SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

Trade Name: Injpime 1 gm

Generic Name: Cefepime For injection USP 1 gm

2. Qualitative and quantitative composition

Each vial contains

Cefepime Hydrochloride USP

Equivalent to Cefepime…….. 1.0 gm

(Sterile Mixture of Cefepime Hydrochoride and L-Arginine)

3. Pharmaceutical form

Dry Powder for Injection

4. Clinical particulars

4.1 Therapeutic indications

Cefepime is indicated for the treatment of the severe infections listed below caused by cefepime-susceptible pathogens.

In adults and children over 12 years of age and with a body weight of ≥ 40 kg:

- Pneumonia
- Complicated urinary tract infections (including pyelonephritis)
- Complicated intra-abdominal infections
- Peritonitis associated with dialysis in patients on CAPD In adults:
- Acute biliary tract infections

In children aged 2 months up to 12 years and with a body weight of ≤40 kg:

- Pneumonia
- Complicated urinary tract infections
- 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. Cefepime may be used in the empirical treatment of adults, adolescents and children aged 2 months to 12 years with febrile neutropenia that is suspected to be due to a bacterial infection. In patients at high risk of severe infections (e.g. patients with recent bone marrow transplantation, hypotension at presentation, underlying haematological malignancy, or severe or

prolonged neutropenia), antimicrobial monotherapy may be inappropriate. No sufficient data exist to

support the efficacy of cefepime monotherapy in such patients. A combination therapy with an aminoglycoside or glycopeptide antibiotic may be advisable, taking into consideration the patient's individual risk profile. Cefepime should be co-administered with other antibacterial agents whenever the possible range of causative bacteria would not fall within its spectrum of activity. Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

After reconstitution cefepime can be administered intravenously as a slow injection over a period of 3 to 5 minutes or as a short infusion over a period of about 30 min. Posology and method of administration are guided by the nature and severity of infection, pathogen susceptibility, renal function and the patient's overall constitution. Dosage in patients with normal renal function:

Adults and adolescents over 40 kg body weight (approximately over 12 years):

Single doses and dosage interval	Very severe infections: •Complicated intra-abdominal infections •Empirical treatment of patients with febrile neutropenia
Severe infections: •Bacteraemia •Pneumonia •Complicated urinary tract infections (including pyelonephritis) •Acute biliary tract infections	
2.0 g every 12 hours	2.0 g every 8 hours

Infants and children (aged from 1 month to 12 years and/or weighing ≤ 40 kg, with normal renal function).

Single doses (mg/kg body weight), dosage interval and treatment duration		
	Severe infections: •Pneumonia •Complicated urinary tract infections (including	Very severe infections: •Bacteraemia •Bacterial meningitis •Empirical treatment

	pyelonephritis)	of patients with febrile neutropenia
Children from 2 months, body weight ≤ 40 kg:	50 mg/kg every 12 hours More severe infections: 50 mg/kg every 8 hours for 10 days	50 mg/kg every 8 hours for 7-10 days
Infants 1 to less than 2 months:	30 mg/kg every 12 hours More severe infections: 30 mg/kg every 8 hours for 10 days	30 mg/kg every 8 hours for 7-10 days

Experience in infants younger than 2 months is limited. Dosage recommendations of 30 mg/kg every 12 or 8 hours were derived from pharmacokinetic data of children older than 2 months and are considered appropriate for infants from 1 to less than 2 months.

For children weighing > 40 kg dosage recommendations for adults are applicable. For patients older than 12 years with a body weight < 40 kg, dosage recommendations for younger patients with a body weight of < 40 kg are applicable. The maximum recommended daily dose of 2 g every 8 h as for adults should not be exceeded.

Dosage in patients with impaired renal function:In patients with impaired renal function, the dose of cefepime should be adjusted to compensate for the slower rate of renal elimination.

Adults and adolescents (>12 years and body weight over 40 kg): For patients with mild to moderate renal impairment an initial dose of 2.0 g cefepime is recommended.

The following table gives the subsequent maintenance dose:

Creatinine clearance [ml/min]	Recommended maintenance dosage: Single doses and interval of administration	
	Severe infections: •Bacteraemia •Pneumonia •Complicated urinary tract infections (including pyelonephritis) •Acute biliary tract infections	Very severe infections: •Complicated intra-abdominal infections •Empirical treatment of patients with febrile neutropenia
> 50 (usual dose, no	2 g every 12 h	2 g every 8 h
30-50	2 g every 24 h	2 g every 12 h
11-29	1 g every 24 h	2 g every 24 h
≤ 10	0.5 g every 24 h	1 g every 24 h

Dialysis patients: In patients undergoing haemodialysis, approximately 68% of the total amount of cefepime present in the body at the start of dialysis will be eliminated during a

3 hour dialysis period. Pharmacokinetic modelling indicates that dose reduction is necessary in these patients. The following dosage is recommended: Loading dose of 1 g on the first day of treatment with cefepime followed by 500 mg per day thereafter except for febrile neutropenia, for which indication the recommended dose is 1 g per day. On days of dialysis, cefepime should be administered after the course of dialysis. If possible, cefepime should be administered at the same time each day.

In patients undergoing continuous ambulatory peritoneal dialysis (CAPD) the following dosage is recommended:

- 1 g cefepime every 48 hours in case of severe infections (bacteraemia, pneumonia, complicated urinary tract infections (including pyelonephritis), acute biliary tract infections)
- 2 g cefepime every 48 hours in case of very severe infections (abdominal infections, peritonitis, empirical treatment of patients with febrile neutropenia) Infants from 1 month and children up to 12 years with a body weight of ≤ 40 kgA dose of 50 mg/kg for patients between 2 months and 12 years (see section 5.2) and a dose of 30 mg/kg for infants aged 1 to 2 months is comparable to a dose of 2 g in adults including the same prolongation of dosing intervals as shown in the table below.

Children from 2 months up to 40 kg body weigth (approx. 12 years)

Single doses (mg/kg body weight) and dosage interval		
Creatinine clearance [ml/min]	Severe infections: •Pneumonia •Complicated urinary tract infections (including pyelonephritis)	Very severe infections: •Bacteraemia •Bacterial meningitis •Empirical treatment of patients with febrile neutropenia
> 50 (usual dose, no adjustment required)	50 mg/kg every 12 h	50 mg/kg every 8 h
30-50	50 mg/kg every 24 h	50 mg/kg every 12 h
11-29	25 mg/kg every 24 h	50 mg/kg every 24 h
≤ 10	12.5 mg/kg every 24 h	25 mg/kg every 24 h

Infants from 1 to less than 2 months

Single doses (mg/kg body weight) and dosage interval		
Creatinine clearance [ml/min]	Severe infections: •Pneumonia •Complicated urinary tract infections (including pyelonephritis)	Very severe infections: •Bacteraemia •Bacterial meningitis •Empirical treatment of patients with febrile neutropenia
> 50 (usual dose, no adjustment required)	30 mg/kg every 12 h	30 mg/kg every 8 h
30-50	30 mg/kg every 24 h	30 mg/kg every 12 h
11-29	15 mg/kg every 24 h	30 mg/kg every 24 h
≤ 10	7.5 mg/kg every 24 h	15 mg/kg every 24 h

Impaired hepatic function:

No dose adjustment is required in patients with impaired hepatic function.

Elderly patients:

Since elderly patients are at increased risk for reduced renal function, the dosage should be chosen with caution and the patient's renal function should be monitored. Dosage adjustment is recommended if renal function is reduced .

Duration of treatment:

The usual duration of therapy is 7 to 10 days. In general, cefepime should be administered not less than 7 days and not longer than 14 days per treatment. For empirical treatment of febrile neutropenia, usual duration of therapy is 7 days or until resolution of neutropenia

4.3 Contraindications

Cefepime is contraindicated in patients who have had previous hypersensitivity reactions to cefepime, to any of the excipients listed in section 6.1., to any other cephalosporin or to any other beta-lactam antibiotics agent (e.g. penicillins, monobactams and carbapenems). Due to its L-arginine content, this product is further contraindicated in patients with L-arginine hypersensitivity and acidosis. Caution is therefore advised in cases of hyperkalemia.

4.4 Special warnings and precautions for use

Hypersensitivity reactions

As with all beta-lactam antibacterial agents, severe and occasionally fatal hypersensitivity reactions have been reported. In case of severe hypersensitivity reactions, treatment with cefepime must be discontinued immediately and adequate emergency measures must be initiated. Before therapy with cefepime is instituted, careful inquiry should be made to

determine whether the patient has had previous hypersensitivity reactions to cefepime, beta-lactams or other medicinal products. In 10 % of the cases there is cross-reactivity between hypersensitivity to penicillin and cephalosporins. Cefepime should be administered with caution to patients with a history of asthma or allergic diathesis. The patient must be carefully monitored during the first administration. If an allergic reaction occurs, treatment must be discontinued immediately. Serious hypersensitivity reactions may require epinephrine and other supportive therapy.

Antibacterial activity of cefepime

5 Due to the relatively limited spectrum of antibacterial activity of cefepime it is not suitable for treatment of some types of infections unless the pathogen is already documented and known to be susceptible or there is a very high suspicion that the most likely pathogen(s) would be suitable for treatment with cefepime (see section 5.1).

Renal impairment

In patients with impaired renal function (creatinine clearance ≤ 50 ml/min) or other conditions that may compromise renal function, the dosage of cefepime should be adjusted to compensate for the slower rate of renal elimination. Because high and prolonged serum antibiotic concentrations can occur from usual dosages in patients with renal insufficiency or other conditions that may compromise renal function, the maintenance dosage should be reduced when cefepime is administered to such patients. Continued dosage should be determined by degree of renal impairment, severity of infection, and susceptibility of the causative organisms (see sections 4.2 and 5.2). During post-marketing surveillance, the following serious adverse events have been reported: reversible encephalopathy (disturbance of consciousness including confusion, hallucinations, stupor, and coma), myoclonus, seizures (including non-convulsive status epilepticus), and/or renal failure (see section 4.8). Most cases occurred in patients with renal impairment who received doses of cefepime that exceeded recommendations. In general, symptoms of neurotoxicity resolved after discontinuation of cefepime and/or after haemodialysis, however, some cases included a fatal outcome.

Renal function should be monitored carefully if drugs with nephrotoxic potential, such as aminoglycosides and potent diuretics are administered with cefepime.

Special precautions for use

Clostridium difficile associated diarrhoea (CDAD) has been reported with use of nearly all antibacterial agents, including cefepime, and may range in severity from mild diarrhoea to fatal colitis. CDAD must be considered in all patients who present with diarrhoea following antibiotic use. Careful medical history is necessary since CDAD has

been reported to occur over two months after the administration of antibacterial agents. If CDAD is suspected or confirmed, ongoing antibiotic use not directed against C. difficile may need to be discontinued.

As with other antibiotics, use of cefepime may result in overgrowth of nonsusceptible organisms. Should superinfection occur during therapy, appropriate measures should be taken.

Geriatric use

Of the more than 6400 adults treated with cefepime e in clinical studies, 35 % were 65 years or older while 16% were 75 years or older. For geriatric patients in clinical studies, who received the usual recommended adult dose, clinical efficacy and safety were comparable to clinical efficacy and safety in non-geriatric adult patients, unless the patients had renal insufficiency. There was a modest prolongation in elimination half-life and lower renal clearance values compared to those seen in younger persons.Dosage adjustments are recommended if renal function is compromised (see section 4.2 - Posology and administration and 5.2- Pharmacokinetic properties). Cefepime is known to be substantially excreted by the kidney and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection and renal function should be monitored (see sections 4.8 Undesirable effects and 5.2 - Pharmacokinetic properties). Serious adverse events, including reversible encephalopathy (disturbance of consciousness including confusion, hallucinations, stupor, and coma), myoclonus, seizures (including nonconvulsive status epilepticus), and/or renal failure have occurred in geriatric patients with renal insufficiency given the usual dose of cefepime (see section 4.8 - Undesirable effects).

Interference with serological testing

A positive Coombs test, without evidence of haemolysis, has been described in patients treated with cefepime twice daily.

Cephalosporin antibiotics may produce a false-positive reaction for glucose in the urine with copper reduction tests (Benedict’s or Fehling’s solution or with Clinitest tablets), but not with enzyme-based tests (glucose oxidase) for glycosuria. Therefore, it is recommended that glucose tests based on enzymatic glucose oxidase reactions be used.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed. Positive Coombs test without haemolysis was detected in patients receiving cefepime two times daily (see section 4.8). The result of glucose determination from urine may be false positive therefore glucose oxidase

method is suggested. Concomitant treatment with bacteriostatic antibiotics may interfere with the action of beta lactam antibiotics.

4.6 Fertility, pregnancy and lactation

Fertility No impairment of fertility has been seen in rats. There are no data on the use of cefepime in human fertility. Pregnancy Reproductive studies in mice, rats, and rabbits showed no evidence of fetal damage, however there are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed. Lactation Cefepime is excreted in human breast milk in very low concentrations. Caution should be used when cefepime is administered to a nursing woman, then the infant should be monitored closely

4.7 Effects on ability to drive and use machines

The effects of medicinal product on ability to drive and use machines have not been studied. However, possible adverse reactions like altered state of consciousness, dizziness, confusional state or hallucinations may alter the ability to drive and use machines (see sections 4.4, 4.8 and 4.9).

4.8 Undesirable effects

Undesirable effects are classified into the following categories, according to system organ class, MedDRA terminology and MedDRA frequencies: Very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to ≤1/100), rare (≥1/10,000 to ≤1/1,000), very rare (≤ 1/10,000) and not known (frequency cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

System Organ Class	Frequency	MedDRA Term
Infections and infestations	Uncommon Rare	Oral candidiasis, vaginal infection Candidiasis
Blood and lymphatic system	Very common Common	Coombs test positive Prothrombin time prolonged, partial thromboplastin time prolonged, anaemia, eosinophilia

	Uncommon Not known	Thrombocytopenia, leukopenia, neutropenia Aplastic anaemiaa, haemolytic anaemiaa, agranulocytosis
Metabolism and nutrition disorders	Not known	Urine glucose false positive
Psychiatric disorders	Not known	Confusional state, hallucination
Hepatobiliary disorders	Common	Alanine aminotransferase increased, Aspartate aminotransferase increased, Blood bilirubin increased
Renal and urinary disorders	Uncommon Not known	Blood urea increased, blood creatinine increased Renal failure, nephropathy toxic

Pediatrics

The safety profile of cefepime in infants and children is similar to that seen in adults. The most frequently reported adverse event considered related to cefepime in clinical trials was rash.

4.9 Overdose

In case of severe overdosage, especially in patients with compromised renal function, hemodialysis will aid in the removal of cefepime from the body; peritoneal dialysis is of no value. Accidental overdosing has occurred when large doses were given to patients with impaired renal function (see sections 4.2 - Posology and administration and 4.4 - Special warnings and precautions for use). Symptoms of overdose include encephalopathy (disturbance of consciousness including confusion, hallucinations, stupor, and coma), myoclonus, and seizures (see section 4.8).

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Fourth-generation cephalosporins,

ATC code: J01DE01

Mechanism of action

The mechanism of action of cefepime is based on inhibition of bacterial cell wall synthesis (in the growth phase), due to inhibition of penicillin-binding proteins (PBPs) e.g. transpeptidases. This results in a bactericidal action.

PD/PK relationship Efficacy is largely dependent on the length of time during which drug levels exceed the minimal inhibitory concentration (MIC) of the pathogen concerned. Mechanism of resistance Cefepime has a low affinity for chromosomally-encoded beta-lactamases and is highly resistant to hydrolysis by most beta-lactamases. Bacterial resistance to cefepime may be due to one or more of the following mechanisms: •reduced affinity of penicillin-binding proteins for cefepime, •production of β-lactamases which are able to hydrolyse cefepime efficiently (e.g, several of the extended-spectrum and chromosomally-mediated β-lactamases), •outer membrane impermeability, which restricts access of cefepime to penicillin binding proteins in gram-negative organisms, efflux pumps for active substances.

There is partial or complete cross resistance between cefepime and other cephalosporins and penicillins. Cefepime testing is performed using the standard dilution series. The following minimum inhibitory concentrations have been determined for susceptible and resistant germs: EUCAST (European Committee on Antimicrobial Susceptibility Testing) breakpoints (2014-01-01)

Pathogen	**susceptible**	**resistant**
Enterobacteriaceae	≤ 1 mg/l	> 4 mg/l
Pseudomonas spp.	≤ 8 mg/l [1]	> 8 mg/l
Staphylococcus spp.	note [2]	note [2]
Streptococcus groups A, B, C and G	note [3]	note [3]
Streptococcus pneumoniae	≤ 1 mg/l [4]	> 2 mg/l
Viridans group streptococci	≤ 0.5 mg/l	> 0.5 mg/l
Haemophilus influenzae	≤ 0.25 mg/l [4]	> 0.25 mg/l
Moraxella catarrhalis	≤ 4 mg/l	> 4 mg/l
PK/PD (non-species related) breakpoints [5]	≤ 4 mg/l	> 8 mg/l

1 Breakpoints relate to high dose therapy.

2 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.

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

4 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

The prevalence of resistance in individualized bacterial strains may vary according to the region and time, so it is recommended to obtain local information about the susceptibility of the strains before initiating the treatment. Cefepime is usually active against the following microorganisms *in vitro* (status: December 2012).

Commonly susceptible species
Aerobic Gram-positive microorganisms
Staphylococcus aureus (methicillin-susceptible)
Streptococcus pneumoniae (incl. penicillin-resistant strains) 0
Streptococcus pyogenes O
Aerobic Gram-negative microorganisms
Citrobacter freundii
Enterobacter aerogenes
Haemophilus influenzae
Moraxella catarrhalis 0
Morganella morganii
Proteus mirabilis %
Proteus vulgaris 0
Serratia liquefaciens 0
Serratia marcescens
Species in which acquired resistance may pose a problem during use
Aerobic Gram-positive microorganisms
Staphylococcus aureus 3
Staphylococcus epidermidis +
Staphylococcus haemolyticus +
Staphylococcus hominis +
Aerobic Gram-negative microorganisms
Acinetobacter baumannii
Enterobacter cloacae
Escherichia coli %
Klebsiella oxytoca %
Klebsiella pneumoniae %
Pseudomonas aeruginosa
Naturally resistant species

Aerobic Gram-positive microorganisms
Enterococcus spp.
Listeria monocytogenes
*Staphylococcus aureus (*methicillin-resistant*)*
Aerobic Gram-negative microorganisms
Stenotrophomonas maltophilia
Anaerobic microorganisms
Bacteroides fragilis
Clostridium difficile
Other microorganisms
Chlamydia spp.
Chlamydophila spp.
Legionella spp.
Mycoplasma spp.

O There were no current data available at the time of publishing this table. Susceptibility is assumed in the

primary literature, standard works and therapeutic recommendations.+ Rate of resistance is over 50% in at least one region.

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

3 In an outpatient setting, the rate of resistance is <10%.

5.2 Pharmacokinetic properties

The pharmacokinetic properties of cefepime are linear within the range of 250 mg to 2 g i.v.; they do not differ with regard to duration of treatment.

Absorption

After i.v.administration of 2 g over 30 minutes to healthy volunteers, peak plasma concentrations (Cmax) were 126 - 193 µg/ml.

Distribution

Cefepime is well distributed in bodily fluids and tissues. Within the range of 250 mg to 2 g, the relative tissue distribution of cefepime does not vary in relation to the administered dose. The mean steady-state volume of distribution is 18 l. There is no evidence of any

accumulation in healthy subjects given doses of up to 2 g i.v.at 8-hourly intervals over a 9-day period. Serum protein binding of cefepime is < 19% and is not dependent on serum concentrations. The mean elimination half-life is approximately 2 hours.

Biotransformation

Cefepime is metabolised to a minor extent. The primary urinary metabolite is N-methylpyrrolidine oxide, a tertiary amine, accounting for only around 7% of the dose.

Elimination

Mean total body clearance is 120 ml/min. The mean renal clearance of cefepime is 110 ml/min; this shows that cefepime is almost exclusively eliminated via renal mechanisms, mainly by glomerular filtration. Urine recovery of unchanged cefepime is approximately 85% of the dose, leading to high urinary concentrations of cefepime. Following i.v. administration of 500 mg cefepime, cefepime was no longer detectable after 12 hours in plasma and after 16 hours in urine.

Elderly patients:

Distribution of cefepime has been tested in elderly male and female patients (> 65 years). Safety and efficacy in elderly patients is comparable with adults, whilst a slight prolongation of the elimination half-life and lower renal clearance values were observed in elderly patients. Dose adjustment is required when there is concomitant impairment of renal function (see section 4.2. Posology and method of administration ”Adults with impaired renal function” and 4.4. Special warnings and precautions for use ”Elderly patients”).

Paediatrics:

The pharmacokinetics with respect to single and multiple doses of cefepime have been evaluated in patients aged between 2 months and 16 years who received doses of 50 mg/kg, administered via I.V. infusion; multiple doses were administered every 8 or 12 hours for a period of at least 48 hours. The mean plasma concentrations of cefepime after the first dose were similar to those in steady-state, and a slight accumulation was observed with the administration of additional doses. The values of the other pharmacokinetic parameters in infants and children, determined both after the first dose and in steady-state, did not differ, regardless of the dosage schedule (every 12 hours or every 8 hours). There were no differences in the pharmacokinetic values, neither between

the patients of different ages, nor between males and females. After the administration of a single I.V. dose, the average total body clearance was 3.3 ml/min/kg and the distribution volume was 0.3 l/kg. The total average elimination half-life was 1.7 hours.
The proportion of cefepime recovered unchanged in the urine was 60.4% of the administered dose and renal clearance was the main route of elimination with an average value of 2.0 ml/min/kg.

Impaired renal function:
Studies in objects with various degrees of renal insufficiency have indicated a significant prolongation of the elimination half-life. There is a linear relationship between the individual body clearance and the creatinine clearance in subjects with renal impairment. The average elimination half-life in dialysis patients is 13 hours (haemodialysis) and 19 hours for continuous ambulatory peritoneal dialysis.

Impaired hepatic function
With single-dose administration of 1 g, the kinetics of cefepime is unchanged in patients with cystic fibrosis and hepatic dysfunction. Thus, no dose adjustment is required.

5.3 Preclinical safety data

Although no long-term animal studies have been performed to evaluate carcinogenic potential, in vivo and in vitro testing has shown that cefepime is not genotoxic. Studies in animals have shown that daily doses of up to 10 times the recommended dose in humans do not have any direct or indirect harmful effects on reproduction, embryonal/foetal development, duration of gestation or peri-/postnatal development.

6. Pharmaceutical particulars

6.1 List of excipients

None

6.2 Incompatibilities

Solutions of Cefepim MIP must not be mixed with the following antibiotics: metronidazole, vancomycin, gentamicin, tobramycin sulphate and netilmicin sulphate, because physical or chemical incompatibilities may arise. Should concomitant therapy be indicated, such agents must be administered separately. All parenteral products should be visually inspected for particles prior to administration. This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store below 30°C.Protect from Sunlight.

6.5 Nature and contents of container

20 ml USP type I Glass vial

6.6 Special precautions for disposal and other handling

Preparation of the solution for i.v. injection The vial contents are dissolved in 10 ml solvent as indicated in the table below. The prepared solution is injected slowly over a 3 to 5-minute period - either directly into a vein or directly into the cannula of an infusion system whilst the patient is receiving an infusion with a compatible i.v. solution.

Preparation of the solution for i.v. infusion

For intravenous infusion, reconstitute the 1 g or 2 g cefepime solution, as noted above for direct intravenous administration; and add the required quantity of the resulting solution to a container with one of the compatible i.v. fluids (recommended final volume: about 40-50 ml). The prepared solution should be administered over a period of approximately 30 minutes.

Compatibility with intravenous liquids

The following solvents are suitable for preparation of the solution:

- Water for injections
- Glucose solution 50 mg/ml (5%)
- Sodium chloride solution 9 mg/ml (0.9%).

The reconstitution/dilution is to be made under aseptic conditions. Add the recommended volume of reconstitution solution and shake gently until the contents of the vial have dissolved completely. For single use only. Any remaining solution should be discarded. Any unused product or waste material should be disposed of in accordance with local requirements. See 6.2 for incompatibilities. Inspect the vial before use. It must only be used if the solution is free from particles. Use only clear solutions. Like other cephalosporins, cefepime solutions can develop a yellow to amber colour, depending on storage conditions. However, this has no negative influence on the effect of the product**.**

7. Applicant/Manufacturer

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8. Marketing authorisation number(s)

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9. Date of first authorisation/renewal of the authorization

Date of First Authorization:14-03-2019

10. Date of revision of the text

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