

# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Cefotaxime 2 g Powder for Solution for Injection or Infusion

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains cefotaxime sodium equivalent to 2 g cefotaxime.

## 3 PHARMACEUTICAL FORM

Powder for solution for injection or infusion.

White or slightly yellow powder.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

For the treatment of the following severe infections when known or thought very likely to be due to organisms that are susceptible to cefotaxime (see section 5.1)

- Infections of the lower respiratory tract
- Infections of the kidneys and other upper urinary tract infections
- Infections of the skin and soft tissue
- Genital infections caused by gonococci, particularly when penicillin has failed or is unsuitable
- Intra-abdominal infections (incl. peritonitis) (cefotaxime should be used in combination with another antibiotic that can provide anaerobic cover in the treatment of intra-abdominal infections)
- Acute meningitis.

Consideration should be given to official local guidance on the appropriate use of antibiotics when using cefotaxime.

### 4.2 Posology and method of administration

Cefotaxime sodium may be administered intravenously by bolus injection or infusion or intramuscularly.

Cefotaxime 500 mg and 1 g are suitable for i.v. and i.m. injection. Cefotaxime 2 g is suitable for i.v. injection and i.v. infusion.

The intramuscular method of administration is reserved for exceptional clinical situations and should undergo a risk-benefit assessment. It is recommended that no more than 4 ml is injected unilaterally. If the daily dose exceeds 2 g cefotaxime or if cefotaxime is injected more frequently than twice per day, the i.v. route is recommended.

Intramuscular administration of cefotaxime reconstituted with lidocaine should not be administered to children in the first year of age.

#### *Dosage with individual and daily administration*

Dosage and type of administration depends on the severity of the infection, the sensitivity of the bacterium and the condition of the patient.

For the dosages and routes of administration which are not possible with this strength, other strengths are available.

The duration of the treatment depends on the course of disease. As a general rule cefotaxime is administered for a further 3 to 4 days after improvement/regression of the symptoms.

**Adults and adolescents (12 to 16-18 years)** in general receive 1 g cefotaxime every 12 hours. In severe cases, the daily dose can be increased up to 12 g. Daily doses up to 6 g can be divided into at least two individual administrations at 12 hour intervals. Higher daily doses must be divided into at least 3 to 4 individual administrations at 8 or 6-hour intervals, respectively.

The following table may serve as a guide to dosages:

<b>Type of infection</b>	<b>Single dose cefotaxime</b>	<b>Dose Interval</b>	<b>Daily dose cefotaxime</b>
Typical infections, in which a sensitive bacterium is proven or suspected	1 g	12 h	2 g
Infections, in which various bacteria with high to medium sensitivity are demonstrated or suspected	2 g	12 h	4 g
Unclear bacterial illnesses which cannot be localised and where the patient is critically ill	2-3 g	8 h 6 h	6-9 g 8-12 g

**Infants, toddlers (28 days to 23 months) and children (2 to 11 years)** receive 50 to 100 mg cefotaxime according to the severity of the infection (up to 150 mg) per kilogram of body weight per day, in 2 to 4 divided doses (every 12 - 6 hours). The following table may serve as a guide to dosages:

<b>Type of infection</b>	<b>Dose interval</b>	<b>Daily dose cefotaxime</b>
Typical infections, in which a sensitive bacterium is proven or suspected	6 - 12 h	50 mg/kg
Infections, in which various bacteria with high to medium sensitivity are demonstrated or suspected	6 - 12 h	100 mg/kg
Unclear bacterial illnesses which cannot be localised and where the patient is critically ill	6 - 8 h	150 mg/kg *

\* In individual cases -particularly in life-threatening situations- it may be necessary to increase the daily dose to 200 mg cefotaxime per kilogram of body weight without exceeding the maximum daily dosage of 12 g.

**Pre term new born infants and term new born infants (0-27 days)** receive in general doses of 50 mg cefotaxime per kilogram of body weight per day in 2 to 4 divided doses (every 12-6 hours). In case of life-threatening situations it may be necessary to increase the daily dose. For severe infections 150 mg/kg/day has been given. The following table may serve as a guide to dosages:

<b>Type of infection</b>	<b>Age</b>	<b>Dose interval</b>	<b>Daily dose cefotaxime</b>
Typical infections due to sensitive bacteria <b>or</b> in cases with high to medium sensitivity demonstrated or suspected	0 - 7 days	6 - 12 h	50 mg/kg
	8 days – 1 month		
Unclear bacterial illnesses which cannot be localised and where the patient is critically ill	0 - 7 days	6 - 12 h	100 mg/kg *
	8 days – 1 month		150 mg/kg *



In individual cases -particularly in life-threatening situations- it may be necessary to increase the daily dose to 200 mg cefotaxime per kilogram of body weight. This dosage should not be exceeded in view of not fully matured kidney clearance.

### ***Gonorrhoea***

Uncomplicated gonorrhoea: a single intramuscular injection of 0.5 to 1 gram cefotaxime, although 1 gram is recommended as preferable. In cases of disseminated gonococcal infection, local official guidelines should be followed. The possibility of syphilis needs to be ruled out before starting cefotaxime therapy.

### **Special dosage recommendations**

#### ***Dosage in the case of impaired renal function***

For adult patients with a creatinine clearance of 20 ml/minute or less, the maintenance dose is to be reduced to half the normal dose.

For adult patients with a creatinine clearance of 5 ml/minute or less, after an initial loading dose of 1 g, the daily dose should be halved without change in the frequency of dosing, i.e. 1 g 12 hourly becomes 0.5 g 12 hourly, 1 g 8 hourly becomes 0.5 g 8 hourly, 2 g 8 hourly becomes 1 g 8 hourly etc. As in all other patients, dosage may require further adjustment according to the course of the infection and the general condition of the patient.

#### ***Haemodialysis***

In patients on haemodialysis, 0.5-2 g is given by i.v. injection at the end of every dialysis. This dose is repeated every 24 hours.

#### ***Elderly patients***

No dosage adjustments are needed in patients with normal renal function.

### **Method of administration**

See also section 6.6. Instructions for use and handling.

#### **Intravenous use**

##### ***Intravenous injection***

For i.v. injection, Cefotaxime 500 mg powder for solution for injection is dissolved in at least 2 ml water for injection, Cefotaxime 1 g powder for solution for injection in at least 4 ml and Cefotaxime 2 g powder for solution for injection in at least 10 ml and subsequently injected directly into the vein over 3 to 5 minutes or after clamping of the infusion tube into the distal end of the tube.

##### ***Infusion***

Short term infusion: 2 g cefotaxime is dissolved in 40 to 50 ml water for injection or a compatible infusion solution (see section 6.6 Instructions for use and handling) and subsequently i.v. infused over approximately 20 minutes.

For infusion by intravenous drip, 2 g cefotaxime is dissolved in 100 ml sodium chloride 9 mg/ml (0.9%) or glucose 50 mg/ml (5%) solution and subsequently i.v. infused over 50 to 60 minutes. Another compatible infusion solution can also be used for the solution.

##### ***Intramuscular injection***

For intramuscular injection, 0.5 g Cefotaxime 500 mg powder for solution for injection and 1 g Cefotaxime 1 g powder for solution for injection is dissolved in 2 and 4 ml water for injection, respectively. Afterwards, the injection should take place deep into the gluteal muscle. Pain with the i.m. injection can be avoided by dissolving Cefotaxime 500 mg powder for solution for injection in 2 ml or Cefotaxime 1 g powder for solution for injection in 4 ml of 1% lidocaine solution. An intravascular injection is to be avoided in this case because of possible adverse effects. If Cefotaxime is intramuscularly administered after reconstitution with lidocaine, the SPC of lidocaine should be checked for the necessary product information.

### **Combination therapy**

A combination therapy of cefotaxime with aminoglycosides is indicated without availability of an antibiogram in the case of severe, life-threatening infections. Kidney function must be monitored when using in combination with aminoglycosides.

The duration of the treatment depends on the course of the illness.

### **4.3 Contraindications**

Hypersensitivity to cefotaxime or to any of the cephalosporins.

Previous immediate and/or severe hypersensitivity reaction to penicillin or to any other type of beta-lactam drug.

### **4.4 Special warnings and precautions for use**

Cefotaxime should be given with caution to patients who have had any other type of hypersensitivity reaction to a penicillin or any other beta-lactam drug. Before therapy with cefotaxime is instituted, careful inquiry should be made to determine whether the patient had any previous hypersensitivity reactions to cefotaxime, any other cephalosporin, or to any penicillin or other beta-lactam drug.

Cefotaxime should be used with caution in patients with allergic diatheses and asthma.

Antibiotic-associated diarrhoea, colitis and pseudomembranous colitis have all been reported with the use of cefotaxime. These diagnoses should be considered in any patient who develops severe and/or bloody diarrhoea during or shortly after treatment.

The presence of *Clostridium difficile* should be investigated and cefotaxime should be discontinued immediately. Appropriate treatment measures should be initiated including specific antibiotic therapy if considered necessary. Antiperistaltics are contraindicated.

Cefotaxime should be used with caution in individuals with a previous history of gastro-intestinal disease, particularly colitis.

As with other cephalosporins, prolonged use of cefotaxime may result in the overgrowth of non-susceptible organisms, such as enterococci and *Candida* spp.

Since haematological abnormalities may develop during treatment with cefotaxime, blood count should be monitored if treatment lasts for longer than 7 days. In cases of neutropenia ( $<1400$  neutrophils/mm<sup>3</sup>), treatment should be interrupted.

Fast infusion into a central vein can cause arrhythmia.

Patients with severe renal dysfunction (creatinine clearance of 20 ml/minute or less) require dose adjustment. See section 4.2.

If cefotaxime is intramuscularly administered after reconstitution with lidocaine, the SPC of lidocaine should be checked for the necessary product information.

This product contains sodium, which should be taken into account when prescribing to patients requiring sodium restriction. Cefotaxime 2 g powder for solution for intravenous infusion contains 2096 mg cefotaxim-sodium which is equivalent to 4,4 mmol sodium (101,2 mg sodium).

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

### *Cefotaxime/other antibiotics*

As far as possible, cefotaxime should not be combined with substances having a bacteriostatic action (e.g. tetracycline, erythromycin, chloramphenicol or sulfonamides), since an antagonistic effect has been observed regarding the anti-bacterial effect *in vitro*. A synergistic effect can result with a combination with aminoglycosides.

An increased risk of oto- and nephrotoxicity have been reported when high doses of cephalosporins have been used concomitantly with aminoglycosides. A dose adjustment may be necessary, and the kidney function must be monitored (see 4.2 Posology and method of administration).

### *Cefotaxime/probenecid*

The simultaneous administration of probenecid leads to higher, more prolonged concentrations of cefotaxime in the serum by inhibiting renal clearance.

### *Cefotaxime/potentially nephrotoxic drugs and loop diuretics*

In combination with potentially nephrotoxic drugs (for example, aminoglycoside antibiotics, polymyxin B and colistin) and with loop diuretics the kidney function should be monitored, since the nephrotoxicity of these substances quoted may be accentuated.

### *Influence on laboratory diagnostic tests*

False positives may occur in the Coombs-test in rare cases during treatment with cefotaxime.

In glucose determinations in urine and blood, false positive as well as false negative results may also be obtained, depending on the method; these may be avoided by the use of enzymatic methods.

## 4.6 Fertility, pregnancy and lactation

### *Pregnancy*

Cefotaxime crosses the placenta. Although reproduction studies in animals have not revealed any evidence of harm to the foetus, cefotaxime should be used during pregnancy only if clearly needed and the expected benefit to the mother outweighs any potential risk to the foetus.

### *Lactation*

Cefotaxime is excreted in human milk in low concentrations.

Use during lactation can lead in infants to an effect on the physiological intestinal flora with diarrhoea, to *Saccharomyces* colonisation and may also lead into sensitisation. Caution should be exercised when administered to nursing women. A decision should be made whether to discontinue nursing or discontinue treatment taking into account the importance of cefotaxime to the nursing women.

## 4.7 Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

In individual cases, in administration of high doses and particularly with simultaneous kidney function impairment, attacks of cramp (tonic/clonic), muscle spasms (myoclonias) and giddiness have been reported. The indicated activities should therefore be discontinued under these circumstances.

## 4.8 Undesirable effects

Adverse reactions to cefotaxime have occurred relatively infrequently and have generally been mild and transient and occur in about 5% of patients treated with cefotaxime.

The side effects, described below, are classified according to following frequencies:

Very common: >10%; Common: >1%, <10%; Uncommon: >0.1%, <1%; Rare: >0.01%, <0.1%; Very rare, including isolated reports: <0.01%.

**Blood and lymphatic system disorders***Rare*

Haemolytic anaemia, granulocytopenia, leukocytopenia, eosinophilia, thrombocytopenia. Agranulocytosis may develop, particularly after prolonged therapy. These occurrences are reversible. If therapy lasts for more than 7 days blood picture checks should be instituted.

**Immune system disorders***Rare*

Severe acute hypersensitivity reaction (anaphylaxis). An anaphylactic shock is life threatening and necessitates corresponding emergency measures.

Allergic skin-reactions (e.g. urticaria, exanthema), itching and drug-fevers.

*Very rare, including isolated cases*

Erythema multiforme (mild to severe forms i.e Stevens-Johnsons syndrome) and toxic-epidermal necrolysis.

In patients with an inclination to allergies an allergic reaction is more likely.

**Nervous system disorders***Rare*

Seizures have been reported, especially with high doses and in patients with renal function impairment.

**Cardiac disorders***Very rare*

A very small number of cases of arrhythmias have occurred following rapid bolus infusion through a central venous catheter.

**Gastrointestinal disorders***Common*

Gastrointestinal disturbances, like loss of appetite, nausea, sickness, stomach ache or diarrhoea, which are usually mild in nature and frequently fade away during or otherwise after termination of the therapy.

*Rare*

Pseudomembranous colitis. See also section 4.4 Special warnings and precautions for use.

**Renal and urinary disorders***Rare*

Increased serum creatinine and urea concentrations,

*Very rare, including isolated cases*

Acute interstitial nephritis

**Hepato-biliary disorders***Rare*

Slight, transient increases in serum bilirubin and/or liver enzymes (SGOT, SGPT, Gamma GT, alkaline phosphatase, LDH).

**General disorders and administration site conditions***Common*

Transient pain may be experienced at the site of injection. This is more likely to occur with higher doses. Occasionally, phlebitis has been reported in patients receiving intravenous cefotaxime. However, this has rarely been a cause for discontinuation of treatment.

Pain and hardening of the tissue (induration) occasionally arise at the injection site after intramuscular injection.

**Other advice**

Liver and kidney function should be monitored in the event of prolonged use.

## 4.9 Overdose

In the event of overdosing it may be necessary, in addition to removing the drug, to take steps to accelerate elimination.

Cefotaxime is haemodialysable.

### a) symptoms of overdosing

Intoxication, *sensu strictu*, is not known in man. With certain risk patterns and with the administration of very high doses, central nervous system excitation conditions, myoclonia and cramp can occur, as have also been described for other betalactams. The risk of the appearance of these undesirable effects is increased in patients with severely restricted kidney function, epilepsy and meningitis.

### b) emergency measures

Centrally initiated cramps can be treated with diazepam or phenobarbital, but not with phenytoin. With anaphylactic reactions the usual emergency measures must be commenced, preferably with the first indications of the shock.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutical group: Third generation cephalosporins.

ATC classification: J01DD01

#### **Mode of action**

Cefotaxime inhibits the action of certain bacterial cell wall synthetic enzymes and so interrupts cell wall biosynthesis. Bacterial cell lysis results.

#### **Mechanisms of resistance**

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

- Hydrolysis by  $\beta$ -lactamases. Cefotaxime may be efficiently hydrolysed by the production of certain extended-spectrum  $\beta$ -lactamases. Also, the induction and/or constitutive expression of chromosomally-encoded (AmpC) enzymes can efficiently hydrolyse the drug
- An impermeability-based mechanism of resistance
- Efflux pump mechanisms.

More than one of these possible mechanisms may co-exist in a single bacterium.

Cefotaxime-resistant bacteria may exhibit varying degrees of cross-resistance with other  $\beta$ -lactams. Cefotaxime-resistant gram-negative bacteria show complete cross-resistance to other broad-spectrum third generation cephalosporins (e.g. ceftazidime, ceftriaxone).

The use of cefotaxime as monotherapy in infections caused by gram negative bacteria containing inducible encoded AmpC-like  $\beta$ -lactamases like *Enterobacter cloacae*, *Enterobacter* spp., *Serratia* spp., and *Citrobacter* spp. should be discouraged despite apparent *in vitro* susceptibility, as mutants with stably depressed (hyperproduced)  $\beta$ -lactamase may be selected during therapy.

#### Breakpoints

National Committee for Clinical Laboratory Standards (NCCLS):

Enterobacteriaceae\*, *Pseudomonas aeruginosa* and other Non-Fermenters, *Staphylococcus* spp.: susceptible  $\leq$  8 mg/l; intermediate 16-32 mg/l; resistant  $\geq$  64 mg/l

*Haemophilus influenzae*: susceptible  $\leq$  2 mg/l

*Neisseria gonorrhoeae*: susceptible  $\leq$  0.5 mg/l

*Streptococcus pneumoniae* (non-meningitis): susceptible  $\leq$  1 mg/l; intermediate 2 mg/l; resistant  $\geq$  4 mg/l

*Streptococcus pneumoniae* (meningitis): susceptible  $\leq$  0.5 mg/l; intermediate 1 mg/l; resistant  $\geq$  2 mg/l

*Streptococcus* spp. (beta-haemolytic group): susceptible  $\leq$  0.5 mg/l

*Streptococcus* spp. (viridans group): susceptible  $\leq 1$  mg/l; intermediate 2 mg/l; resistant  $\geq 4$  mg/l.

\*Strains of *Escherichia coli* and *Klebsiella* spp. that produce ESBLs may be clinically resistant to therapy with cefotaxime despite *in vitro* susceptibility.

#### *In-vitro* antibacterial spectrum

A general overview of the antibacterial spectrum of cefotaxime is given below. It should be considered that the prevalence of acquired resistance may vary geographically within the European Union and with time for selected species, so that local information on resistance is desirable, particularly when treating severe infections. The information given in the table below provides an approximate guidance on the probabilities whether micro organisms will be susceptible to cefotaxime.

<p><b>Commonly susceptible species</b></p> <p><b>Gram positive aerobes</b></p> <p><i>Staphylococcus aureus</i> (MSSA)</p> <p><i>Streptococcus agalactiae</i></p> <p><i>Streptococcus pneumoniae</i> (including penicillinresistant strains)</p> <p><i>Streptococcus pyogenes</i></p> <p><b>Gram-negative aerobes</b></p> <p><i>Haemophilus influenzae</i></p> <p><i>Moraxella catarrhalis</i><sup>o</sup></p> <p><i>Morganella morganii</i></p> <p><i>Neisseria gonorrhoeae</i><sup>o</sup></p> <p><i>Neisseria meningitidis</i><sup>o</sup></p> <p><i>Proteus mirabilis</i><sup>%</sup></p> <p><b>Species for which acquired resistance may be a problem</b></p> <p><b>Gram-positive aerobes</b></p> <p><i>Staphylococcus aureus</i><sup>3</sup></p> <p><i>Staphylococcus epidermidis</i><sup>+</sup></p> <p><i>Staphylococcus haemolyticus</i><sup>+</sup></p> <p><i>Staphylococcus hominis</i><sup>+</sup></p> <p><b>Gram-negative aerobes</b></p> <p><i>Citrobacter freundii</i></p> <p><i>Enterobacter aerogenes</i></p> <p><i>Enterobacter cloacae</i></p> <p><i>Escherichia coli</i><sup>%</sup></p> <p><i>Klebsiella oxytoca</i><sup>%</sup></p> <p><i>Klebsiella pneumoniae</i><sup>%</sup></p> <p><i>Proteus vulgaris</i></p> <p><i>Serratia marcescens</i></p> <p><b>Anaerobes</b></p> <p><i>Bacteroides fragilis</i></p> <p><b>Inherently resistant species</b></p> <p><b>Gram-positive aerobes</b></p> <p><i>Enterococcus</i> spp.</p> <p><i>Listeria monocytogenes</i></p> <p><i>Staphylococcus aureus</i> (MRSA)</p>	
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<p><b>Gram-negative aerobes</b>  <i>Acinetobacter baumannii</i>  <i>Pseudomonas aeruginosa</i>  <i>Stenotrophomonas maltophilia</i></p>	
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<p><b>Anaerobes</b>  <i>Clostridium difficile</i></p>	
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<p><b>Others</b>  <i>Chlamydia</i> spp.  <i>Chlamydophila</i> spp.  <i>Legionella pneumophila</i>  <i>Mycoplasma</i> spp.  <i>Treponema pallidum</i></p>	
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° No current surveillance data available. Susceptibility is anticipated according to the current scientific knowledge.

+ In at least one region resistance rate is above 50%.

% Extended Spectrum beta-lactamase (ESBL) producing strains are always resistant.

∞ resistance rates <10% in community acquired infections

## 5.2 Pharmacokinetic properties

Cefotaxime is applied parenterally.

### **Absorption**

After intravenous injection of 1 g cefotaxime, the serum concentrations after 5 min amounted to about 81-102 mg/l and after 15 min to 46 mg/l. Eight minutes after intravenous injection of 2 g cefotaxime, serum concentrations of 167-214 mg/l were recorded. After intramuscular administration, the maximum serum concentrations (approximately 20 mg/l after 1 g) were reached within 30 minutes.

### **Distribution**

The apparent distribution volume is 21-37 l.

With infected meninges, cefotaxime and desacetyl-cefotaxime penetrate into the fluid space and then reach therapeutically effective concentrations there (e.g. with infections which are caused by gram-negative bacteria and pneumococci).

The serum protein binding amounts to approximately 25-40%.

Cefotaxime pervades tissue rapidly, passes the placenta barrier and reaches high concentrations in foetal tissues (up to 6 mg/kg). It is only expressed at a low percentage in the mother's milk (concentrations in the mother's milk: 0.4 mg/l after 2 g).

### **Metabolism**

Cefotaxime is metabolized to a considerable extent in man. Approximately 15-25% of a parenteral dose is excreted as O-desacetyl-cefotaxime. The metabolite possesses anti-bacterial activity.

In addition to desacetyl-cefotaxime, there are two other inactive lactones. From desacetyl-cefotaxime, a lactone is produced as an ephemeral intermediate, which still cannot be proven either in the urine or in the plasma, because it is subject to a rapid conversion to stereo isomers of the ring opening (beta-lactam ring) lactone. These are likewise eliminated in the urine.

**Excretion**

The excretion of cefotaxime and desacetyl-cefotaxime takes place mainly by the renal route. A small percentage (approximately 2%) is eliminated with bile. In urine collected over 6-hours, 40-60% of a dose was recovered in unchanged form and approximately 20% as desacetyl-cefotaxime. After intravenous administration of radioactively marked cefotaxime somewhat more than 80% was recovered in the urine, from it, 50-60% appeared as unchanged mother substance and the remainder as three metabolites.

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

The serum half-lives of cefotaxime and its active metabolite amount to 50-80 minutes and 125 minutes, respectively. In geriatric patients (> 80 years), the half-lives were found to be 120-150 minutes and 5 hours for the active metabolite.

With severe kidney malfunctions (creatinine clearance 3-10 ml/min) the half-life of the cefotaxime can be extended to 2.5-10 hours. Cefotaxime only accumulates under these conditions to a small extent, in contrast to the active and inactive metabolites.

Both cefotaxime and desacetyl-cefotaxime are to a large extent removed from the blood by haemodialysis.

**5.3 Preclinical safety data**

The toxicity of cefotaxime after single doses is very low. Cefotaxime has no mutagenic potential, as indicated by a negative micronucleus test. Studies in rats and mice gave no indication of cefotaxime having teratogenic properties. Fertility was not impaired. In perinatal and postnatal studies in rats, pups born to the high dose animals had significantly lower weights at birth and remained smaller than control pups during the 21 days of nursing.

**6 PHARMACEUTICAL PARTICULARS****6.1 List of excipients**

Not applicable.

**6.2 Incompatibilities**

Cefotaxime should not be mixed in alkaline solutions such as sodium bicarbonate injection.

Cefotaxime should also not be admixed with aminoglycosides. However, they may be administered separately to the same patient.

**6.3 Shelf life**Unopened

2 years

Opened and reconstituted product

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

Chemical and physical in-use stability has been demonstrated for 6 hours at 2-8 °C, when dissolved in water for injection and 1% lidocaine HCl solution. When reconstituted with other compatible solutions (see section 6.6), the product should be used immediately.

The colour of the solution may change to light yellow, however, the efficacy and safety of the antibiotic are not influenced.

## 6.4 Special precautions for storage

Do not store above 25 °C.

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

## 6.5 Nature and contents of container

Transparent type II glass vial with bromobutyl rubber stopper and aluminium seal with a flip off cap, containing cefotaxime sodium, equivalent to 2 g cefotaxime.

The vials are packed in a carton box containing 1, 5 or 10 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

The product is compatible with the following solutions:

- Water for Injections
- Sodium chloride 9 mg/ml (0.9% w/v), solution for infusion
- Glucose 50 mg/ml (5% w/v), solution for infusion
- Lidocaine HCl 10 mg/ml (1% w/v), solution for injection (see also section 4.4 Special warnings and precautions for use).

The compatibility with other infusion fluids should be checked before use.

Reconstitute the powder with the solvent by shaking vigorously for at least 30 seconds to ensure complete dissolution. See also section 4.2 Posology and method of administration for further instructions. Only clear solutions, practically free from particles, should be used.

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

## 7 MARKETING AUTHORISATION HOLDER

Teva Pharma  
Computerweg 10  
P.O. Box 43028  
3540 AA Utrecht  
The Netherlands

## 8 MARKETING AUTHORISATION NUMBER

PA 749/12/3

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10th November 2006

Date of last renewal: 12th July 2010

## 10 DATE OF REVISION OF THE TEXT

November 2011