SUMMARY OF PRODUCT CHARACTERISTICS

Cefazolin - Fresenius

Powder for solution for IV/IM injection.

1. Trade name of the medicinal product

Cefazolin - Fresenius

2. Qualitative and quantitative composition

Cefazolin (as sodium cefazolin) 1000 mg

Each vial contains 48.4 mg of sodium

3. Pharmaceutical form

Powder for solution for IV/IM injection.

4. Clinical particulars

4.1 Therapeutic indications

Cefazolin - Fresenius is indicated in the treatment of the following serious infections due to susceptible organisms:

Respiratory Tract Infections: Due to *S.Aureus* (methicillin sensitive).

Species for which acquired resistance can be a problem: *S. pneumoniae*, *H.influenzae,* and group A beta-hemolytic streptococci.

Injectable benzathine penicillin is considered to be the drug of choice in treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever.

Data establishing the efficacy of Cefazolin - Fresenius in the subsequent prevention of rheumatic fever are not available at present.

Urinary Tract Infections: Due to *E coli*.

Skin and Skin Structure Infections: Due to *S. Aureus* (methicillin sensitive).

Species for which acquired resistance can be a problem: group A beta-hemolytic streptococci, and other strains of streptococci.

Biliary Tract Infections: Due to E coli, S. aureus. Species for which acquired resistance can be a problem: various strains of streptococci.

Bone and Joint Infections: Due to *S. aureus*.

Genital Infections: (i.e., prostatitis, epididymitis) due *to E. coli.*

Septicemia: Due to, S. *aureus* (methicillin sensitive), *E coli.* Species for which acquired resistance can be a problem: S. *pneumonia.*

Endocarditis: Due to *S. aureus* (methicillin sensitive).

Species for which acquired resistance can be a problem: group A beta-hemolytic streptococci.

Perioperative Prophylaxis: The prophylactic administration of Cefazolin - Fresenius preoperatively, intraoperatively, and postoperatively may reduce the incidence of certain postoperative infections in patients undergoing surgical procedures which are classified as contaminated or potentially contaminated (e.g., vaginal hysterectomy, and cholecystectomy in high-risk patients such as those older than 70 years, with acute cholecystitis, obstructive jaundice, or common duct bile stones).

The perioperative use of Cefazolin - Fresenius may also be effective in surgical patients in whom infection at the operative site would present a serious risk (e.g., during open-heart surgery and prosthetic arthroplasty).

4.2 Posology and Method of Administration

Posology:

Usual Adult dosage:

Type of Infection Dose frequency	Dose	Frequency
Moderate to severe infections	500 mg to 1 gram	every 6 to 8 hours
Mild infections caused by susceptible gram - positive cocci	250 mg to 500 mg	every 8 hours
Acute, uncomplicated urinary tract infections	1 gram	every 12 hours
Pneumococcal pneumonia	500 mg	every 12 hours
Severe, life -threatening infections (e.g.,endocarditis , septicemia)*	1 gram to 1.5 grams	every 6 hours

* In rare instances, doses of up to 12 grams per day have been used.

Perioperative Prophylactic Use: To prevent postoperative infection in contaminated or potentially contaminated surgery, recommended doses are:

a. 1 gram IV or IM administered 1/2 hour to 1 hour prior to the start of surgery.

b. For lengthy operative procedures (e.g., 2 hours or more), 500 mg to 1 gram IV or IM during surgery (administration modified depending on the duration of the

operative procedure),

c. 500 mg to 1 gram IV or IM every 6 to 8 hours for 24 hours postoperatively.

It is important that (1) the preoperative dose be given just (1/2 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-Fresenius 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. The prophylactic administration of Cefazolin - Fresenius should usually be discontinued within a 24- hour period after the surgical procedure. In surgery where the occurrence of infection may be particularly devastating (e.g., open-heart surgery and prosthetic arthroplasty), the prophylactic administration of Cefazolin-Fresenius may be continued for 3 to 5 days following the completion of surgery.

If there are signs of infection, specimens for cultures should be obtained for the identification of the causative organism so that appropriate therapy may be instituted

Dosage Adjustment for Patients with Reduced Renal Function: Cefazolin-Fresenius may be used in patients with reduced renal function with the following dosage adjustments:

Crearinine clearance (ml /min)	Serum creatinine (mg%)	Dosage
55 or greater	1.5 or less	Full doses
35 to 54	1.6 to 3.0	Full doses restricted to at least 8 hour intervals
11 to 34	3.1 to 4.5	1/2 of the usual dose every 12 hours
10 or less	4.6 or greater	1/2 of the usual dose every 18 to 24 hours

All reduced dosage recommendations apply after an initial loading dose appropriate to the severity of the infection. Patients undergoing peritoneal dialysis see section 5.2 Pharmacokinetic Properties.

Pediatric Dosage: In pediatric patients, a total daily dosage of 25 to 50 mg per kg (approximately 10 to 20 mg per pound) of body weight, divided into 3 or 4 equal doses, is effective for most mild to moderately severe infections. Total daily dosage may be increased to 100 mg per kg (45 mg per pound) of body weight for severe infections. Since safety for use in premature infants and in neonates has not been

established, the use of Cefazolin-Fresenius in these patients is not recommended.

Pediatric Dosage Guide					
Weight		**25 mg/kg /day** **Divided into 3 doses**		**25 mg /kg /day** **Divided into 4 doses**	
lbs	Kg	Approximate Single dose mg/q8h	Vol.(ml)needed With dilution of 125 mg/ml	Approximate Single Dose mg/q6h	Vol.(ml) needed with dilution of 125 mg/ml
10	4.5	40 mg	0.35 ml	30 mg	0.25 ml
20	9.0	75 mg	0.60 ml	55 mg	0.45 ml
30	13.6	115 mg	0.90 ml	85 mg	0.70 ml
40	18.1	150 mg	1.20 ml	115 mg	0.90 ml
50	22.7	190 mg	1.50 ml	140 mg	1.10 ml

Weight		**50 mg/kg /day** **Divided into 3 doses**		**50 mg /kg /day** **Divided into 4 doses**	
lbs	Kg	Approximate Single dose mg/q8h	Vol.(ml)needed With dilution of 225 mg/ml	Approximate Single Dose mg/q6h	Vol.(ml) needed with dilution of 225 mg/ml
10	4.5	75 mg	0.35 ml	55 mg	0.25 ml
20	9.0	150 mg	0.70 ml	110 mg	0.50 ml
30	13.6	225 mg	1.00 ml	170 mg	0.75 ml
40	18.1	300 mg	1.35 ml	225 mg	1.00 ml

50	22.7	375 mg	1.70 ml	285 mg	1.25 ml

In pediatric patients with mild to moderate renal impairment (creatinine clearance of 70 to 40 ml /min.), 60 percent of the normal daily dose given in equally divided doses every 12 hours should be sufficient. In patients with moderate impairment (creatinine clearance of 40 to 20 mL/min.), 25 percent of the normal daily dose given in equally divided doses every 12 hours should be adequate. Pediatric patients with severe renal impairment (creatinine clearance of 20 to 5 mL/min.) may be given 10 percent of the normal daily dose every 24 hours. All dosage recommendations apply after an initial loading dose.

Method of Administration:

Cefazolin may be administered by deep intramuscular injection, intravenously or by infusion.

IM Administration:

Intramuscular injection is contraindicated in children under the age of 30 months.

Dilute 1000mg of Cefazolin in 4 ml Lidocaine 0,5 % and administer by deep intramuscular injection. The reconstituted solution with 4 ml Lidocaine 0,5 % is stable for 24 hours below 25°C or 72 hours in the refrigerator (2° C - 8° C).

Reconstituted solution may present a yellow coloration that does not imply that the product potency is adversely affected.

IV Administration:

Cefazolin can be given by direct injection (bolus) or by continuous or intermittent infusion.

Do not use intravenously the solution reconstituted with lidocaine hydrochloride, which is specific for intramuscular administration.

Direct (bolus) IV injection:

Dilute 1000mg of Cefazolin in 10 ml of Water for injections or 4ml Sodium chloride 0.9% and administer slowly (3 to 5 minutes), directly in the vein or in the infusion system.

The reconstituted solution with 10 ml of Water for injections is stable for 24 hours below 25°C or 72 hours in the refrigerator (2° C - 8°C).

The reconstituted solution with 4 ml of Sodium chloride 0.9% is stable for 12 hours below 25°C or 72 hours in the refrigerator (2° C - 8°C).

Intermittent or continuous IV infusion.

Dilute 1000mg dosage of Cefazolin in 100 ml in one of the following intravenous solutions:

- Sodium chloride 0.9%
- Dextrose 5%

In these intravenous solutions, Cefazolin is stable for 12 hours below 25°C.

4.3 Contra-indications

- Cefazolin Labesfal is contraindicated in patients who have hypersensivity reaction to the active substance or to any of the solvents/ intravenous solutions mentioned in section 4.2.

-Hypersensitivity to cephalosporins.

-Hypersensitivity to lidocaine (IM administration)

-Do not use the IM presentation in children with less than 30 months (solvent is lidocaine chloridrate).

4.4 Special Warnings and Precautions for Use Warnings

• Before therapy with Cefazolin-Fresenius is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cefazolin, cephalosporins, penicillins, or other drugs. Cephalosporin administration is formally contraindicated in patients who have had a previous immediate hypersensivity reaction to cephalosporins, if this product is given to penicillin-sensitive patients, caution should be exercised because cross-hypersensitivity among beta-lactam antibiotics has been clearly documented and may occur in up to 10% of patients with a history of penicillin allergy. In case of doubt, medical surveillance is required during first administration in order to treat anaphylactic shock that might occur.If an allergic reaction to Cefazolin-Fresenius occurs, discontinue treatment with the drug. Serious acute hypersensitivity reactions may require treatment with epinephrine and other emergency measures, including oxygen, iv fluids, iv antihistamines, corticosteroids, pressor amines, and airway management, as clinically indicated.

• Pseudomembranous colitis has been reported with nearly all antibacterial agents, including cefazolin, and may range in severity from mild to life-threatening.

Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.

Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is a primary cause of "antibiotic-associated colitis."

After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an oral antibacterial drug clinically effective against C. *difficile* colitis.

Precautions

- **General:** Prolonged use of Cefazolin - Fresenius may result in the overgrowth of nonsusceptible organisms. Careful clinical observation of the patient is essential.
- When Cefazolin - Fresenius is administered to patients with low urinary output because of impaired renal function, lower daily dosage is required. As with other ß - lactam antibiotics, seizures may occur if inappropriately high doses are administered to patients with impaired renal function (see 4.2 Posology and Method of Administration).
- Geriatric Use: Reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. This drug 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 it maybe useful to monitor renal function.
- Cefazolin - Fresenius, as with all cephalosporins, should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.
- Cephalosporins may be associated with a fall in prothrombin activity. Those at risk include patients with renal or hepatic impairment or poor nutritional state, as well as patients receiving a protracted course of antimicrobial therapy, and patients previously stabilized on anticoagulant therapy. Prothrombin time should be monitored in patients at risk and exogenous vitamin K administered as indicated.
- Prescribing Cefazolin - Fresenius in the absence of a proven or strongly suspected

bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

- Renal function should be monitored during treatment, in cases of association of cefazolin with other antibacterials potentially nephrotoxic (aminoglycosides in particular) or diuretics like furosemide or etacrinic acid.

Due to the poor diffusion of cefazolin through cerebrospinal fluid, this medicine is not indicated on meningitis treatment, even if caused by sensitive germs.

4.5 Interactions with other medicinal products and other forms of interactions

Probenecid may decrease renal tubular secretion of cephalosporins when used concurrently, resulting in increased and more prolonged cephalosporin blood levels

- Although no specific interaction with cefazolin has been reported, cases of nephrotoxicity after concomitant administration of other cephalosporins and aminoglycosides had been described.
- Cefazolin has been associated with an increase of prothrombin time and haemorrhagic episodes. These effects may potentiate the effects of warfarin and other oral anticoagulants.

. *Drug/Laboratory Test Interactions*. A false positive reaction for glucose in the urine may occur with Benedict's solution, Fehling's solution or with CLINITEST® tablets, but not with enzyme-based tests such as Clinistix®.

Positive direct and indirect antiglobulin (Coombs) tests have occurred; these may also occur in neonates whose mothers received cephalosporins before delivery.

4.6 Fertility, Pregnancy and Lactation

Cefazolin use during pregnancy and lactation should be made only when necessary because the drug crosses the placental barrier and is excreted in breast milk.

Pregnancy:

The harmlessness of Cefazolin administration in premature infants and in children less than 3 months has not been established.

Studies in animals have not revealed any evidence of teratogenic or fetotoxic effect.

There are, however, 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:

Cefazolin is excreted in human milk. Caution should be exercised when Cefazolin - Fresenius is administered to a nursing woman.

Fertility

No data is available regarding the effects of Cefazolin - Fresenius on human fertility.

Labor and Delivery: When cefazolin has been administered prior to caesarean section, drug levels in cord blood have been approximately one quarter to one third of maternal drug levels.

The drug appears to have no adverse effect on the fetus.

4.7 Effects on ability to drive and use machines

Seizures may occur when high doses of cefazolin are given to patients with renal dysfunction.

4.8 Undesirable Effects

The following reactions have been reported:

Gastrointestinal: diarrhea, oral candidiasis (oral thrush), vomiting, nausea, stomach cramps, anorexia, and pseudomembranous colitis. Onset of pseudomembranous colitis symptoms may occur during or after antibiotic treatment (see Warnings). Nausea and vomiting have been reported rarely.

Allergic: Anaphylaxis, eosinophilia, itching, drug fever, skin rash, Stevens-Johnson syndrome,

Hematologic: Neutropenia, leukopenia, thrombocytopenia, thrombocythemia,

Hepatic: Transient rise in SGOT, SGPT, and alkaline phosphatase levels has been observed (without clinical evidence of liver damage).As with other cephalosporins, reports of hepatitis have been received.

Renal: As with other cephalosporins, reports of increased BUN and creatinine levels, as well as renal failure, have been received.

Local Reactions: Rare instances of phlebitis have been reported at site of injection. Pain at the site of injection after intramuscular administration has occurred infrequently. Some induration has occurred.

Other Reactions: Genital and anal pruritus (including vulvar pruritus, genital moniliasis, and vaginitis).

Infections and infestations: As with other antibiotics, prolonged use may result in overgrowth of non-susceptible microorganisms.

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.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il/ and emailed to the Registration Holder's Patient Safety Unit at: drugsafety@neopharmgroup.com.

4.9 Overdose

Symptoms of overdose: Overdose can cause pain, inflammatory reactions and phlebitis at the injection site. Administration of very high parenteral doses of cephalosporins can result in dizziness. Shivering, paresthesia and headache. Particularly in patients with renal disease cephalosporin overdose can induce convulsions.

In case of seizures, administration of the drug should be discontinued immediately and anticonvulsant therapeutic should be instituted.

If overdose occurs in patients with renal insufficiency, haemodialysis may be needed.

Overdosage may lead to the following abnormal laboratory test results: elevated creatinine, BUN, liver enzyme values and bilirubin; positive Coombs test; thrombocytosis and thrombocytopenia, eosinophilia, leukopenia and a prolonged prothrombin time.

Severe acute hypersensivity reactions may require administration of epinephrine, corticosteroids or other emergency

5 Pharmacological Properties

5.1 Pharmacodynamic Properties

Pharmacoterapeutic group: 1.1.2.1 Antiinfectives for systemic use. Antibacterials for systemic use, ß-lactam. First generation cephalosporins, semisynthetic

ATC code: J01DB04

Cefazolin is a first generation cephalosporin, and like cephalosporins and penicillins, exerts antibacterial activity by inhibiting the synthesis of the bacterial cell wall.

Cefazolin binds with high affinity to penicillin binding proteins on the bacterial cell wall, interrupting pepti- doglycan synthesis.

Transpeptidase enzym, responsible for binding glicine to pentapeptide (d-alanine) is

inhibited by cephalosporins. As a result, bacterial cell wall is destroyed.

Mechanism of resistance

The beta-lactam antibiotics contain a so-called beta- lactam ring which is essential for the antimicrobial action. If this ring is split open, it loses its antibiotic effect. Various bacteria have enzymes (beta- lactamases) that can split open this ring, thus they become resistant to this type of antibiotic.

As with all cephalosporins and other beta-lactam antibiotics, different resistance mechanism acquired by groups of bacteria include: changes in targets (penicillin-binding proteins, PBPs), enzymatic degradation of the ring by beta-lactamases and changed access to the target site.

There is cross-resistance between cephalosporins and penicilins. Gram-negative microorganisms containing inducible chromosome for beta-lactamases, such as Enterobacter spp, Serratia spp, Citrobacter spp and spp Providence, should be regarded as resistant to cefazolin despite in vitro susceptibility.

Susceptibility testing breakpoints

Minimum inhibitory concentration (MIC) breakpoints established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) are as follows:

Organism	MIC Breakpoints (mg/ml)		
	S	EU	R
Staphylococcus spp.	Note 1	-	Note 1
Streptococcus species, A,B,C and G	Note 2	-	Note 2
Viridans group streptococci	≤ 0.5	-	> 0.5
Non -species related	≤1	-	> 2

breakpoints			

S=susceptible ,1 =intermediate, R= resistent

1 Susceptibility of staphylococcus to cephalosporins in inferred from the cefoxitin susceptibility.

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

Microbiological susceptibility

The prevalence of acquired resistance may vary geographically and with time for the selected species and local information on resistance is desirable, particularly when treating severe infections. If necessary, expert advice should be sought when the local prevalence of resistance is such tnat the utility of the agent in at least some types of infections is questionable.

Commonly susceptible species
Gram-positive Staphylococcus aureus (methicillin-sensitive)
Species for which acquired resistance can be a problem
Haemophilus influenzae Neisseria gonorrhoeae Group A B, C and G streptococci, ß−haemolytic Streptococcus pneumonia Staphylococcus epidermidis (methicillin-sensitive)
Inherently resistant organisms
Citrobacter spp Enterobacter spp (Enterobacter cloacae, Enterobacter aerogenes) Ella Morgan moganii Proteus stuartii

Proteus vulgaris
Pseudomonas aeruginosa
Serratia
Staphylococcus, methicillin-resistant
Indole positive Proteus spp
Enterobacteriaceae spp (Klebsiella pneumoniae)
Enterobacteriaceae spp (Proteus mirabilis)

Some strains of listed species may be more or less sensitive to the product that is declared for the majority of these microorganisms. For this reason, susceptibility testing is recommended.

Pharmacokinetic/pharmacodynamic 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).

5.2 Pharmacokinetic Properties

Absorption and distribution:

IM administration:

After intramuscular administration of cefazolin to normal volunteers, the mean serum concentrations were 37 mcg/mL at 1 hour and 3 mcg/mL at 8 hours following a 500-mg dose, and 64 mcg/mL at 1 hour and 7 mcg/mL at 8 hours following a 1 -gram dose.

IV administration:

Studies have shown that following intravenous administration of cefazolin to normal volunteers, mean serum concentrations peaked at approximately 185 mcg/mL and were approximately 4 mcg/mL at 8 hours for a 1-gram dose.

In a study (using normal volunteers) of constant intravenous infusion with dosages of 3.5 mg/kg for 1 hour (approximately 250 mg) and 1.5 mg/kg the next 2 hours (approximately 100 mg), cefazolin produced a steady serum level at the third hour of approximately 28 mcg/mL.

Studies in patients hospitalized with infections indicate that cefazolin produces mean peak serum levels approximately equivalent to those seen in normal volunteers.

The serum half-life for cefazolin is approximately 1.8 hours following IV administration and approximately 2.0 hours following IM administration

Bile levels in patients without obstructive biliary disease can reach or exceed serum levels by up to 5 times; however, in patients with obstructive biliary disease, bile levels of cefazolin are considerably lower than serum levels (< 1.0 mcg/mL).

After administration of therapeutic doses in patients with inflamed meninges, concentrations ranges of Cefazolin measured in cerebrospinal fluid vary from 0 to 0.4 micrograms/ml.

In synovial fluid, the level of cefazolin becomes comparable to that reached in serum at about 4 hours after drug administration.

Studies of cord blood show prompt transfer of cefazolin across the placenta, cefazolin is present in very low concentrations in the milk of nursing mothers.

Cefazolin binds to plasma proteins at about 70%- 86%.

The volume of distribution is approximately 11 L/1.73 m2

Biotransformation:

Cefazolin is not metabolized in the body.

Flimination:

Cefazolin is excreted unchanged in the urine. In the first 6 hours approximately 60% of the drug is excreted in the urine and this increases to 70% to 80% within 24 hours. Cefazolin achieves peak urine concentrations of approximately 2,400 mcg/mL and

4,000 mcg/mL respectively following 500-mg and 1-gram intramuscular doses.

Cefazolin is mainly removed from the serum by glomerular filtration, the renal clearance is 65 ml/ min/1.73 m2.

In patients undergoing peritoneal dialysis (2 L/hr.), cefazolin produced mean serum levels of approximately 10 and 30 mcg/mL after 24 hours instillation of a dialyzing solution containing 50 mg/L and 150 mg/L, respectively. Mean peak levels were 29 mcg/mL (range 13 to 44 mcg/mL) with 50 mg/L (3 patients), and 72 mcg/mL (range 26 to 142 mcg/mL) with 150 mg/L (6 patients). Intraperitoneal administration of cefazolin is usually well tolerated.

Controlled studies on adult normal volunteers, receiving 1 gram 4 times a day for 10

days, monitoring CBC, SGOT, SGPT, bilirubin, alkaline phosphatase, BUN, creatinine, and urinalysis, indicated no clinically significant changes attributed to cefazolin.

6 Pharmaceutical particulars

6.1 List of excipients

See 2_Qualitative and quantitative composition and the recommended solvents/ intravenous solutions mentioned in section 4.2.

6.2 Incompatibilities

Cefazolin solutions should not be mixed with blood, proteins hydrolyse or other liquids containing proteins.

Cefazolin is incompatible of with aminoglycosides, tetracyclines, eritromycin, ascorbic acid, B vitamin, bleomycin sulphate, calcium gluceptate, calcium gluconate and cimetidine chloridrate.

6.3 Shelf-life

2 years.

6.4 Special precautions for storage

Store below 25°C.

From a microbiological point of view, unless the method of opening and reconstitution/dilution precludes the risk of microbial contamination, 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.

Chemical and physical in-use stability has been demonstrated as follows:

- In-use stability after reconstitution for IM administration / Direct (bolus) IV injection:

Diluent and volume	**Purpose of use**	**Stability after reconstitution**
4 ml lidocaine 0.5%	IM administration	24 h below 25°C or 72 h in the refrigerator (2°C - 8°C).
10 ml water for injections	Direct IV injection	24 h below 25° C or 72 h in the refrigerator (2°C-8°C).
4 ml sodium chloride 0.9%	Direct IV injection	12 h below 25° C or 72 h in the refrigerator (2°C- 8°C).

- In-use stability after reconstitution for intermittent IV infusion in 100 ml of Sodium chloride 0,9% / Dextrose 5% has been demonstrated for 12 hours below 25°C.
- Obtained solutions should be protected from light.

6.5 Nature and contents of container

Sterile powder is packaged in glass vials with 1000 mg of sodium cefazolin

Pack sizes: 1,5,10,50, vials

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and handling

Do not use after the expiry date which is stated on the carton.

Reconstituted solutions should be inspected visually. Only clear solutions free of visible particles should be used.

Keep out of the reach and sight of children.

7. Marketing authorisation holder

NEOPHARM (ISRAEL) 1996 LTD

HASHILOACH 6, POB 7063 PETACH TIQVA 4917001

Manufacturer

Labesfal - Lahoratorios Almiro S.A Fresenius Kabi Group

Lageao, 3465- 157 Santiago de Besteiros, Portugal

8. Marketing authorisation number

149-89-33775-00

9. Date of revision of the text

Revised in June 2022 according to MOH guidelines

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