

1. NAME OF THE MEDICINAL PRODUCT

Zinacef Injection 750 mg

Zinacef Injection 1.5 g

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Vials containing 750 mg or 1.5 g cefuroxime as cefuroxime sodium. Cefuroxime is a white to faintly yellow powder to which appropriate amounts of water are added to prepare an off-white suspension for intramuscular use or a yellowish solution for intravenous administration. Variations in the intensity of this colour do not indicate any change in either the efficacy or safety of the product.

3. PHARMACEUTICAL FORM

Powder for solution/suspension for injection

Powder for solution for infusion

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ZINACEF is a bactericidal cephalosporin antibiotic which is resistant to most beta-lactamases and is active against a wide range of Gram-positive and Gram-negative organisms.

It is indicated for the treatment of infections before the infecting organism has been identified or when caused by sensitive bacteria. Susceptibility to *ZINACEF* will vary with geography and time and local susceptibility data should be consulted where available (see *Pharmacological properties*, *Pharmacodynamics*).

Indications include:

- respiratory tract infections for example, acute exacerbation of chronic bronchitis, infected bronchiectasis, bacterial pneumonia, lung abscess and post-operative chest infections
- ear, nose and throat infections for example, sinusitis, tonsillitis, pharyngitis and otitis media
- urinary tract infections for example, acute and chronic pyelonephritis, cystitis and asymptomatic bacteriuria
- soft-tissue infections for example, cellulitis, erysipelas and wound infections
- bone and joint infections for example, osteomyelitis and septic arthritis
- obstetric and gynaecological infections, pelvic inflammatory diseases
- gonorrhoea particularly when penicillin is unsuitable
- other infections including septicaemia, meningitis and peritonitis
- prophylaxis against infection in abdominal, pelvic, orthopaedic, cardiac, pulmonary, oesophageal and vascular surgery where there is increased risk from infection.

Usually *ZINACEF* will be effective alone, but when appropriate it may be used in combination with an aminoglycoside antibiotic, or in conjunction with metronidazole (orally or by suppository or injection), especially for prophylaxis in colonic or gynaecological surgery.

Where appropriate *ZINACEF* is effective when used prior to oral therapy with *ZINNAT* (cefuroxime axetil) in the treatment of pneumonia and acute exacerbations of chronic bronchitis.

4.2 Posology and method of administration

Pharmaceutical forms:

ZINACEF Injection: Powder for suspension or solution for injection and Powder for solution for infusion

ZINACEF Injection is for intravenous (i.v.) and/or intramuscular (i.m.) administration only.

ZINACEF is also available as the axetil ester (*ZINNAT*) for oral administration. This permits the use of sequential therapy with the same antibiotic, when a change from parenteral to oral therapy is clinically indicated.

No more than 750 mg should be injected at one intramuscular site.

General dosing recommendations

- **Adults**

Many infections respond to 750 mg three times daily by i.m. or i.v. injection. For more severe infections, the dose should be increased to 1.5 g three times daily given i.v. The frequency of administration may be increased to 6-hourly if necessary, giving total daily doses of 3 to 6 g. Where clinically indicated, some infections respond to 750 mg or 1.5 g twice daily (i.v. or i.m.) followed by oral therapy with *ZINNAT*.

- **Infants and Children**

30 to 100 mg/kg/day given as 3 or 4 divided doses. A dose of 60 mg/kg/day is appropriate for most infections.

- **Neonates**

30 to 100 mg/kg/day given as 2 or 3 divided doses (see *Pharmacokinetics*).

GONORRHOEA

- **Adults**

1.5 g as a single dose (as 2 x 750 mg injections given i.m. with different sites, e.g. each buttock).

MENINGITIS

ZINACEF is suitable for sole therapy of bacterial meningitis due to sensitive strains.

- **Adults:** 3 g given i.v. every 8 hours.
- **Infants and Children:** 150 to 250 mg/kg/day given i.v. in 3 or 4 divided doses
- **Neonates:** The dosage should be 100 mg/kg/day given i.v.

PROPHYLAXIS

- **Adults**

The usual dose is 1.5 g given i.v. with induction of anaesthesia for abdominal, pelvic and orthopaedic operations. This may be supplemented with two 750 mg i.m. doses 8 and 16 hours later.

In cardiac, pulmonary, oesophageal and vascular operations, the usual dose is 1.5 g given i.v. with induction of anaesthesia, continuing with 750 mg given i.m. three times daily for a further 24 to 48 hours.

In total joint replacement, 1.5 g *ZINACEF* powder may be mixed dry with each pack of methyl methacrylate cement polymer before adding the liquid monomer.

SEQUENTIAL THERAPY

- **Adults**

Duration of both parenteral and oral therapy is determined by the severity of the infection and the clinical status of the patient.

Pneumonia

1.5 g *ZINACEF* twice daily (given i.v. or i.m.) for 48 to 72 hours, followed by 500 mg twice daily *ZINNAT* (cefuroxime axetil) oral therapy for 7 to 10 days.

Acute exacerbations of chronic bronchitis

750 mg *ZINACEF* twice daily (given i.v. or i.m.) for 48 to 72 hours, followed by 500 mg twice daily *ZINNAT* (cefuroxime axetil) oral therapy for 5 to 10 days.

Renal impairment

Cefuroxime is excreted by the kidneys. Therefore, as with all such antibiotics, in patients with markedly impaired renal function it is recommended that the dosage of *ZINACEF* should be reduced to compensate for its slower excretion.

It is not necessary to reduce the standard dose (750 mg to 1.5 g three times daily) until the creatinine clearance falls to 20 ml/min or below.

In adults with marked impairment (creatinine clearance 10 to 20 ml/min) 750 mg twice daily is recommended and with severe impairment (creatinine clearance < 10 ml/min) 750 mg once daily is adequate.

For patients on haemodialysis a further 750 mg dose should be given i.v. or i.m. at the end of each dialysis. In addition to parenteral use, *ZINACEF* can be incorporated into the peritoneal dialysis fluid (usually 250 mg for every 2 litres of dialysis fluid).

For patients in renal failure on continuous arteriovenous haemodialysis or high-flux haemofiltration in intensive therapy units a suitable dosage is 750 mg twice daily. For low-flux haemofiltration follow the dosage recommended under impaired renal function.

Hepatic impairment

Cefuroxime is primarily eliminated by the kidney. In patients with hepatic dysfunction this is not expected to effect the pharmacokinetics of cefuroxime.

Method of administration

Cefuroxime should be administered by intravenous injection over a period of 3 to 5 minutes directly into a vein or via a drip tube or infusion over 30 to 60 minutes, or by deep intramuscular injection. For instructions on reconstitution of the medicinal product before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to cefuroxime or to any of the excipients listed in section 6.1.

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 useHypersensitivity reactions

As with all beta-lactam antibacterial agents, serious and occasionally fatal hypersensitivity reactions have been reported.

There have been reports of hypersensitivity reactions which progressed to Kounis syndrome (acute allergic coronary arteriospasm that can result in myocardial infarction, see section 4.8). In case of severe hypersensitivity reactions, treatment with cefuroxime 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 cefuroxime, to other cephalosporins or to any other type of beta-lactam agent. Caution should be used if cefuroxime is given to patients with a history of non-severe hypersensitivity to other beta-lactam agents.

Concurrent treatment with potent diuretics or aminoglycosides

Cephalosporin antibiotics at high dosage should be given with caution to patients receiving concurrent treatment with potent diuretics such as furosemide or aminoglycosides. Renal function should be monitored in the elderly and those with known pre-existing renal impairment (see section 4.2).

Overgrowth of non-susceptible microorganisms

Use of *ZINACEF* may result in the overgrowth of *Candida*. Prolonged use may also result in the overgrowth of other non-susceptible organisms (e.g. enterococci and *Clostridium difficile*), which may require interruption of treatment (see section 4.8).

Antibacterial agent-associated pseudomembranous colitis has been reported with the use of cefuroxime 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 cefuroxime (see section 4.8). Discontinuation of therapy with cefuroxime and the administration of specific treatment for *Clostridium difficile* should be considered. Medicinal products that inhibit peristalsis should not be given.

Intracameral use and ocular toxicity

Cefuroxime is not formulated for intracameral use. Individual cases and clusters of serious ocular adverse reactions have been reported following unapproved intracameral use of cefuroxime sodium compounded from vials approved for intravenous/intramuscular administration. These reactions included macular oedema, retinal oedema, retinal detachment, retinal toxicity, visual impairment, visual acuity reduced, vision blurred, corneal opacity and corneal oedema.

Intra-abdominal infections

Due to its spectrum of activity, cefuroxime is not suitable for the treatment of infections caused by Gram-negative non-fermenting bacteria (see section 5.1).

Interference with diagnostic tests

The development of a positive Coomb's Test associated with the use of cefuroxime may interfere with cross matching of blood (see section 4.8).

Slight interference with copper reduction methods (Benedict's, Fehling's, Clinitest) may be observed. However, this should not lead to false-positive results, as may be experienced with some other cephalosporins.

As a false negative result may occur in the ferricyanide test, it is recommended that either the glucose oxidase or hexokinase methods are used to determine blood/plasma glucose levels in patients receiving cefuroxime sodium.

Severe cutaneous adverse reactions (SCAR), such as Stevens Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) and acute generalised exanthematous pustulosis (AGEP) have been reported in patients receiving cefuroxime (see section 4.8). If signs and symptoms suggestive of these reactions appear, cefuroxime should be withdrawn immediately and an alternative treatment should be considered.

4.5 Interaction with other medicinal products and other forms of interaction

Cefuroxime is excreted by glomerular filtration and tubular secretion. Concomitant use of probenecid is not recommended. Concurrent administration of probenecid prolongs the excretion of the antibiotic and produces an elevated peak serum level.

Potential nephrotoxic drugs and loop diuretics

High-dose treatments with cephalosporins should be carried out with caution on patients who are taking strong-acting diuretics (such as furosemide) or potential nephrotoxic preparations (such as aminoglycoside antibiotics), since impairment of renal function through such combinations cannot be ruled out.

Other Interactions

Determination of blood/plasma glucose levels: refer to section 4.4.

Concomitant use with oral anticoagulants may give rise to increased international normalised ratio (INR).

4.6 Fertility, pregnancy and lactation

Pregnancy

There are limited amounts of data from the use of cefuroxime in pregnant women. Studies in animals

have shown no reproductive toxicity (see section 5.3). Cefuroxime sodium should be prescribed to pregnant women only if the benefit outweighs the risk.

Cefuroxime has been shown to cross the placenta and attain therapeutic levels in amniotic fluid and cord blood after intramuscular or intravenous dose to the mother.

Breastfeeding

Cefuroxime is excreted in human milk in small quantities. Adverse reactions at therapeutic doses are not expected, although a risk of diarrhoea and fungus infection of the mucous membranes cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from cefuroxime therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

Fertility

There are no data on the effects of cefuroxime sodium on fertility in humans. Reproductive studies in animals have shown no effects on fertility.

4.7 Effects on ability to drive and use machines

No studies on the effects of cefuroxime on the ability to drive and use machines have been performed. However, based on known adverse reactions, cefuroxime is unlikely to have an effect on the ability to drive and use machines.

4.8 Undesirable effects

The most common adverse reactions are neutropenia, eosinophilia, transient rise in liver enzymes or bilirubin, particularly in patients with pre-existing liver disease, but there is no evidence of harm to the liver and injection site reactions.

The frequency categories assigned to the adverse reactions below are estimates, as for most reactions suitable data for calculating incidence are not available. In addition, the incidence of adverse reactions associated with *ZINACEF* may vary according to the indication.

Data from clinical trials were used to determine the frequency of very common to rare undesirable effects adverse reactions. The frequencies assigned to all other undesirable effects (i.e., those occurring at <1/10,000) were mainly determined using post-marketing data and refer to a reporting rate rather than a true frequency.

Treatment related adverse reactions, all grades, are listed below by MedDRA body system organ class, frequency and grade of severity. The following convention has been used for the classification of frequency:

Very common	≥1/10
Common	≥1/100 to <1/10
Uncommon	≥1/1,000 to <1/100
Rare	≥1/10,000 to <1/1000,
Very rare	<1/10,000
Not known	cannot be estimated from the available data

Infections and infestations

Not known: *Candida* overgrowth, overgrowth of *Clostridium difficile*

Blood and lymphatic system disorders

Common:	Neutropenia, eosinophilia, decreased haemoglobin concentration
Uncommon:	Leukopenia, positive Coomb's test
Not known:	Thrombocytopenia, haemolytic anaemia

Immune system disorders

Not known: Drug fever, interstitial nephritis, anaphylaxis, cutaneous vasculitis

Cardiac disorders

Very rare: Kounis syndrome

Gastrointestinal disorders

Uncommon: Gastrointestinal disturbance
 Very rare: Pseudomembranous colitis (see section 4.4)

Hepatobiliary disorders

Common: Transient rise in liver enzymes
 Uncommon: Transient rise in bilirubin

Skin and subcutaneous tissue disorders

Uncommon: Skin rash, urticaria and pruritus
 Very rare: Erythema multiforme, angioneurotic oedema, severe cutaneous adverse reactions, including Stevens Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalised exanthematous pustulosis (AGEP) (see section 4.4)

Renal and urinary disorders

Not known: Elevations in serum creatinine, elevations in blood urea nitrogen and decreased creatinine clearance (see *Warnings and Precautions*)

General disorders and administration site conditions

Common: Injection site reactions which may include pain and thrombophlebitis

Description of selected adverse reactions

Cephalosporins as a class tend to be absorbed onto the surface of red cell membranes and react with antibodies directed against the agent to produce a positive Coomb's test (which can interfere with cross matching of blood) and very rarely haemolytic anaemia.

Transient rises in serum liver enzymes or bilirubin have been observed which are usually reversible.

Pain at the intramuscular injection site is more likely at higher doses. However it is unlikely to be a cause for discontinuation of treatment.

Paediatric population

The safety profile for cefuroxime sodium in children is consistent with the profile in adults.

4.9 Overdose

Overdose can lead to neurological sequelae including encephalopathy, convulsions and coma. Symptoms of overdose can occur if the dose is not reduced appropriately in patients with renal impairment (see sections 4.2 and 4.4).

Serum levels of cefuroxime can be reduced by haemodialysis or peritoneal dialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Pharmacotherapeutic group: antibacterials for systemic use, other beta-lactam antibacterials, second-generation cephalosporins

ATC code: J01DC02

Mechanism of action

Cefuroxime inhibits bacterial cell wall synthesis following attachment to penicillin binding proteins (PBPs). This results in the interruption of cell wall (peptidoglycan) biosynthesis, which leads to bacterial cell lysis and death.

Mechanism of resistance

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

- hydrolysis by beta-lactamases including (but not limited to) extended-spectrum beta-lactamases (ESBLs), and Amp-C enzymes, that may be induced or stably derepressed in

- certain aerobic Gram-negative bacterial species;
- reduced affinity of penicillin-binding proteins for cefuroxime;
- outer membrane impermeability, which restricts access of cefuroxime to penicillin binding proteins in Gram-negative bacteria;
- bacterial efflux pumps.

Organisms that have acquired resistance to other injectable cephalosporins are expected to be resistant to cefuroxime. Depending on the mechanism of resistance, organisms with acquired resistance to penicillins may demonstrate reduced susceptibility or resistance to cefuroxime.

Cefuroxime sodium breakpoints

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

Microorganism	Breakpoints (mg/L)	
	<u>Susceptible</u>	<u>Resistant</u>
<i>Enterobacteriaceae</i> ¹	≤8 ²	>8
<i>Staphylococcus</i> spp.	Note ³	Note ³
<i>Streptococcus</i> A, B, C and G	Note ⁴	Note ⁴
<i>Streptococcus pneumoniae</i>	≤0.5	>1
<i>Streptococcus</i> (other)	≤0.5	>0.5
<i>Haemophilus influenzae</i>	≤1	>2
<i>Moraxella catarrhalis</i>	≤4	>8
Non-species related breakpoints ¹	≤4 ⁵	>8 ⁵

¹ The cephalosporin breakpoints for Enterobacteriaceae will detect all clinically important resistance mechanisms (including ESBL and plasmid mediated AmpC). Some strains that produce beta-lactamases are susceptible or intermediate to 3rd or 4th generation cephalosporins with these breakpoints and should be reported as found, i.e. the presence or absence of an ESBL does not in itself influence the categorization of susceptibility. In many areas, ESBL detection and characterization is recommended or mandatory for infection control purposes.

² Breakpoint relates to a dosage of 1.5 g × 3 and to *E. coli*, *P. mirabilis* and *Klebsiella* spp. only

³ Susceptibility of staphylococci to cephalosporins is inferred from the methicillin susceptibility except for ceftazidime and cefixime and ceftibuten, which do not have breakpoints and should not be used for staphylococcal infections.

⁴ The susceptibility of streptococcus groups A, B, C and G to cephalosporins is inferred from the benzylpenicillin susceptibility.

⁵ Breakpoints apply to daily intravenous dose of 750 mg × 3 and a high dose of at least 1.5 g × 3.

Microbiological susceptibility

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

Cefuroxime is usually active against the following microorganisms *in vitro*.

Commonly Susceptible Species
<u>Gram-Positive Aerobes:</u> <i>Staphylococcus aureus</i> (methicillin-susceptible) ^{\$} <i>Streptococcus pyogenes</i> <i>Streptococcus agalactiae</i>
<u>Gram-Negative Aerobes:</u> <i>Haemophilus parainfluenzae</i> <i>Moraxella catarrhalis</i>
Organisms for which acquired resistance may be a problem
<u>Gram-Positive Aerobes:</u> <i>Streptococcus pneumoniae</i> <i>Streptococcus mitis</i> (viridans group)
<u>Gram-Negative Aerobes:</u> <i>Citrobacter</i> spp. not including <i>C. freundii</i> <i>Enterobacter</i> spp. not including <i>E. aerogenes</i> and <i>E. cloacae</i> <i>Escherichia coli</i> <i>Haemophilus influenzae</i> <i>Klebsiella pneumoniae</i> <i>Proteus mirabilis</i> <i>Proteus</i> spp. not including <i>P. penneri</i> and <i>P. vulgaris</i> <i>Providencia</i> spp. <i>Salmonella</i> spp.
<u>Gram-Positive Anaerobes:</u> <i>Peptostreptococcus</i> spp. <i>Propionibacterium</i> spp.
<u>Gram-Negative Anaerobes:</u> <i>Bacteroides</i> spp. <i>Fusobacterium</i> spp.
Inherently resistant microorganisms
<u>Gram-Positive Aerobes:</u> <i>Enterococcus faecalis</i> <i>Enterococcus faecium</i>
<u>Gram-Negative Aerobes:</u> <i>Acinetobacter</i> spp. <i>Burkholderia cepacia</i> <i>Campylobacter</i> spp. <i>Citrobacter freundii</i> <i>Enterobacter aerogenes</i> <i>Enterobacter cloacae</i> <i>Morganella morganii</i> <i>Proteus penneri</i> <i>Proteus vulgaris</i> <i>Pseudomonas aeruginosa</i> <i>Serratia marcescens</i> <i>Stenotrophomonas maltophilia</i>
<u>Gram-Positive Anaerobes:</u> <i>Clostridium difficile</i>
<u>Gram-Negative Anaerobes:</u> <i>Bacteroides fragilis</i>
<u>Others:</u> <i>Chlamydia</i> species <i>Mycoplasma</i> species <i>Legionella</i> species

\$ All methicillin-resistant *S. aureus* are resistant to cefuroxime.

In vitro the activities of cefuroxime sodium and aminoglycoside antibiotics in combination have been shown to be at least additive with occasional evidence of synergy.

5.2 Pharmacokinetics properties

Peak levels of cefuroxime are achieved within 30 to 45 minutes after i.m. administration.

Protein binding has been variously stated as 33 - 50% depending on the methodology used. Concentrations of cefuroxime in excess of the minimum inhibitory levels for common pathogens can be achieved in bone, synovial fluid and aqueous humour. Cefuroxime passes the blood-brain barrier when the meninges are inflamed.

Cefuroxime is not metabolised and is excreted by glomerular filtration and tubular secretion.

The serum half-life after either i.m. or i.v. injection is approximately 70 minutes.

In the first weeks of life the serum half-life of cefuroxime can be 3 to 5 times that in the adult.

Concurrent administration of probenecid prolongs the excretion of the antibiotic and produces an elevated peak serum level.

There is an almost complete recovery (85 to 90%) of unchanged cefuroxime in urine within 24 hours of administration. The major part is excreted in the first 6 hours.

Serum levels of cefuroxime are reduced by dialysis.

5.3 Preclinical safety data

No additional data of relevance.

6. PHARMACEUTICAL INFORMATION

6.1 List of Excipients

None.

Each 750 mg vial contains 42 mg sodium (1.8 mEq).

Each 1.5 g vial contains 83 mg of sodium (3.6 mEq).

6.2 Incompatibilities

ZINACEF should not be mixed in the syringe with aminoglycoside antibiotics.

The pH of 2.74% w/v Sodium Bicarbonate Injection BP considerably affects the colour of the solution and therefore this solution is not recommended for the dilution of *ZINACEF*. However, if required, for patients receiving Sodium Bicarbonate Injection by infusion *ZINACEF* may be introduced into the tube of the giving set.

6.3 Shelf-Life

24 months. The expiry date of the powder is indicated on the packaging.

The unopened pack storage temperature requirements are indicated on the packaging.

If unopened product previously stored below 30°C

Shelf life after reconstitution and dilution under controlled and validated aseptic conditions:

Suspension and solution for Injection - 5 hours below 25°C or 72 hours at 2 to 8°C

Solution for Infusion - Use immediately or within 24 hours at 2° to 8°C

Shelf life if reconstitution and dilution has not taken place in controlled and validated aseptic conditions:

The product should be used immediately or within 24 hours if stored at 2° to 8°C.

6.4 Special precautions for storage

Store below 30°C. Protect from light.

The storage conditions are detailed on the packaging.

Store in original package to protect from light.

Some increase in the colour of prepared solutions and suspensions of *ZINACEF* may occur on storage.

6.5 Nature and contents of container

ZINACEF Injection 750 mg and 1.5 g are available in single vial packs.

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

Add 3 ml Water for Injections to 750 mg *ZINACEF*. Shake gently to produce an off-white opaque suspension.

Intravenous:

Dissolve *ZINACEF* in Water for Injections using at least 6 ml for 750 mg, or 15 ml for 1.5 g. Shake gently to produce a yellowish solution.

Intravenous infusion:

Dissolve 1.5 g of *ZINACEF* in 15 ml of Water for Injections. Add the reconstituted solution of *ZINACEF* to 50 or 100 ml of a compatible infusion fluid (see information on Compatibility below). These solutions may be given directly into the vein or introduced into the tubing of the giving set if the patient is receiving parenteral fluids.

Compatibility

1.5g *ZINACEF* constituted with 15 ml Water for Injections may be added to metronidazole injection (500 mg/100 ml).

1.5g *ZINACEF* is compatible with azlocillin 1 g (in 15 ml) or 5 g (in 50 ml).

ZINACEF (5 mg/ml) is compatible with 5% w/v or 10% w/v xylitol injection.

ZINACEF may be constituted for i.m. use with aqueous solutions containing up to 1% lidocaine hydrochloride.

ZINACEF is compatible with the following more commonly used i.v. infusion fluids:

- Sodium Chloride Injection BP 0.9% w/v
- 5% Dextrose Injection BP
- 0.18% w/v Sodium Chloride plus 4% Dextrose Injection BP
- 5% Dextrose and 0.9% Sodium Chloride Injection
- 5% Dextrose and 0.45% Sodium Chloride Injection
- 5% Dextrose and 0.225% Sodium Chloride Injection
- 10% Dextrose Injection
- 10% Invert Sugar in Water for Injection
- Ringer's Injection USP
- Lactated Ringer's Injection USP
- M/6 Sodium Lactate Injection
- Compound Sodium Lactate Injection BP (Hartmann's Solution).

The stability of *ZINACEF* in Sodium Chloride Injection BP 0.9% w/v and in 5% Dextrose Injection is not affected by the presence of hydrocortisone sodium phosphate.

ZINACEF has also been found compatible admixed in i.v. infusion with: Heparin (10 and 50 units/ml) in 0.9% Sodium Chloride Injection; Potassium Chloride (10 and 40 mEqL) in 0.9% Sodium Chloride Injection.

Not all presentations are available in every country.

7. MANUFACTURER

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8. DATE OF REVISION OF THE TEXT

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