated disease (CDAD). CDAD may range in severity from mild to life threatening, the most severe form of which is pseudo-membranous colitis.
The diagnosis of this rare but possibly fatal condition can be confirmed by endoscopy and/or histology.
It is important to consider this diagnosis in patients who present with diarrhoea during or subsequent to the administration of cefotaxime.
If a diagnosis of pseudomembranous colitis is suspected, cefotaxime should be stopped immediately and appropriate specific antibiotic therapy should be started without delay.
Clostridium difficile associated disease can be favoured by faecal stasis.
Medicinal products that inhibit peristalsis should not be given.

* Haematological reactions

Since Leukopenia, neutropenia and, more rarely, agranulocytosis may develop during treatment with cefotaxime, blood count should be monitored if treatment lasts for longer than 7 days. In case of neutropenia (< 1400 neutrophils/mm^3), treatment should be stopped.
Some cases of eosinophilia and thrombocytopenia, rapidly reversible on stopping treatment, have been reported. Cases of haemolytic anemia have also been reported (see section 4.8).

* Patients with renal insufficiency

The dosage should be modified according to the creatinine clearance calculated (see section 4.2). Caution should be exercised if cefotaxime is administered together with aminoglycosides; probenecid or other nephrotoxic drugs (see section 4.5). Renal function must be monitored in these patients, the elderly, and those with pre-existing renal impairment.

- Neurotoxicity

High doses of beta-lactam antibiotics, including cefotaxime, particularly in patients with renal insufficiency, may result in encephalopathy (e.g. impairment of consciousness, abnormal movements and convulsions) (see section 4.8).

* Precautions for administration

During post-marketing surveillance, potentially life-threatening arrhythmia has been reported in a very few patients who received rapid intravenous administration of cefotaxime through a central venous catheter. The recommended time for injection or infusion should be followed (see section 4.2).

- Sodium intake

The sodium content of cefotaxime (2.09 mmol/g) should be taken into account when prescribing to patients requiring sodium retention.

- Effects on laboratory tests

As with other cephalosporins a positive Coombs' test has been found in some patients treated with cefotaxime. This phenomenon can interfere with the cross-matching of blood.
Urinary glucose testing with non-specific reducing agents may yield false-positive results. This phenomenon is not seen when a glucose-oxidase specific method is used.

4.5 Interaction with other medicinal products and other forms of interaction

With other medicaments:

- Uricosurics

Probenecid interferes with the renal tubular transfer of cefotaxime, thereby increasing cefotaxime exposure about 2-fold and reducing renal clearance to about half at therapeutic doses. Due to the large therapeutic index of cefotaxime, no dosage adjustment is needed in patients with normal renal function. Dosage adjustment may be needed in patients with renal impairment (see sections 4.4 and 4.2).

- Aminoglycoside antibiotics and diuretics:

As with other cephalosporins, cefotaxime may potentiate the nephrotoxic effects of nephrotoxic drugs such as aminoglycosides or potent diuretics (e.g. furosemide). Renal function must be monitored in these patients (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety of cefotaxime has not been established in human pregnancy.
Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. There are, however, no adequate and well controlled studies in pregnant women.
Cefotaxime crosses the placental barrier. Therefore, cefotaxime should not be used during pregnancy unless the anticipated benefit outweighs any potential risks.

Breast-feeding
Cefotaxime is excreted into human breast milk.
Effects on the physiological intestinal flora of the breast-fed infant leading to diarrhoea, colonisation by yeast-like fungi, and sensitisation of the infant cannot be excluded.
Therefore, a decision must be made whether to discontinue breast-feeding or to discontinue 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

There is no evidence that cefotaxime directly impairs the ability to drive or to operate machines.
High doses of cefotaxime, particularly in patients with renal insufficiency, may cause encephalopathy (e.g. impairment of consciousness, abnormal movements and convulsions) (see section 4.8). Patients should be advised not to drive or operate machinery if any such symptoms occur.

4.8 Undesirable effects

System organ class	***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 (< /10, 000)***	***Not known (cannot be estimated from available data)****
Infections and infestations						Superinfection (see section 4.4)
Blood and the lymphatic system disorders			Leukopenia Eosinophilia Thrombo-cytopenia			Neutropenia Agranulocytosis (see section 4.4) Haemolytic anaemia
Immune system disorders			Jarisch-Herxheimer reaction			Anaphylactic reactions Angioedema Bronchospasm Anaphylactic shock
Nervous system disorders			Convulsions (see section 4.4)			Headache Dizziness Encephalopathy (e.g. impairment of consciousness, abnormal movements) (see section 4.4)
Cardiac disorders						Arrhythmia following rapid bolus infusion through central venous catheter
Gastro-intestinal disorders			Diarrhea			Nausea, Vomiting Abdominal pain Pseudo-membranous colitis (see section 4.4)

Hepato-bilary disorders			Increase in liver enzymes (ALAT, ASAT, LDH, gamma-GT and/or alkaline phosphatase) and/or bilirubin			Hepatitis* (sometimes with jaundice)
Skin and subcutaneous tissue disorders			Rash Pruritus Urticaria			Erythema multiforme Stevens-Johnson syndrome Toxic epidermal necrolysis (see section 4.4)
Renal and urinary disorders			Decrease in renal function/ increase of creatinine (particularly when co-prescribed with amino-glycosides)			Interstititial nephritis
General disorders and administration site conditions	*For IM formulations:* Pain at the injection site		Fever Inflammatory reactions at the injection site, including phlebitis/ thrombo-phlebitis			*For IM formulations (since the solvent contains lidocaine):* Systemic reactions to lidocaine

Jarisch-Herxheimer reaction

For the treatment of borreliosis, a Jarisch-Herxheimer reaction may develop during the first days of treatment. The occurrence of one or more of the following symptoms has been reported after several week's treatment of borreliosis: skin rash, itching, fever, leucopenia, increase in liver enzymes, difficulty of breathing, joint discomfort.

Hepatobiliary disorders

Increase in liver enzymes (ALAT, ASAT, LDH, gamma-GT and/or alkaline phosphatase) and/or bilirubin have been observed. These laboratory abnormalities may rarely exceed twice the upper limit of the normal range and elicit a pattern of liver injury, usually cholestatic and most often asymptomatic.

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 Yellow Card Scheme: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Symptoms of overdose may largely correspond to the profile of side effects.

There is a risk of reversible encephalopathy in cases of administration of high doses of β-lactam antibiotics including cefotaxime.

In case of overdose, cefotaxime must be discontinued, and supportive treatment initiated, which includes measures to accelerate elimination, and symptomatic treatment of adverse reactions (e.g. convulsions).

No specific antidote exists. Serum levels of cefotaxime can be reduced by haemodialysis or peritoneal dialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:
Third-generation cephalosporins.
ATC Code:
J01DD01

Mode of action
The bactericidal activity of cefotaxime results from the inhibition of bacterial cell wall synthesis (during the period of growth) caused by an inhibition of penicillin-binding proteins (PBPs) like transpeptidases.

Pharmacokinetics and pharmacodynamics relationship
The extent of the bactericidal activity depends on the period of time when the serum level exceeds the minimal inhibitory concentration (MIC) of the pathogen.

Mechanism of resistance
A resistance to cefotaxime may be caused by following mechanisms:

- inactivation by β-lactamases. Cefotaxime can be hydrolysed by certain β-lactamases, especially by extended-spectrum β-lactamases (ESBLs) which can be found in strains of Escherichia coli or Klebsiella pneumoniae, or by chromosomal encoded inducible or constitutive β-lactamases of the AmpC type which can be detected in Enterobacter cloacae. Therefore infections caused by pathogens with inducible, chromosomal encoded AmpC-β-lactamases should not be treated with cefotaxime even in case of proven in-vitro-susceptibility because of the risk of the selection of mutants with constitutive, derepressed AmpC- β-lactamases-expression.
- reduced affinity of PBPs against cefotaxime. The acquired resistance of Pneumococci and other Streptococci is caused by modifications of already existing PBPs as a consequence of a mutation process. In contrast to this concerning the methicillin-(oxacillin-)resistant Staphylococcus, the creation of an additional PBP with reduced affinity against cefotaxime is responsible for resistance.
- inadequate penetration of cefotaxime through the outer cell membrane of gram-negative bacteria so that the inhibition of the PBPs is insufficient.
- the presence of transport mechanism (efflux pumps) being able to actively transport cefotaxime out of the cell.

A complete cross resistance of cefotaxime occurs with ceftriaxone and partially with other penicillins and cephalosporins.

Breakpoints:
The following minimal inhibitory concentrations were defined for sensitive and resistant germs:

EUCAST (European Committee on Antimicrobial Susceptibility Testing) break points V3.1(2013-02-11):

Pathogen	**Susceptible**	**Resistant**
Enterobacteriaceae	≤ 1 mg/l	> 2 mg/l
Staphylococcus spp.	--*	--*

Streptococcus (group A, B, C, G)	--**	--**
Viridans group streptococci	≤ 0.5 mg/l	> 0.5 mg/l
Streptococcus pneumoniae	≤ 0.5 mg/l***	> 2 mg/l
Haemophilus influenzae	≤ 0.12 mg/l***	> 0.12 mg/l
Moraxella catarrhalis	≤ 1 mg/l	> 2 mg/l
Neisseria gonorrhoeae	≤ 0.12 mg/l	> 0.12 mg/l
Neisseria meningitidis	≤ 0.12 mg/l***	> 0.12 mg/l
Not species-specific breakpoints****	≤ 1 mg/l	> 2 mg/l

* Susceptibility of staphylococci to cephalosporins is inferred from the cefoxitin susceptibility except for ceftazidime, cefixime and ceftibuten, which do not have breakpoints and should not be used for staphylococcal infections. Some methicillin-resistant S. aureus are susceptible to ceftaroline.
** The beta-lactam susceptibility of streptococcus groups A, B, C and G is inferred from the penicillin susceptibility.
*** Isolates with MIC values above the susceptible breakpoint are very rare or not yet reported. The identification and antimicrobial susceptibility tests on any such isolate must be repeated and if the result is confirmed the isolate sent to a reference laboratory. Until there is evidence regarding clinical response for confirmed isolates with MIC values above the current resistant breakpoint they should be reported resistant.
**** Breakpoints apply to a daily intravenous dose of 1 g x 3 and a high dose of at least 2 g x 3.

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. If the efficacy of cefotaxime is questionable due to the local prevalence of resistance, expert opinion should be sought regarding the choice of therapy. In particular in the case of severe infections or failure of therapy a microbiological diagnosis including a verification of the germ and its susceptibility should be aspired.

Commonly susceptible species
Gram-positive aerobes
Staphylococcus aureus (methicillin-susceptible)
Streptococcus agalactiae°
Streptococcus pneumoniae (incl. penicillin-resistant strains)
Streptococcus pyogenes°
Gram-negative aerobes
Borrelia burgdorferi°
Haemophilus influenzae
Moraxella catarrhalis°
Neisseria gonorrhoeae°
Neisseria meningitidis°
Proteus mirabilis%
Proteus vulgaris°
Species for which acquired resistance may be a problem
Gram-positive aerobes
*Staphylococcus aureus*ɔ
Staphylococcus epidermidis+
Staphylococcus haemolyticus+
Staphylococcus hominis+
Gram-negative aerobes
Citrobacter freundii
Enterobacter aerogenes

Enterobacter cloacae
Escherichia coli[%]
Klebsiella oxytoca[%]
Klebsiella pneumoniae[%]
Morganella morganii
Serratia marcescens
Anaerobes
Bacteroides fragilis
Inherently resistant species
Gram-positive aerobes
Enterococcus spp.
Listeria monocytogenes
Staphylococcus aureus (methicillin-resistant)
Gram-negative aerobes
Acinetobacter baumannii
Pseudomonas aeruginosa
Stenotrophomonas maltophilia
Anaerobes
Clostridium difficile
Others
Chlamydia spp.
Chlamydophila spp.
Legionella pneumophila
Mycoplasma spp.
Treponema pallidum

° Literature data, reference books and therapy guidelines support susceptibility.
+ In at least one region the resistance rate is > 50%.
% Extended Spectrum Beta-Lactamase (ESBL) producing strains are always resistant.
ɘ In the community area the resistance rate is <10%.

5.2 Pharmacokinetic properties

Absorption:

Cefotaxime is for parenteral application. Mean peak concentrations 5 minutes after intravenous injection are about 81-102 mg/l following a 1 g dose of cefotaxime and about 167-214 mg/l 8 minutes after a 2 g dose. Intramuscular injection produces mean peak plasma concentrations of 20 mg/l within 30 minutes following a 1 g dose.

Distribution:

Cefotaxime gives good penetration into different compartments. Therapeutic drug levels exceeding the minimum inhibitory levels for common pathogens can rapidly be achieved. Cerebrospinal fluid concentrations are low when the meninges are not inflamed but cefotaxime usually passes the blood-brain barrier in levels above the MIC of the sensitive pathogens when the meninges are inflamed (3-30µg/ml). Cefotaxime concentrations (0.2-5.4µg/ml), inhibitory for most Gram-negative bacteria, are attained in purulent sputum, bronchial secretions and pleural fluid after doses of 1 or 2 g.

Concentrations likely to be effective against most sensitive organisms are similarly attained in female reproductive organs, otitis media effusions, prostatic tissue, interstitial fluid, peritoneal fluid and gall bladder wall, after therapeutic doses. High concentrations of cefotaxime and O-desacetyl-cefotaxime are attained in bile. Cefotaxime passes the placenta and attains high concentrations in foetal fluid and tissues (up to 6 mg/kg). Small amounts of cefotaxime diffuse into the breast milk.

Protein binding for cefotaxime is approximately 25-40%.

The apparent distribution volume for cefotaxime is 21-37 l after 1 g intravenous infusion over 30 minutes.

Biotransformation:

Cefotaxime is partly metabolised in human beings. Approximately 15-25% of a parenteral dose are metabolised to the O-desacetylcefotaxime metabolite, which also has antibiotic properties.

Elimination:

The main route of excretion of cefotaxime and O-desacetylcefotaxime is the kidney. Only a small amount (2%) of cefotaxime is excreted in the bile. In the urine collected within 6 hours 40-60% of the administered dose of cefotaxime is recovered as unchanged cefotaxime and 20% is found as O-desacetylcefotaxime. After administration of radioactive labelled cefotaxime more than 80 % can be recovered in the urine, 50-60% of this fraction is unchanged cefotaxime and the rest contains metabolites.

The total clearance of cefotaxime is 240-390 ml/min and the renal clearance is 130-150 ml/min.

The serum half-lives of cefotaxime and O-desacetylcefotaxime are normally about 50-80 and 90 minutes respectively. In elderly, the serum half-life of cefotaxime is 120-150min.

In patients with impaired renal function (creatinine clearance 3-10 ml/min) the serum half-life of cefotaxime can be increased to 2.5-3.6 hours.

In neonates, the pharmacokinetics are influenced by gestation and chronological age, the half-life being prolonged in premature and low birth weight neonates of the same age.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, and toxicity to reproduction.

Cefotaxime passes through the placenta. After intravenous administration of 1 g Cefotaxime during the birth values of 14 µg/ml were measured in the umbilical cord serum in the first 90 minutes after application, which dropped to approximately 2.5 µg/ml by the end of the second hour after application. In the amniotic fluid, the highest concentration of 6.9 µg/ml was measured after 3 - 4 hours. This value exceeds the MIC for most gram-negative bacteria.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

None.

6.2 Incompatibilities

Cefotaxime should not be added with other antibiotics, in the same syringe or solution for infusion. This concerns especially aminoglycosides.
Cefotaxime should not be mixed with solutions containing sodium bicarbonate.

6.3 Shelf life

Unopened:
2 years.

Opened & Reconstituted product:
For immediate use.

6.4 Special precautions for storage

Unopened:
Do not store above 25°C. Keep vial in the outer carton in order to protect from light.

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

6.5 Nature and contents of container

Nature
2 g powder for solution for injection or infusion:
20 ml vials of clear glass hydr. class III with halogenated butyl rubber stopper.
50 ml vials of clear glass hydr. class II with halogenated isobutene-isoprene rubber stopper.

Content
1 vial per carton
1 vial per carton in pack of 5 cartons
1 vial per carton in pack of 10 cartons
1 carton of 10 vials
1 carton of 25 vials
1 carton of 50 vials
1 carton of 100 vials

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Aseptic techniques should be used to reconstitute the solution. The reconstituted solution should be administered immediately.

Cefotaxime is compatible with several commonly used intravenous infusion fluids:
- Water for Injection
- 0.9 % Sodium Chloride solution
- 5 % Glucose solution
- 5 % Glucose/0.9 % Sodium Chloride solution
- Ringer-lactate solution
- 5 % Metronidazole solution
- Dextran 40 in 0.9 % Sodium Chloride solution
- Dextran 40 in 5 % Glucose solution

The compatibility of cefotaxime in other infusion fluids should be checked before use.

Following reconstitution the solution should be clear and pale yellowish to brown-yellowish. Do not use if any particulate matter is visible. Withdraw only one dose.

Any unused solution should be discarded.

See point 4.2 for the instructions for reconstitution.

7 MARKETING AUTHORISATION HOLDER

Sandoz GmbH
Biochemiestrasse 10
A-6250 Kundl
Austria

8 MARKETING AUTHORISATION NUMBER

PA 0111/005/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 06 December 2002

Date of last renewal: 17 December 2006

10 DATE OF REVISION OF THE TEXT

September 2015