# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Cefotaxime hameln 2 g powder for solution for injection/infusion

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains cefotaxime sodium equivalent to 2 g cefotaxime.

Each 2 g vial contains 96 mg sodium (4.18 mmol).

## 3 PHARMACEUTICAL FORM

Powder for solution for injection/infusion.
A white or slightly yellow powder.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Cefotaxime is indicated in the treatment of the following severe infections either when known or thought very likely to be caused by bacteria that are susceptible to cefotaxime (see section 4.4 and 5.1):
- Bacterial pneumonia
- Complicated infections of the urinary tract including pyelonephritis
- Severe skin and soft tissue infections
- Genital infections, including gonorrhoea
- Intra-abdominal infections (such as peritonitis)
- Bacterial meningitis
- Endocarditis
- Borreliosis

Treatment of patients with bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above.
Perioperative prophylaxis. For surgical operations with increased risk of infections with anaerobic pathogens, e.g. colorectal surgery, a combination with an appropriate drug with activity against anaerobes is recommended.

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

### 4.2 Posology and method of administration

Posology

Cefotaxime hameln may be administered by intravenous bolus injection or intravenous infusion or by intramuscular injection after reconstitution of the solution
The dosage, route and frequency of administration should be determined by the severity of infection, the sensitivity of causative organism and condition of the patient. Therapy may be initiated before the results of sensitivity tests are known.

Adults and adolescents over 12 years of age
Adults and adolescents usually receive 2 to 6 g cefotaxime daily. The daily dose should be divided in two single doses every 12 hours.
- Common infections in presence (or suspicion) of sensitive bacteria: 1 g every 12 hours.
- Infections in presence (or suspicion) of several sensitive or moderately sensitive bacteria: 1 – 2 g every 12 hours.
- Severe infections or for infections that cannot be localised: 2 – 3 g as a single dose every 6 to 8 hours (maximum daily dose: 12 g).

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

Paediatric population

Children: The usual dosage range is 100-150 mg/kg/day in 2 to 4 divided doses. However, in very severe infections doses of up to 200 mg/kg/day may be required.

Neonates: The recommended dosage is 50 mg/kg/day in 2 to 4 divided doses. In severe infections 150-200 mg/kg/day, in divided doses, have been given.

Elderly
No dosage adjustment is required, provided that the function of the kidneys and the liver is normal.

**Other special recommendations**
*Gonorrhoea*
For gonorrhoea, a single injection (intramuscularly or intravenously) of 0.5-1 g cefotaxime. For complicated infections, consideration should be given to available official guidelines. Syphilis should be excluded before initiating treatment.

*Bacterial meningitis*
Adults: Daily dose of 6 – 12 g cefotaxime divided into equal doses every 6 – 8 hours (2 to 3 g 3 – 4 times daily).
Children: 150 – 200 mg / kg / day divided into equal doses every 6 – 8 hours.
Newborns: 0 – 7 days: 50 mg / kg every 12 hours, 7 – 28 days: 50 mg / kg every 8 hours.

*Perioperative prophylaxis*
1 – 2 g as single dose as close to start of surgery as possible. In those cases where the operation time exceeds 90 minute an additional dose of prophylactic antibiotic should be given.

*Intra-abdominal infections*
Intra-abdominal infections should be treated with cefotaxime in combination with other antibiotics with coverage for anaerobic bacteria.

Dosage in renal function impairment
In patients with a creatinine clearance less than 10 ml/minute, after an initial normal dose, the maintenance doses have to be reduced to one half of the normal dose, without change of the dose interval.

Dosage in haemodialysis or peritoneal dialysis
1 to 2 g daily, depending on the severity of the infection; on the day of haemodialysis, cefotaxime must be administered after the dialysis session.

**Duration of therapy**
The duration of therapy with cefotaxime depends on the clinical condition of the patient and varies according to the bacteriological progress. 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-day period).

**Method of administration**
Cefotaxime hameln 1 g powder for solution for injection/infusion can be given by **intramuscular injection, intravenous injection or intravenous infusion.**
Cefotaxime hameln 2 g powder for solution for injection/infusion can be given by **intravenous injection or infusion.**

Intravenous infusion
In order to avoid any risk of infection, the reconstitution of the solution for infusion should be done in close aseptic conditions. Do not postpone the infusion after the reconstitution of the solution.
For *short intravenous infusion*: Following reconstitution, the solution should be administered over 20 minutes.
For *long lasting intravenous infusion*: Following reconstitution, the solution should be administered over 50 – 60 minutes.

Intravenous injection
For intermittent i.v. injections, the solution must be injected over a period of 3 to 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 (recommended only for 1 g vials)

The intramuscular method of administration is restricted to exceptional clinical situations (e.g. gonorrhoea). It is not indicated in severe infections and should undergo a risk-benefit assessment. It is recommended that no more than 4 ml are injected unilaterally. If the daily dose exceeds 2 g cefotaxime or if cefotaxime is injected more frequently than twice per day, the intravenous route is recommended. In case of severe infections, intramuscular injection is not recommended.
The solution should be administered by deep intramuscular injection. Solutions with lidocaine must **not** be administered intravenously. Cefotaxime reconstituted with lidocaine should not be administrated to children less than 30 months. The product information of the chosen lidocaine containing medicinal product must be regarded.

For instructions on reconstitution and dilution of the medicinal product before administration, see section 6.6. Cefotaxime and aminoglycosides should not be mixed in the same syringe or perfusion fluid.

**4.3 Contraindications**

- Hypersensitivity to the active substance, to other cephalosporins.
- Previous, immediate and/or severe hypersensitivity reaction to penicillin or any beta-lactam antibiotic.

**4.4 Special warnings and precautions for use**

As with other antibiotics, the use of cefotaxime, especially if prolonged, may result in overgrowth of non-susceptible organisms. Repeated evaluation of the patient's condition is essential. If superinfection occurs during therapy, appropriate measures should be taken (see Section 4.8).

· Anaphylactic reactions
Serious, including fatal hypersensitivity reactions have been reported in patients receiving cefotaxime (see sections 4.3 and 4.8).

If a hypersensitivity reaction occurs, treatment must be stopped.

The use of cefotaxime is strictly contra-indicated in subjects with a previous history of immediate type hypersensitivity to cephalosporins.

Since cross allergy exists between penicillins and cephalosporins, use of the latter should be undertaken with extreme caution in penicillin sensitive subjects. Hypersensitivity reactions (anaphylaxis) occurring with these two antibiotic families may be serious or even fatal.

· Severe skin reactions
Severe cutaneous adverse reactions (SCARs) including acute generalized exanthematous pustulosis (AGEP), Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), which can be life-threatening or fatal, have been reported post-marketing in association with cefotaxime treatment. At the time of prescription patients should be advised of the signs and symptoms for skin reactions. If signs and symptoms suggestive of these reactions appear, cefotaxime should be withdrawn immediately. If the patient has developed AGEP, SJS, TEN or DRESS with the use of cefotaxime, treatment with cefotaxime must not be restarted and should be permanently discontinued.
In children, the presentation of a rash can be mistaken for the underlying infection or an alternative infectious process, and physicians should consider the possibility of a reaction to cefotaxime in children that develop symptoms of rash and fever during therapy with cefotaxime.

· *Clostridioides difficile* associated disease (e.g. pseudomembranous colitis)
Diarrhoea, particularly if severe and/or persistent, occurring during treatment or in the initial weeks following treatment, may be symptomatic of *Clostridioides 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. *Clostridioides difficile* associated disease can be favoured by faecal stasis. Medicinal products that inhibit peristalsis should not be given.

· Blood disorders

Leukopenia, neutropenia and, more rarely, bone marrow failure, pancytopenia or agranulocytosis may develop during treatment with cefotaxime. For treatment courses lasting longer than 7-10 days, the blood white cell count should be monitored and treatment stopped in the event of neutropenia.
Some cases of eosinophilia and thrombocytopenia, rapidly reversible on stopping treatment, have been reported. Cases of haemolytic anaemia have also been reported. (see section 4.8).

· Patients with renal insufficiency
The dosage should be modified according to the creatinine clearance calculated.
Caution should be exercised if cefotaxime is administered together with aminoglycosides 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.

· Encephalopathy
Beta-lactams, including cefotaxime, predispose the patient to encephalopathy risk (which may include convulsions, confusion, impairment of consciousness, movement disorders), particularly in case of overdose or renal impairment (see section 4.8). Patients should be advised to contact their doctor immediately prior to continuing treatment if such reactions occur.

· 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).

· Precautions for administration when reconstituted with lidocaine

Do not administer if there is:
- known history of hypersensitivity to lidocaine or other local anaesthetics of the amide type
- non-paced heart block
- severe heart failure

· 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-oxydase specific method is used.

Sodium
This medicinal product contains 48 mg sodium per 1 of powder, equivalent to 2.4% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Cefotaxime hameln is considered high in sodium. This should be particularly taken into account for those on a low salt diet.

This medicinal product is administered only after reconstitution - see section 6.6.
The sodium content of the diluent should be taken into account when calculating the total sodium content of the prepared dilution of the product. For detailed information on the sodium content of the solution used to dilute the product, please refer to the product characteristics of the diluent used.#

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

Probenecid interferes with the renal tubular transfer of cephalosporins, 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).

Bacteriostatic antibiotics: Cefotaxime should not be combined with bacteriostatic antibiotics (e.g. tetracyclines, erythromycin and chloramphenicol) because an antagonistic effect is possible.

Interference with Laboratory Tests: As with other cephalosporins, a positive Coombs' test has been seen in some patients treated with cefotaxime. This phenomenon can interfere with the cross-matching of blood.

A false positive reaction to glucose may occur with reducing substances (e.g. Fehling's solution) but not with the use of specific glucose oxidase methods.

**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. 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 administration, 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. Therefore, cefotaxime should not be used during pregnancy unless the anticipated benefit outweighs any potential risks.

Breast-feeding
Cefotaxime passes into human breast milk.
Effects on the physiological intestinal flora of the breast-fed infant leading to diarrhoea, colonization 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**

In the case of adverse reactions such as dizziness or encephalopathy (which may include convulsions, confusion, impairment of consciousness, movement disorders) the patient should not operate machines or drive a vehicle. 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 (<1/10,000)** | **Not known (cannot be estimated from available data)*** |
|---|---|---|---|---|---|---|
| Infections and infestations | | | | | | Superinfection (see section 4.9) |
| Blood and the lymphatic system disorders | | | Leukopenia<br>Eosinophilia<br>Thrombocytopenia | | | Bone marrow failure<br>Pancytopenia<br>Neutropenia<br>Agranulocytosis<br>(see section 4.4) Haemolytic anaemia |
| Immune system disorders | | | Jarisch-Herxheimer reaction | | | Anaphylactic reactions<br>Angioedema<br>Bronchospasm<br>Anaphylactic shock |
| Nervous system disorders | | | Convulsions (see section 4.4) | | | Headache<br>Dizziness<br>Encephalopathy* (see section 4.4) |
| Cardiac disorders | | | | | | Arrhythmia<br>following rapid bolus infusion through central venous catheter |
| Gastrointestinal | | | Diarrhea | | | Nausea |

| | | | | | | |
|---|---|---|---|---|---|---|
| disorders | | | | | | Vomiting<br>Abdominal pain<br>Pseudomembranous 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<br>Pruritus<br>Urticaria | | | Erythema multiforme<br>Stevens-Johnson syndrome<br>Toxic epidermal necrolysis (see section 4.4)<br>Acute generalised exanthematous pustulosis (AGEP)<br>Drug reaction with eosinophilia and systemic symptoms (DRESS) (see section 4.4) |
| Renal and urinary disorders | | | Decrease in renal function/increase of creatinine (particularly when coprescribed with aminoglycosides) | | | Acute renal failure (see Section 4.4)<br>Interstititial nephritis |
| General disorders and administration site conditions | For IM formulations: Pain at the injection site | | Fever<br>Inflammatory reactions at the injection site, including phlebitis/ thrombophlebitis | | | For IM formulations (where lidocaine is used for re-constitution): Systemic reactions to lidocaine |

* Beta-lactams, including cefotaxime, predispose the patient to encephalopathy risk (which may include convulsions, confusion, impairment of consciousness, movement disorders), particularly in case of overdose or renal impairment.
** postmarketing experience

**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 reported. 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.

**Superinfection**
As with other antibiotics, the use of cefotaxime, especially if prolonged, may result in overgrowth of non-susceptible organisms. Repeated evaluation of the patient's condition is essential. If superinfection occurs during therapy, appropriate measures should be taken.

**For IM Formulations**
If the solvent contains lidocaine, systemic reactions to lidocaine may occur, especially in the event of inadvertent intravenous injection or injection into highly vascularised tissue or in the event of an overdose.

**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
HPRA Pharmacovigilance
Website: www.hpra.ie

**4.9 Overdose**

Symptoms of overdose may largely correspond to the profile of side effects.
There is a risk of encephalopathy in cases of administration of beta-lactam antibiotics including cefotaxime, particularly in case of overdose or renal impairment.

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. Cefotaxime may be removed by haemodialysis. Peritoneal dialysis is ineffective in removing cefotaxime.

**5 PHARMACOLOGICAL PROPERTIES**

**5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: antibacterials for systemic use, other beta-lactam antibacterials, third generation cephalosporins, ATC code: J01DD01

Mechanism 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.

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

- Inactivation by beta-lactamases. Cefotaxime can be hydrolysed by certain beta-lactamases, especially by extended-spectrum beta-lactamases (ESBLs) which can be found in strains of *Escherichia coli* or *Klebsiella pneumoniae*, or by chromosomal encoded inducible or constitutive beta-lactamases of the AmpC type which can be detected in *Enterobacter cloacae*. Therefore infections caused by pathogens with inducible, chromosomal encoded AmpC-beta-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-beta-lactamases-expression.
- Reduced affinity of PBPs to 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 to 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.

Susceptibility testing breakpoints
Minimum Inhibitory Concentration (MIC) breakpoints established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) for cefotaxime can be viewed on the following website:
https://www.ema.europa.eu/documents/other/minimum-inhibitory-concentration-mic-breakpoints_en.xlsx

**5.2 Pharmacokinetic properties**

Pharmacokinetics: After a 1000 mg intravenous bolus, mean peak plasma concentrations of cefotaxime usually range between 81 and 102 microgram/ml. Doses of 500 mg and 2000 mg produce plasma concentrations of 38 and 200 microgram/ml,

respectively. There is no accumulation following administration of 1000 mg intravenously or 500 mg intramuscularly for 10 or 14 days.

The apparent volume of distribution at steady-state of cefotaxime is 21.6 L/1.73 $m^2$ after 1 g intravenous 30 minute infusion.

Concentrations of cefotaxime (usually determined by non-selective assay) have been studied in a wide range of human body tissues and fluids. Cerebrospinal fluid concentrations are low when the meninges are not inflamed, but are between 3 and 30 microgram/ml in children with meningitis.

Cefotaxime usually passes the blood-brain barrier in levels above the MIC of common sensitive pathogens when the meninges are inflamed. Concentrations (0.2-5.4 microgram/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, renal tissue, peritoneal fluid and gall bladder wall, after usual therapeutic doses. High concentrations of cefotaxime and desacetyl-cefotaxime are attained in bile.

Cefotaxime is partially metabolised prior to excretion. The principle metabolite is the microbiologically active product, desacetyl-cefotaxime. Most of a dose of cefotaxime is excreted in the urine about 60% as unchanged drug and a further 24% as desacetyl-cefotaxime. Plasma clearance is reported to be between 260 and 390 ml/minute and renal clearance 145 to 217 ml/minute.

After intravenous administration of cefotaxime to healthy adults, the elimination half-life of the parent compound is 0.9 to 1.14 hours and that of the desacetyl metabolite, about 1.3 hours.

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

In severe renal dysfunction the elimination half-life of cefotaxime itself is increased minimally to about 2.5 hours, whereas that of desacetyl-cefotaxime is increased to about 10 hours. Total urinary recovery of cefotaxime and its principal metabolite decreases with reduction in renal function.

**5.3 Preclinical safety data**

Nonclinical 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.

**6 PHARMACEUTICAL PARTICULARS**

**6.1 List of excipients**

None

**6.2 Incompatibilities**

Aminoglycosides are incompatible with cephalosporins in parenteral mixtures.
This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

**6.3 Shelf life**

Unopened vials: 2 years.

Shelf life after reconstitution:
The reconstituted product is chemically and physically stable:
- at a temperature of 2°C to 8°C for 24 hours;
- at a temperature below 25°C for 2 hours.

See section 6.6 for preparation of solutions.

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

The reconstituted product does not require protection from light.

The solution after reconstitution may be colourless to yellow.

**6.4 Special precautions for storage**

This medicinal product does not require any special temperature storage conditions.
Keep the vial in the outer carton in order to protect from light
For storage conditions after reconstitution of the medicinal product, see section 6.3.

**6.5 Nature and contents of container**

Cefotaxime hameln is supplied in type III colourless glass vials, closed with a bromobutyl rubber stopper and aluminium caps and seal or aluminium caps and plastic flip-off seal.
Each vial contains 1 or 2 g of cefotaxime, respectively.

Pack sizes: 10 vials.

**6.6 Special precautions for disposal and other handling**

After the solvent is added to the vial contents, the vial should be shaken until the powder dissolves; the solution should be clear after 1–2 minutes. The solution of the reconstituted product should be inspected visually for clearness and particulate matter prior to administration. If it is cloudy or it contains particulate matter, the solution is not suitable for use. The solution after reconstitution may be colourless to yellow.
For instructions on administration, see section 4.2.

**Preparation of solution for injection and infusion**

**Intravenous injection** (from 3 to 5 minutes)
The contents of a vial should be dissolved in 4 or 10 ml of water for injection, 9 mg/ml (0.9%) sodium chloride solution for injection or 50 mg/ml (5%) glucose solution for injection.

**Intravenous infusion** (from 20 to 60 minutes)
In order to prepare solutions of cefotaxime for intravenous infusion, the powder is dissolved in water for injection (in the same way as for intravenous injections).
The solution thus obtained should be further diluted with one of the following solutions:
9 mg/ml (0.9%) sodium chloride solution,
50 mg/ml (5%) glucose solution,
50 mg/ml (5%) glucose solution with 9 mg/ml (0.9%) sodium chloride solution 1:1,
50 mg/ml (5%) glucose solution with 9 mg/ml (0.9%) sodium chloride solution 2:1,
Ringer's solution, Compound Sodium Lactate Injection (Ringer-lactate Injection).

| **Antibiotic content per vial** | **Solvent volume** | |
|---|---|---|
| | **Intravenous injection** | **Intravenous infusion** |
| 1 g | 10 ml | 40–100 ml |
| 2 g | 10 ml | 40–100 ml |

**Intramuscular injection** (recommended only for 1 g vials)
The contents of 1 g vial should be dissolved in 4 ml of water for injection, 9 mg/ml (0.9%) sodium chloride solution or 10 mg/ml (1%) lidocaine solution. The product must not be administered intravenously with lidocaine solution.

| **Antibiotic content per vial** | **Solvent volume** |
|---|---|
| | **Intramuscular injection** |
| 1 g | 4 ml |
| 2 g | - |

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

**7 MARKETING AUTHORISATION HOLDER**

hameln pharma gmbh
Inselstraße 1
31787 Hameln
Germany

**8 MARKETING AUTHORISATION NUMBER**

PA2237/008/002

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

Date of first authorisation: