SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Cefazolin 2 g, powder for solution for injection / infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One vial contains 2096.72 mg cefazolin sodium corresponding to 2000 mg cefazolin.

One vial contains 101.6 mg sodium, corresponding to 4.4 mmol.

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Powder for solution for injection / infusion.

White or almost white powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Cefazolin is indicated for the treatment of the following infections caused by cefazolin-susceptible micro-organisms

- Skin and soft tissue infections
- Bone and joint infections

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.

The use of cefazolin should be limited to cases where parenteral treatment is needed.

Susceptibility of causative organism to the treatment should be tested (if possible), although therapy may be initiated before the results are available.

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

4.2 Posology and method of administration

The dosage as well as the method of administration are dependent on the location and severity of the infection and on the clinical and bacteriological progress.

Adults and adolescents (above 12 years of age and ≥ 40 kg bodyweight)

- Infections caused by sensitive micro-organisms: 1 g - 2 g cefazolin per day divided into 2-3 equal doses.
- Infections caused by moderately sensitive micro-organisms : 3 g - 4 g cefazolin per day divided into 3-4 equal doses.

In severe infections, doses of up to 6 g per day can be administered in three or four equal doses (one dose every 6 or 8 hours).

Special dosage recommendations

Peri-operative prophylaxis

- To prevent postoperative infection in contaminated or potentially contaminated surgery, recommended doses are: 1 g cefazolin 30 - 60 minutes before surgery
- In case of long surgical interventions (2 hours or more) additional 0.5 - 1 g cefazolin during the intervention.
- Prolonged continuation of administration beyond the surgical intervention should be supported by national official guidance.

It is important that (1) the preoperative dose be given just (30 min to 1 hour) prior to the start of surgery so that adequate antibiotic levels are present in the serum and tissues at the time of initial surgical incision; and (2) cefazolin be administered, if necessary, at appropriate intervals during surgery to provide sufficient levels of the antibiotic at the anticipated moments of greatest exposure to infective organisms.

Adult patients with renal impairment

Adults with renal impairment may need a lower dose to avoid overlapping.
This lower dose may be guided by determining blood levels. If not possible the dosage of creatinine clearance can be established.

Cefazolin maintenance therapy in patients with renal impairment

Creatinine clearance [ml/min]	Serum creatinine [mg/dl]	Dosage
≥ 55	≤ 1.5	Normal dose and normal dosage interval
35 - 54	1.6 - 3.0	Normal dose, every 8 hours
11 - 34	3.1 - 4.5	Half of the normal dose every 12 hours
≤ 10	≥ 4.6	Half of the normal dose every 18-24 hours

In haemodialysis patients, the treatment schedule depends on the dialysis conditions.

Paediatric population:

Infections caused by sensitive microorganisms

A dose of 25-50 mg / kg body weight divided into two to four equal doses per day is recommended (one dose every 6, 8 or 12 hours).

Infections caused by moderately sensitive microorganisms

A dose of up to 100 mg / kg body weight divided in three or four equal doses is recommended (one dose every 6 or 8 hours).

Prematures and infants below the age of 1 month

Since safety of use in prematures and infants below the age of one month has not been determined, the use of Cefazolin in these patients is not recommended. See also section 4.4.

Guidelines for paediatric dosage

The content of 1 vial (2000 mg cefazolin) is dissolved in 10 ml of a compatible solvent (i.e. concentration approx. 200 mg/ml). The respective volume of this solution to be used is indicated in the following table in addition to the dose in mg.

Alternatively, the dosage can be given as intravenous infusion, using the diluted solution (10 mg/ml) described in section 6.6.

Body weight	5 kg	10 kg	15 kg	20 kg	25 kg
Divided dose every 12 hours at 25 mg / kg body weight per day	63 mg; 0.3 ml	125 mg; 0.65 ml	188 mg; 0.95 ml	250 mg; 1.3 ml	313 mg; 1.55 ml
Divided dose every 8 hours at 25 mg / kg body weight per day	42 mg; 0.2 ml	85 mg; 0.4 ml	125 mg; 0.65 ml	167 mg; 0.85 ml	208 mg; 1.05 ml
Divided dose every 6 hours at 25 mg / kg body weight per day	31 mg; 0.15 ml	62 mg; 0.3 ml	94 mg; 0.45 ml	125 mg; 0.65 ml	156 mg; 0.8 ml
Divided dose every 12 hours at 50 mg / kg body weight per day	125 mg; 0.65 ml	250 mg; 1.3 ml	375 mg; 1.9 ml	500 mg; 2.5 ml	625 mg; 3.15 ml
Divided dose every 8 hours at 50 mg / kg body weight per day	83 mg; 0.4 ml	166 mg; 0.85 ml	250 mg; 1.3 ml	333 mg; 1.65 ml	417 mg; 2.1 ml
Divided dose every 6 hours at 50 mg / kg body weight per day	63 mg; 0.3 ml	125 mg; 0.65 ml	188 mg; 0.95 ml	250 mg; 1.3 ml	313 mg; 1.55 ml
Divided dose every 8 hours at 100 mg / kg body weight per day	167 mg; 0.85 ml	333 mg; 1.7 ml	500 mg; 2.5 ml	667 mg; 3.5 ml	833 mg; 4.15 ml
Divided dose every 6 hours at 100 mg / kg body weight per day	125 mg; 0.65 ml	250 mg; 1.3 ml	375 mg; 1.9 ml	500 mg; 2.5 ml	625 mg; 3.15 ml

Paediatric patients with renal impairment

Children with renal impairment (like adults) may need a lower dose to avoid overlapping.

This lower dose may be guided by determining blood levels. If not possible, the dosage of creatinine clearance may be determined according to the following guidelines.

In children with moderate impairment (creatinine clearance 40-20 ml / min), 25% of the normal daily dose, divided into doses every 12 hours are sufficient.
In children with severe impairment (creatinine 20-5 ml / min) will be 10% of normal daily dose, given every 24 hours are sufficient.
All these guidelines are valid after an initial starting dose.
See also section 4.4.

Elderly patients:
In elderly patients with normal renal function no dosage adjustment is necessary.

Method of administration
Cefazolin 2 g may be administered by slow intravenous injection or by intravenous infusion after dilution.
The volume of diluent to be used for the reconstitution is dependent upon the method of administration.
For instructions on the reconstitution of the medicinal product before administration, please see section 6.6.

Duration of treatment
The duration of the treatment depends on the severity of the infection as well as on the clinical and bacteriological progress.

4.3 Contraindications

Hypersensitivity to cefazolin.

Patients with known hypersensitivity to cephalosporin antibiotics.

History of severe hypersensitivity (e.g. anaphylactic reaction) to any other type of beta-lactam antibacterial agent (penicillins, monobactams and carbapenems).

4.4 Special warnings and precautions for use

Warnings

In case of any known hypersensitivity to penicillins or other beta-lactam antibiotics, attention is to be paid to a possible cross-sensitivity (see section 4.3).

As with all beta-lactam antibacterial agents, serious and occasionally fatal hypersensitivity reactions have been reported. In case of severe hypersensitivity reactions, treatment with cefazolin 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 cefazolin, to other cephalosporins or to any

other type of beta-lactam agent. Caution should be used if cefazolin is given to patients with a history of non-severe hypersensitivity to other beta-lactam agents.

Cefazolin should be administered only with special caution to patients with allergic reactivity (e. g. allergic rhinitis or bronchial asthma) as the risk for a serious hypersensitivity reaction is increased.

Antibacterial agent-associated pseudomembranous colitis has been reported with use of cefazolin and may range in severity from mild to life threatening. This diagnosis should be considered in patients with diarrhoea during or subsequent to the administration of cefazolin (see section 4.8). Discontinuation of therapy with cefazolin and the administration of specific treatment for *Clostridium difficile* should be considered. Medicinal products that inhibit peristalsis should not be given.

Paediatric use: As there are no sufficient experiences available so far, Cefazolin 2 g must not be applied to new-borns and babies in the first month of life.

Precautions

In case of a renal insufficiency with a glomerular filtration rate under 55 ml/min, an accumulation of cefazolin must be taken into consideration. Therefore, the dosage has to be reduced accordingly or the dosage interval has to be prolonged (see section 4.2).

In patients with renal impairment the use of cefazolin may be associated with seizures.

Prolonged prothrombin time may occur in patients with renal or hepatic impairment or poor nutritional state, as well as in patients receiving a protracted course of antimicrobial therapy, and patients previously stabilised on anticoagulant therapy. In these patients the prolongation of prothrombin time has to be monitored under treatment with cefazolin since it can very rarely cause plasmatic blood coagulation diseases (see sections 4.5 and 4.8). Therefore, INT (International Normalised Ratio) has to be measured regularly in patients with diseases which can cause haemorrhages (e.g. gastro-intestinal ulcers) as well as in patients with coagulation defects (inherited: e.g. haemophilia; acquired: e.g. by parenteral feeding, malnutrition, disordered liver or renal function or thrombocytopenia; caused by drugs: e.g. by heparin or other oral anticoagulants). Vitamin K can be substituted (10 mg per week) if necessary.

Long-term and repeated administration can lead to overgrowth of resistant organisms. If superinfection occurs during therapy, appropriate measures should be taken.

Effects on laboratory tests

In rare cases, the non-enzymatic urine sugar test and the Coombs test can show false positive results.

This medicinal product contains 4.2 mmol (or 96 mg) sodium per 2,000 mg dose. To be taken into consideration by patients on a controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

Anticoagulants

Cephalosporins may very rarely cause bleeding disorders (see 4.4). During concomitant use with oral anticoagulants (for e.g. warfarin or heparin) in high doses, the coagulation parameters should be monitored.

Vitamin K1

Some cefalosporins such as cefamandol, cefazolin and cefotetan can cause interference in the metabolism of vitamin K1, especially in cases of vitamin K1 deficiency. This may require vitamin K1 supplementation.

Probenecid

Due to its inhibitory effect on the renal diuresis, the administration of probenicid induces a higher concentration and a longer retention time of cefazolin in the blood.

Aminoglycosides/Diuretics

It cannot be excluded that cefazolin intensifies the nephrotoxic effect of aminoglycosides and quick-acting diuretics (e. g. Furosemid). Therefore, the renal function should be controlled during a concomitant therapy with these drugs.

4.6 Fertility, Pregnancy and lactation

Pregnancy

Cefazolin reaches the embryo/fetus via the placenta. There is not sufficient experience in the human use of cefazolin. As a precautionary measure, cefazolin should only be used during pregnancy after careful benefit/risk assessment, especially during the first trimester of pregnancy.

Lactation

Cefazolin is excreted in maternal milk at low concentrations and therefore it should only be used after careful benefit/risk assessment. Diarrhoea and fungus infection of the mucous membranes could occur in the breast-fed infant, so that nursing might have to be discontinued. The possibility of sensitisation should be borne in mind.

4.7 Effects on ability to drive and use machines

Cefazolin has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Dependent on the dose and duration of the treatment, patients are expected to experience one or several of the adverse reactions mentioned below.

System Organ Class	**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)**
Infections and infestations		Oral candidiasis (prolonged use).	Genital candidiasis (monoliasis), vaginitis	

System Organ Class	**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)**
Blood and lymphatic system disorder			Increase or decrease in blood glucose concentration (hyperglycemia or hypoglycemia). Leukopenia, granulocytopenia, neutropenia, thrombocytopenia, leukocytosis, granulocytosis, monocytosis, lymphocytopenia, basophilia and eosinophilia were observed in blood counts. These effects are rare and reversible.	Coagulation (blood clotting) disorders and bleeding as a consequence. At risk for these side effects are patients with a deficiency of vitamin K or other blood clotting factors, or patients on artificial nutrition, inadequate diet, impaired liver and renal function, thrombocytopenia and patients with disorders or diseases that cause bleeding (e.g., haemophilia, stomach and duodenal ulcers). Also see sections 4.4 and 4.5. Decreased haemoglobin and/or hematocrit, anaemia, agranulocytosis, aplastic anaemia, pancytopenia and hemolytic anaemia.
Immune system disorders		Erythema, erythema multiforme, exanthema, urticaria, reversible local permeability of the blood vessels, joints, or mucous membranes (angioedema), drug-induced fever and interstitial pneumonia or pneumonitis	Toxic epidermal necrolysis (Lyell's syndrome), Stevens-Johnson syndrome.	Anaphylactic shock, swelling of the larynx with narrowing of the airways , increased heart rate, shortness of breath, falling blood pressure, swollen tongue, anal pruritus, genital pruritus, face edema.

System Organ Class	**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)**
Nervous system disorders		Seizures (in patients with renal dysfunction, with inappropriate high treated doses).	Dizziness, malaise, fatigue. Nightmares, vertigo, hyperactivity, nervousness or anxiety, insomnia, drowsiness, weakness, hot flushes, disturbed colour vision, confusion and epileptogenic activity.	
Respiratory, thoracic and mediastinal disorders			Pleural effusion, chest pain, dyspnoea or respiratory distress, cough, rhinitis.	
Gastrointestinal disorders	Loss of appetite, diarrhoea, nausea and vomiting. These symptoms are usually moderate and often disappear during or after treatment.			Pseudomembranous colitis (see section 4.4)
Hepatobiliary disorders			Temporary increase in serum concentrations of AST, ALT, gamma GT, bilirubin and / or LDH and alkaline phosphatase, transient hepatitis, transient cholestatic jaundice.	

System Organ Class	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)
Renal and urinary disorders			Nephrotoxicity, interstitial nephritis, undefined nephropathy, proteinuria, temporary increase in blood urea nitrogen (BUN) usually in patients treated concomitantly with other potential nephrotoxic medicines.	
General disorders and administration site conditions	Pain at the site of intramuscular injection, sometimes with induration	Intravenous administration may cause thrombophlebitis.		

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

4.9 Overdose

Symptoms of an overdose are headache, vertigo, paraesthesia, central nervous states of agitation, myoclonia and convulsions.

In case of poisoning, elimination accelerating measures are indicated. A specific antidote does not exist. Cefazolin can be haemodialysed.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: First-generation cephalosporin.
ATC code: J01DB04.

Cefazolin is a bactericidal cephalosporin antibiotic of the first generation for parenteral administration.

Cephalosporins inhibit cell wall synthesis (in the growth stage) through blocking the penicillin-binding proteins (PBPs) like transpeptidases. The outcome is a bactericidal action.

PK/PD relationship

For cephalosporins, the most important pharmacokinetic-pharmacodynamic index correlating with in vivo efficacy has been shown to be the percentage of the dosing interval that the unbound concentration remains above the minimum inhibitory concentration (MIC) of cefazolin for individual target species (i.e. %T>MIC).

Mechanisms of resistance

Resistance to cefazolin can rest upon one of the following mechanisms:

- Inactivation by beta-lactamases: cefazolin has a high stability against penicillinases of gram-positive bacteria, but only a low stability against plasmid-coded beta-lactamases, e.g. extended-spectrum beta-lactamases or chromosomal-coded beta-lactamases of AmpC-type.
- Reduced affinity of the PBPs to cefazolin: the acquired resistance of pneumococci and other streptococci is caused by modifications of the PBPs due to mutations. The resistance of methicillin (oxacillin)-resistant Staphylococci is due to the formation of an additional PBP with a lower affinity to cefazolin.
- Insufficient penetration of cefazolin through the outer cell wall of gram-negative bacteria can lead to an insufficient inhibition of the PBPs.
- Cefazolin can be transported outside the cell through efflux pumps.

There is a partial or total cross-resistance of cefazolin with other cephalosporins and penicillins.

Breakpoints

The minimum inhibitory concentrations (MIC) breakpoints according to EUCAST (European Committee on Antimicrobial Susceptibility Testing; 2013-02-11) are

Species	sensitive	resistant
Staphylococcus spp.	Note [A]	Note [A]
Streptococcus groups A, B, C and G	Note [B]	Note [B]
Viridans group streptococci	< 0.5 mg/l	> 0.5 mg/l
PK/PD (Non-species related) breakpoints	≤ 1 mg/l	> 2 mg/l

[A] 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.

[B] The beta-lactam susceptibility of *streptococcus* groups A, B, C and G is inferred from the penicillin susceptibility.

Microbiological susceptibility
The following table shows clinically relevant pathogens classified as sensitive or resistant on the basis of *in vitro* and *in vivo* data. Cefazolin is effective against some species *in vitro*, but not clinically, thus these species are classified here as resistant.
The prevalence of acquired resistance may vary geographically and with time for selected species and local information is desirable, particularly when treating severe infections. If necessary, expert advice should be sought when the local prevalence of resistance is such that the efficacy of cefazolin is questionable. Especially in case of severe infections or failure of therapy, a microbiological diagnosis including identification of the microorganism and its susceptibility to cefazolin should be conducted.

Commonly susceptible species
Aerobe Gram-positive
Staphylococcus aureus (methicillin-sensitive*)*

Species for which acquired resistance may be a problem
Aerobe Gram-positive
Group A, B, C and G beta-haemolytic streptococci
Staphylococcus epidermidis (methicillin-sensitive)
Streptococcus pneumoniae

Aerobe Gram-negative
Haemophilus influenzae

Inherently resistant organisms
Aerobe Gram-positive
Staphylococcus aureus, methicillin-resistant

Aerobe Gram-negative
Citrobacter spp.
Enterobacter spp.
Klebsiella pneumoniae
Morganella morganii
Proteus mirabilis
Proteus stuartii
Proteus vulgaris
Pseudomonas aeruginosa
Serratia spp.

5.2 Pharmacokinetic properties

Absorption
Cefazolin is administered parenterally. After administration of 500 mg intramuscular injection, maximum serum levels obtained after approximately an hour were 20-40 micrograms / ml. After administration of 1 g maximum

serum levels of 37-63 micrograms / ml were obtained. In one continuous intravenous infusion of cefazolin study in healthy adults at doses of 3.5 mg / kg for one hour (approx 250 mg) followed by 1.5 mg / kg for the next two hours (approx 100 mg) a stable serum concentration of approx. 28 micrograms / ml was demonstrated in the third hour. The following table shows the meanserum concentration of cefazolin after intravenous injection of a single dose of 1 g.

Serum concentration (µg/ml) after intravenous administration of 1 g					
5 min	15 min	30 min	1 hr	2 hr	4 hr
188.4	135.8	106.8	73.7	45.6	16.5

Distribution
Cefazolin for 70% - 86% bound to plasma proteins. The volume of distribution is approximately 11 l / 1.73 m^2. When cefazolin is administered to patients without obstruction of the bile ducts the antibiotic levels 90-120 minutes after administration were generally higher than antibiotic levels in the serum. Conversely, where obstruction exists the concentrations of antibiotic in the bile were much lower than serum levels. After administration of therapeutic doses in patients with inflamed meninges, varying concentrations of cefazolin from 0 to 0.4 micrograms / ml were measured in cerebrospinal fluid. Cefazolin can easily pass through inflamed synovial membranes and the antibiotic concentration achieved in joints is similar to serum levels.

Biotransformation
Cefazolin is not metabolised.

Elimination
The serum half-life is about 1 hour 35 minutes. Cefazolin is excreted in a microbiologically active form in the urine. Approximately 56-89% of an intramuscular dose of 500 mg is excreted in the first six hours, 80% to almost 100% is excreted within 24 hours. After intramuscular administration of 500 mg and 1 g urine levels can reach 500-4000 µg / ml. Cefazolin is mainly removed from the serum by glomerular filtration, the renal clearance is 65 ml/min/1.73 m^2.

5.3 Preclinical safety data

The acute toxicity of cefazolin is low. By intravenous application the LD50 in rats is 2400-3700 mg/ kg body weight. Studies of chronic toxicity in different animal species (rat, dog) revealed no evidence of toxic effects. However, in dogs, muscle injury by repeated intramuscular administration was observed. Studies on the renal toxicity in rabbits showed a low nephrotoxic potential of cefazolin. Mutagenicity or animal experimental studies on the tumorigenic potential of cefazolin are not

available. Animal studies showed no evidence of teratogenic effects of cefazolin. Fertility studies and studies on peri- and postnatal toxicity showed no evidence of harmful effects of cefazolin.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

None.

6.2 Incompatibilities

Cefazolin is incompatible with amikacin disulfate, amobarbital-sodium, bleomycin sulphate, calcium gluceptate, calcium gluconate, cimetidin hydrochloride, colistin methat-sodium, erythromycin gluceptate, kanamycin sulphate, oxytetracyclin hydrochloride, pentobarbital-sodium, polymyxin-B-sulphate and tetracycline hydrochloride.

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

6.3 Shelf life

3 years.

Shelf-life of the reconstituted solution for injection/infusion

The chemical and physical stability of the prepared solution is 12 hours at 25°C and 24 hours at 2-8°C. From a microbiological point of view, the prepared solution should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

6.4 Special precautions for storage

Do not store above 30°C. Keep the vial in the outer carton in order to protect from light.

For storage conditions after reconstitution, see section 6.3.

6.5 Nature and contents of container

The product is supplied in 15 ml (type I) and 100 ml colourless glass vials (type II) closed with a chlorobutyl rubber stopper which is sealed with an aluminium flip-off cap, containing a white or almost white powder.

Packages with 1, 5 and 10 vials.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Preparation of the solution

For each route of administration see the table for addition volumes and solution concentrations, which may be useful when fractional doses are required.

Intravenous injection

The dry powder is dissolved in at least 10 ml water for injections, physiological sodium chloride solution (0.9%) or 5% glucose solution.

Reconstitution table for intravenous injection

Content per vial	Minimum amount of diluent to be added	Approximate concentration
2 g	10 ml	200 mg/ml

Cefazolin is to be injected slowly over three to five minutes. In no case should the solution be injected in less than 3 minutes. This should be done directly into the vein or into the tube from which the patient receives intravenous solution.

Single doses exceeding 1 g should be given as intravenous infusion over 30 to 60 minutes.

Intravenous infusion

The dry powder is dissolved in 8 ml water for injections and diluted to 50-100 ml with a compatible diluent. For infusion, the powder can be reconstituted with the solvent directly in the vial.

Dilution table for intravenous infusion

Content per vial	Reconstitution	Dilution	Approximate concentration
	Minimum amount of diluent to be added	Amount of diluent to be added	

2 g	8 ml	50 ml - 100 ml	34 mg/ml - 19 mg/ml

If smaller doses are needed, it is recommended to use half of the reconstituted solution (about 4 ml with 1 g cefazolin; i.e. half of the vial content) and to add a compatible diluent to a final volume of 100 ml (resulting concentration about 10 mg/ml). The required amount of this diluted solution can then be administered to the patient over the prescribed time.

Compatibility with intravenous liquids

The following solvents are suitable for the preparation of the solution:

- water for injections
- 50 mg/ml (5%) glucose solution
- 9 mg/ml (0.9 %) sodium chloride solution.

The reconstituted solution is clear, pale yellow and should be protected from light.

As for all parenteral medicinal products, inspect the reconstituted solution visually for particulate matter and discoloration prior to administration. The solution should only be used if the solution is clear and practically free from particles.

The reconstituted product is for single use only. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

PL 26928/0014

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