# National Agency for Food & Drug Administration & Control (NAFDAC)

## SUMMARY OF PRODUCT CHARACTERISTICS

## OF

## CEFUROXIME SODIUM FOR INJECTION 750MG

**Reyoung Pharmaceutical Co., Ltd**

# CONTENT

# Cefuroxime Sodium for Injection 750mg

## 1. NAME OF THE MEDICINAL PRODUCT

Cefuroxime Sodium for Injection 750mg, powder for solution for injection

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains, as the active ingredient, cefuroxime sodium equivalent to 750mg of cefuroxime.

## 3. PHARMACEUTICAL FORM

Powder for solution for injection

## 4. Clinical particulars

### 4.1 Therapeutic indications

Cefuroxime is indicated for the treatment of infections listed below in adults and children, including neonates (from birth) (see sections 4.4 and 5.1).

• Community acquired pneumonia

• Acute exacerbations of chronic bronchitis

• Complicated urinary tract infections, including pyelonephritis

• Soft-tissue infections: cellulitis, erysipelas and wound infections

• Intra-abdominal infections (see section 4.4)

• Prophylaxis against infection in gastrointestinal (including oesophageal), orthopaedic, cardiovascular and gynaecological surgery (including caesarean section)

In treatment and prevention of infections in which it is very likely that anaerobic organisms will be encountered, cefuroxime should be administered with additional appropriate antibacterial agents.

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

### 4.2 Posology and method of administration

**Posology**

Table 1. Adults and children ≥ 40kg

| **Indication** | **Dosage** |
|---|---|
| Community acquired pneumonia and acute exacerbations of chronic bronchitis | 750 mg every 8 hours (intravenously or intramuscularly) |

| | |
|---|---|
| Soft-tissue infections: cellulitis, erysipelas and wound infections | |
| Intra-abdominal infections | |
| Complicated urinary tract infections, including pyelonephritis | 1.5g every 8 hours (intravenously or intramuscularly) |
| Severe infections | 750 mg every 6 hours (intravenously)<br>1.5 g every 8 hours (intravenously) |
| Surgical prophylaxis for gastrointestinal, gynaecological (including caesarean section) and orthopaedic operations | 1.5 g with the induction of anaesthesia. This may be supplemented with two 750 mg doses (intramuscularly) after 8 hours and 16 hours. |
| Surgical prophylaxis for cardiovascular and oesophageal operations | 1.5 g with induction of anaesthesia followed by 750 mg (intramuscularly) every 8 hours for a further 24 hours. |

Table 2. Children < 40kg

| | Infants and toddlers > 3 weeks and children < 40 kg | Infants (birth to 3 weeks) |
|---|---|---|
| Community acquired pneumonia | 30 to 100 mg/kg/day (intravenously) given as 3 or 4 divided doses; a dose of 60 mg/kg/day is appropriate for most infections | 30 to 100 mg/kg/day (intravenously) given as 2 or 3 divided doses (see section 5.2) |
| Complicated urinary tract infections, including pyelonephritis | | |
| Soft-tissue infections: cellulitis, erysipelas and wound infections | | |
| Intra-abdominal infections | | |

Renal impairment

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

Table 3. Recommended doses for Cefuroxime in renal impairment

| Creatinine clearance | $T_{1/2}$ (hrs) | Dose mg |
|---|---|---|
| > 20 mL/min/1.73 $m^2$ | 1.7–2.6 | It is not necessary to reduce the standard dose (750 mg to 1.5 g three times daily). |
| 10-20 mL/min/1.73 $m^2$ | 4.3–6.5 | 750 mg twice daily |
| < 10 mL/min/1.73 $m^2$ | 14.8–22.3 | 750 mg once daily |
| Patients on haemodialysis | 3.75 | A further 750 mg dose should be given intravenously or intramuscularly at the end of each dialysis; in addition to parenteral |

| | | |
|---|---|---|
| | | use, cefuroxime sodium can be incorporated into the peritoneal dialysis fluid (usually 250 mg for every 2 litres of dialysis fluid). |
| Patients in renal failure on continuous arteriovenous haemodialysis (CAVH) or high-flux haemofiltration (HF) in intensive therapy units | 7.9–12.6 (CAVH) 1.6 (HF) | 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 affect 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.

1.5 g powder for solution for infusion.

For instructions on preparation 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 use

Hypersensitivity reactions

As with all beta-lactam antibacterial agents, serious and occasionally fatal hypersensitivity reactions have been reported. 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 impairment has been reported during use of these combinations. 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 cefuroxime may result in the overgrowth of Candida. Prolonged use may also result in the overgrowth of other non-susceptible microorganisms (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 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.

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.

Important information about excipients

Cefuroxime powder for solution for injection and infusion contains sodium. This should be considered for patients who are on a controlled sodium diet.

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

Cefuroxime may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral contraceptives.

Cefuroxime is excreted by glomerular filtration and tubular secretion. Concomitant use of probenicid 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-dosage 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: Please refer to section 4.4.

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

**4.6 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 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 cefuroxime sodium may vary according to the indication.

Data from clinical trials were used to determine the frequency of very common to rare adverse reactions. The frequencies assigned to all other adverse reactions (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 utilised 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 < 1/1,000; very rare < 1/10,000 and not known (cannot be estimated from the available data).

| System organ class | Common | Uncommon | Not known |
|---|---|---|---|
| Infections and infestations | | | Candida overgrowth, overgrowth of Clostridium difficile |
| Blood and lymphatic system disorders | neutropenia, eosinophilia, decreased haemoglobin concentration | leukopenia, positive Coomb's test | thrombocytopenia, haemolytic anaemia |
| Immune system disorders | | | drug fever, interstitial nephritis, anaphylaxis, cutaneous vasculitis |
| Gastrointestinal disorders | | gastrointestinal disturbance | pseudomembranous colitis |
| Hepatobiliary disorders | transient rise in liver enzymes | transient rise in bilirubin | |
| Skin and subcutaneous tissue disorders | | skin rash, urticaria and pruritus | erythema multiforme, toxic epidermal necrolysis and Stevens-Johnson syndrome, angioneurotic oedema |
| Renal and urinary disorders | | | elevations in serum creatinine, elevations in blood urea nitrogen and decreased creatinine clearance (see section 4.4) |
| General disorders and administration site conditions | injection site reactions which may include pain and thrombophlebitis | | |
| Description of selected adverse reactions<br>Cephalosporins as a class tend to be absorbed onto the surface of red cell membranes and react with antibodies directed against the drug to produce a positive Coomb's test (which can interfere with cross matching of blood) and very rarely haemolytic anaemia.<br>Transient rises in serum liver enzymes or bilirubin have been observed which are usually reversible.<br>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.

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

**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, Second-generation cephalosporins, ATC code

**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.

Mechanisms 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 de-repressed 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

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

| Microorganism | Breakpoints (mg/L) | |
|---|---|---|
| | S | R |
| Enterobacteriaceae[1] | <8[2] | >8 |
| Staphylococcus spp. | Note[3] | Note[3] |
| Streptococcus A, B, C and G | Note[4] | Note[4] |
| Streptococcus pneumoniae | ≤0.5 | >1 |
| Streptococcus (other) | ≤0.5 | >0.5 |
| Haemophilus influenzae | ≤1 | >2 |
| Moraxella catarrhalis | ≤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 categorisation of susceptibility. In many areas, ESBL detection and characterisation 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 beta-lactam susceptibility of beta-haemolytic streptococci groups A, B, C and G is inferred from the penicillin susceptibility.
[5] Breakpoints apply to daily intravenous dose of 750 mg ×3 and a high dose of at least 1.5 g ×3.

S=susceptible, R=resistant.

Microbiological susceptibility

The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is therefore 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 |
|---|
| Gram-positive aerobes:<br>Staphylococcus aureus (methicillin-susceptible) *<br>Streptococcus pyogenes<br>Streptococcus agalactiae<br>Streptococcus mitis (viridans group) |
| Gram-negative aerobes:<br>Haemophilus influenzae<br>Haemophilus parainfluenzae<br>Moraxella catarrhalis |
| Microorganisms for which acquired resistance may be a problem |
| Gram-positive aerobes:<br>Streptococcus pneumoniae |
| Gram-negative aerobes:<br>Citrobacter freundii<br>Enterobacter cloacae<br>Enterobacter aerogenes<br>Escherichia coli<br>Klebsiella pneumoniae<br>Proteus mirabilis<br>Proteus spp. (other than P. vulgaris )<br>Providencia spp.<br>Salmonella spp. |
| Gram-positive anaerobes:<br>Peptostreptococcus spp.<br>Propionibacterium spp. |
| Gram-negative anaerobes:<br>Fusobacterium spp.<br>Bacteroides spp. |
| Inherently resistant microorganisms |
| Gram-positive aerobes:<br>Enterococcus faecalis<br>Enterococcus faecium |
| Gram-negative aerobes:<br>Acinetobacter spp.<br>Morganella morganii<br>Proteus vulgaris<br>Pseudomonas aeruginosa<br>Serratia marcescens |

| |
|---|
| Gram-positive anaerobes:<br>Clostridium difficile |
| Gram-negative anaerobes:<br>Bacteroides fragilis |
| Others:<br>Chlamydia spp.<br>Mycoplasma spp.<br>Legionella spp. |

* 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 Pharmacokinetic properties**

**Absorption**

After intramuscular (IM) injection of cefuroxime to normal volunteers, the mean peak serum concentrations ranged from 27 to 35 μg/mL for a 750 mg dose and from 33 to 40 μg/mL for a 1000 mg dose, and were achieved within 30 to 60 minutes after administration. Following intravenous (IV) doses of 750 and 1500 mg, serum concentrations were approximately 50 and 100 μg/mL, respectively, at 15 minutes. AUC and $C_{max}$ appear to increase linearly with increase in dose over the single dose range of 250 to 1000 mg following IM and IV administration. There was no evidence of accumulation of cefuroxime in the serum from normal volunteers following repeat intravenous administration of 1500 mg doses every 8 hours.

**Distribution**

Protein binding has been stated as 33 to 50%, depending on the methodology used. The average volume of distribution ranges from 9.3 to 15.8 L/1.73 $m^2$ following IM or IV administration over the dosage range of 250 to 1000 mg. Concentrations of cefuroxime in excess of the minimum inhibitory levels for common pathogens can be achieved in the tonsilla, sinus tissues, bronchial mucosa, bone, pleural fluid, joint fluid, synovial fluid, interstitial fluid, bile, sputum and aqueous humour. Cefuroxime passes the blood-brain barrier when the meninges are inflamed.

**Biotransformation**

Cefuroxime is not metabolised.

**Elimination**

Cefuroxime is excreted by glomerular filtration and renal tubular secretion. The serum half-life after either intramuscular or intravenous injection is approximately 70 minutes. There is an almost complete recovery (85 to 90%) of unchanged cefuroxime in urine within 24 hours of administration. The majority of the cefuroxime is excreted within the first 6 hours. The average renal clearance ranges from 114 to 170 mL/min/1.73 $m^2$ following IM or IV administration over the dosage range of 250 to 1000 mg.

Special patient populations

Gender

No differences in the pharmacokinetics of cefuroxime were observed between males and females following a single IV bolus injection of 1000 mg of cefuroxime as the sodium salt.

Elderly

Following IM or IV administration, the absorption, distribution and excretion of cefuroxime in elderly patients are similar to younger patients with equivalent renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in cefuroxime dose selection, and it may be useful to monitor renal function (see section 4.2).

Paediatrics

The serum half-life of cefuroxime has been shown to be substantially prolonged in neonates according to gestational age. However, in older infants (aged >3 weeks) and in children, the serum half-life of 60 to 90 minutes is similar to that observed in adults.

Renal impairment

Cefuroxime is primarily excreted by the kidneys. As with all such antibiotics, in patients with markedly impaired renal function (i.e. $C1_{cr}$ <20 mL/minute) it is recommended that the dosage of cefuroxime should be reduced to compensate for its slower excretion (see section 4.2). Cefuroxime is effectively removed by haemodialysis and peritoneal dialysis.

Hepatic impairment

Since cefuroxime is primarily eliminated by the kidney, hepatic dysfunction is not expected to have an effect on the pharmacokinetics of cefuroxime.

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 (%T) that the unbound concentration remains above the minimum inhibitory concentration (MIC) of cefuroxime for individual target species (i.e. %T>MIC).

**5.3 Preclinical safety data**

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and toxicity to reproduction and development. No carcinogenicity studies have been performed; however, there is no evidence to suggest carcinogenic potential.

Gamma glutamyl transpeptidase activity in rat urine is inhibited by various cephalosporins, however the level of inhibition is less with cefuroxime. This may have significance in the interference in clinical laboratory tests in humans.

## 6. PHARMACEUTICAL PARTICULARS

**6.1 List of excipients**

None

**6.2 Incompatibilities**

Cefuroxime should not be mixed in the syringe or giving set with aminoglycosides prior to or during administration.

**6.3 Shelf life**

36 months for the medicinal product as packaged for sale. After reconstitution the product should be used immediately, but if not practicable, the diluted product may be stored for 24 hours at 2 - 8 ºC, after which time unused material should be discarded.

**6.4 Special precautions for storage**

Keep at room temperature (below 30 ºC), protected from light.

**6.5 Nature and contents of container**

Type II 10ml vials ealed with a butyl rubber stopper.

**6.6 Special precautions for disposal**

Instruction for constitution

Table 4. Addition volumes and solution concentrations, which may be useful when fractional doses are required.

| Addition volumes and solution concentrations, which may be useful when fractional doses are required | | | | |
|---|---|---|---|---|
| Vial size | | Displacement (ml) | Amount of water to be added (ml) | Approximate cefuroxime concentration (mg/mL)** |
| 250 mg powder for solution for injection | | | | |
| 250mg | intramuscular<br>intravenous | 0.2 ml | 1 mL<br>2 mL | 216<br>116 |
| 750 mg powder for solution for injection | | | | |
| 750mg | intramuscular<br>intravenous bolus | 0.6ml | 3 mL<br>6 mL | 216<br>116 |
| 1.5 g powder for solution for injection or infusion | | | | |
| 1.5g | intramuscular<br>intravenous bolus<br>intravenous infusion | 1.2ml | 6 mL<br>15mL<br>15 mL* | 216<br>94<br>94 |

* Reconstituted solution to be added to 35ml of compatible infusion fluid (see information on compatibility, below)

** The resulting volume of the solution of cefuroxime in reconstitution medium is increased due the displacement factor of the drug substance resulting in the listed concentrations in mg/ml.

Compatibility

Cefuroxime sodium (5 mg/ml) in 5% w/v or 10% w/v xylitol injection may be stored for up to 24 h at 25ºC.

Cefuroxime sodium is compatible with aqueous solutions containing up to 1% lidocaine hydrochloride.

Cefuroxime sodium is compatible with the following infusion fluids. It will retain potency for up to 24 hours at room temperature in:

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

Cefuroxime sodium has also been found compatible for 24 h at room temperature when 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.

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

## 7. APPLICANT/MANUFACTURER

**Name and address of Applicant:**

ZADIP HEALTHCARE LIMITED

NO.3 OSUIGWE AMOBI STREET, TRANS NKISI LAYOUT 33 ONITSHA, ANAMBRA, NIGERIA

**Name and address of Manufacturer:**

REYOUNG PHARMACEUTICAL CO., LTD

No.1 Ruiyang Road, Yiyuan County, Shandong Province, P.R. China

# Sterile water for injection 10ml

## 1. Name of the medicinal product

Sterile Water for Injections

## 2. Qualitative and quantitative composition

Each ampoule contains 10ml Sterile Water for Injections

## 3. Pharmaceutical form

Solvent for parenteral use.

Clear, colourless, odourless, sterile solution intended for parenteral administration to human beings.

## 4. Clinical particulars

### 4.1 Therapeutic indications

Sterile Water for Injections is indicated to be used as a vehicle for dilution and reconstitution of suitable medicinal products for parenteral administration.

### 4.2 Posology and method of administration

**Posology**

The dosage administered will be dictated by the nature of the additive used. The administration rate will be dependent upon the dose regimen of the prescribed drug. Following suitable admixture of prescribed additives, the dosage is usually dependent upon the age, weight and clinical condition of the patient as well as laboratory determinations.

The solution should only be used if it is clear without visible particles.

**Method of administration**

For parenteral use.

The directions for use will be dependent upon the appropriate medicinal product to which this solvent is added, which will dictate the appropriate volumes as well as administration route.

### 4.3 Contraindications

Sterile Water for Injections should not be administered alone because it may cause haemolysis. The contraindications related to the added medicinal product should be considered.

**4.4 Special warnings and precautions for use**

Water for Injections is hypotonic and it should not be administered alone, because it may cause haemolysis.

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

None known.

The possible clinical interactions between the different medicinal products to be dissolved should be considered.

**4.6 Fertility, pregnancy and lactation**

May be used during fertility, pregnancy and lactation.

The risks during use are determined by the nature of the added medicinal products.

**4.7 Effects on ability to drive and use machines**

Not relevant.

**4.8 Undesirable effects**

May cause haemolysis if administered alone.

The nature of the additive will determine the likelihood of any other undesirable effects.

**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.

**4.9 Overdose**

No effects are anticipated if used as instructed.

Haemolysis may occur following infusion of large volumes of hypotonic solutions using sterile water for injections as diluent.

The signs and symptoms of overdose will also be related to the nature of the medicinal product being added. In the event of accidental overdose, the treatment

should be discontinued and the patient should be observed for the appropriate signs and symptoms related to the medicinal product administered.

**5. Pharmacological properties**

**5.1 Pharmacodynamic properties**

Pharmacotherapeutic Group: Solvents and diluting agents, including irrigating solutions, ATC code: V07AB.

Sterile Water for Injections being only the vehicle for the administration of the added medicinal product, the pharmacodynamics will depend on the nature of the drug added.

**5.2 Pharmacokinetic properties**

Sterile Water for Injections being only the vehicle for the administration of the added medicinal product, the pharmacokinetics will depend on the nature of the drug added.

**5.3 Preclinical safety data**

Sterile Water for Injections being only the vehicle for the administration of the added medicinal product, the preclinical safety data will depend on the nature of the drug added.

**6. Pharmaceutical particulars**

**6.1 List of excipients**

None.

**6.2 Incompatibilities**

Sterile Water for Injections must not be mixed with other medicinal products unless their compatibility has been established.

**6.3 Shelf life**

Unopened

4 years.

Opened

From a microbiological point of view, unless the method of opening/reconstitution/dilution precludes the risk of microbial contamination, the product 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℃. Do not freeze.

**6.5 Nature and contents of container**

Clear glass ampoules.

Pack sizes: 10 mL

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

For single use.

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

Keep out of sight and reach of children.

**7. Applicant/Manufacturer**

**Name and address of Applicant:**

ZADIP HEALTHCARE LIMITED

NO.3 OSUIGWE AMOBI STREET, TRANS NKISI LAYOUT 33 ONITSHA, ANAMBRA, NIGERIA

**Name and address of Manufacturer:**

REYOUNG PHARMACEUTICAL CO., LTD

No.1 Ruiyang Road, Yiyuan County, Shandong Province, P.R. China