SCHEDULING STATUS: **S4**

1. NAME OF THE MEDICINE

CEFTRIAXONE 1000 INJECTION RESMED

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains:

Dry, sterile Ceftriaxone Sodium USP equivalent to Ceftriaxone 1000 mg (i.m. or i.v.).

Sugar free. Sodium content approximately 83 mg (3,6mEq) per vial.

3. PHARMACEUTICAL FORM

Injection.

White to yellowish orange crystalline powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Ceftriaxone 1000 Injection Resmed is indicated for the treatment of the following infections when caused by susceptible organisms:

Bacterial septicaemia caused by Methicillin Sensitive *Staphylococcus aureus* (MSSA), *Streptococcus pneumoniae*, *Escherichia coli*, *Haemophilus influenzae* or *Klebsiella pneumoniae*.

Meningitis caused by *Haemophilus influenzae*, *Neisseria meningitidis,* or *Streptococcus pneumoniae.*

Intra-abdominal infections caused by *Escherichia coli*, *Klebsiella pneumoniae, Clostridium* species (Note: most strains of Clostridium difficile are resistant) or *Peptostreptococcus* species.

Skin and skin structure infections caused by Methicillin Sensitive *Staphylococcus aureus* (MSSA), *Streptococcus pyogenes*, *Streptococcus viridans* group, *Escherichia coli*, *Enterobacter cloacae*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Proteus mirabilis*,

Morganella morganii, *Pseudomonas aeruginosa*, *Serratia marcescens*, or *Peptostreptococcus* species.

Bone and joint infections caused by Methicillin Sensitive *Staphylococcus aureus* (MSSA), *Streptococcus pneumoniae*, *Escherichia coli*, *Proteus mirabilis*, *Klebsiella pneumoniae* or *Enterobacter* species.

Renal and urinary tract infections (complicated and uncomplicated) caused by *Escherichia coli*, *Proteus mirabilis*, *Proteus vulgaris*, *Morganella morganii* or *Klebsiella pneumoniae*.

Respiratory tract infections caused by *Streptococcus pneumoniae*, Methicillin Sensitive *Staphylococcus aureus* (MSSA), *Haemophilus influenza*e, *Haemophilus parainfluenzae*, *Klebsiella pneumoniae*, *Escherichia coli*, *Enterobacter aerogenes*, *Proteus mirabilis* or *Serratia marcescens*.

Ear, nose and throat infections (**acute bacterial otitis media**) caused by *Streptococcus pneumoniae*, *Haemophilus influenzae* (including beta-lactamase producing strains) or *Moraxella catarrhalis* (including beta-lactamase producing strains).

Uncomplicated gonorrhoea (cervical/urethral and rectal) caused by *Neisseria gonorrhoeae*, including both beta-lactamase- and non-beta-lactamase-producing strains, and pharyngeal gonorrhoea caused by non-beta-lactamase-producing strains of *Neisseria gonorrhoeae.*

Surgical prophylaxis

The pre-operative administration of a single 1 g dose of Ceftriaxone 1000 Injection Resmed may reduce the incidence of post-operative infections.

4.2 Posology and method of administration

Posology

Standard Dosage

Adults and children over 12 years:

The usual dosage is 1 – 2 g Ceftriaxone 1000 Injection Resmed once daily (every 24 hours).

In severe cases or in infections caused by moderately sensitive organisms, the dosage may be raised to 4 g, once daily.

Neonates, infants and children up to 12 years:

The following dosage schedules are recommended for once daily administration:

Neonates (up to 14 days):

20 – 50 mg/kg bodyweight once daily. The daily dose should not exceed 50 mg/kg.

It is not necessary to differentiate between premature and term infants.

Infants and children (15 days to 12 years):

20 – 80 mg/kg once daily. For children with bodyweights of 50 kg or more, the usual adult dose should be used. Intravenous doses of ≥ 50 mg/kg bodyweight should be given by infusion over at least 30 minutes.

Elderly patients: No dose modification is needed in the elderly.

Duration of therapy

The duration of therapy varies according to the course of the disease. Administration of Ceftriaxone 1000 Injection Resmed should be continued for a minimum of 48 to 72 hours after the patient has become afebrile or evidence of bacterial eradication has been obtained.

Special dosage instructions

Meningitis:

In bacterial meningitis in *neonates, infants and children*, treatment begins with doses of 100 mg/kg (not to exceed 4 g) once daily.

As soon as the causative organism has been identified and its sensitivity determined, the dose can be adapted accordingly.

For bacterial meningitis in *adults*, the recommended dose is 4 g once daily.

Gonorrhoea:

For the treatment of uncomplicated gonorrhoea (both beta-lactamase-producing and non-beta-lactamase-producing strains), a single intramuscular (i.m.) dose of 125 mg Ceftriaxone 1000 Injection Resmed is recommended.

Peri-operative prophylaxis:

A single dose of 1 – 2 g Ceftriaxone 1000 Injection Resmed administered 30 – 90 minutes prior to surgery.

In colorectal surgery, administration of Ceftriaxone 1000 Injection Resmed with or without a 5-nitroimidazole, e.g., metronidazole, has been proven effective.

Impaired renal and hepatic function:

In patients with impaired renal function, there is no need to reduce the dosage of Ceftriaxone 1000 Injection Resmed provided that hepatic function is intact.

In cases of severe renal failure (creatinine clearance < 10 ml/min) the Ceftriaxone 1000 Injection Resmed dosage should not exceed 2 g daily.

In patients with liver damage, there is no need for the dosage to be reduced, provided that renal function is intact.

Method of Administration

For intramuscular and intravenous injection.

Ceftriaxone 1000 Injection Resmed must be reconstituted prior to use. For reconstitution see section 6.6.

4.3 Contraindications

Hypersensitivity to ceftriaxone, or to any of the excipients of Ceftriaxone 1000 Injection Resmed listed in section 6.1. Hypersensitivity to cephalosporins. Hypersensitivity to penicillins, due to the possibility of cross-reactivity.

Hyperbilirubinaemic neonates, especially prematures, should not be treated with Ceftriaxone 1000 Injection Resmed. *In vitro* studies have shown that ceftriaxone can displace bilirubin from its binding to serum albumin and bilirubin encephalopathy can possibly develop in the patients. Ceftriaxone 1000 Injection

Resmed should not be administered concurrently with calcium-containing solutions or products in newborns because of the risk of precipitation of ceftriaxone-calcium salt (see section 4.4.

4.4 Special warnings and precautions for use

Ceftriaxone must not be mixed or administered simultaneously with calcium-containing solutions or products, even via different lines. Calcium-containing solutions or products must not be administered within 48 hours of last administration of ceftriaxone.

Cases of fatal reactions with ceftriaxone-calcium precipitates in lung and kidneys in both term and premature neonates have been described. In some cases, the infusion lines and times of administration of ceftriaxone and calcium containing solutions differed (see section 4.3).

Do not use diluents containing calcium, such as Ringer's solutions or Hartman's solution to reconstitute Ceftriaxone 1000 Injection Resmed. Particulate formation can result.

Interaction with Calcium-Containing Products:

There are no reports to date of intravascular or pulmonary precipitations in patients, other than neonates, treated with ceftriaxone and calcium-containing IV solutions. However, the theoretical possibility exists for an interaction between ceftriaxone and IV calcium-containing solutions in patients other than neonates.

Therefore, Ceftriaxone 1000 Injection Resmed and calcium-containing solutions, including continuous calcium-containing infusions such as parenteral nutrition, should not be mixed or co-administered to any patient, irrespective of age, even via different infusion lines at different sites.

As a further theoretical consideration and based on 5 half-lives of ceftriaxone, Ceftriaxone 1000 Injection Resmed and IV calcium-containing solutions should not be administered within 48 hours of each other in any patient (see sections 4.3 and 6.6).

No data are available on potential interactions between ceftriaxone and oral calcium-containing products or interactions between intramuscular ceftriaxone and calcium-containing products (IV or oral).

Hypersensitivity reactions

Serious and occasionally fatal hypersensitivity reactions have been reported (see section 4.8). In case of severe hypersensitivity reactions, treatment with Ceftriaxone 1000 Injection Resmed 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 ceftriaxone, to other cephalosporins or to any other type of beta-lactam medicine. Caution should be used if Ceftriaxone 1000 Injection Resmed is given to patients with a history of non-severe hypersensitivity to other beta-lactam medicines.

Severe cutaneous adverse reactions (Stevens Johnson syndrome or Lyell's syndrome/toxic epidermal necrolysis and drug reaction with eosinophilia and systemic symptoms (DRESS)) which can be life-threatening or fatal have been reported in association of ceftriaxone treatment; however, the frequency of these events is not known (see section 4.8).

Paediatric population

Safety and effectiveness of Ceftriaxone 1000 Injection Resmed in neonates, infants and children have been established for the dosages described under Posology and Method of Administration (see section 4.2). Studies have shown that ceftriaxone can displace bilirubin from serum albumin.

Ceftriaxone 1000 Injection Resmed is contraindicated in premature and full-term neonates at risk of developing bilirubin encephalopathy (see section 4.3).

Immune mediated haemolytic anaemia

An immune mediated haemolytic anaemia has been observed in patients receiving cephalosporin class antibacterials. (see section 4.8). Severe cases of haemolytic

anaemia, including fatalities, have been reported during ceftriaxone treatment in both adults and children.

If a patient develops anaemia while on Ceftriaxone 1000 Injection Resmed, the diagnosis of a cephalosporin-associated anaemia should be considered, and Ceftriaxone 1000 Injection Resmed discontinued until the aetiology is determined.

Long term treatment

During prolonged treatment complete blood count should be performed at regular intervals.

Severe renal and hepatic insufficiency

In severe renal and hepatic insufficiency, close clinical monitoring for safety and efficacy is advised (see section 4.2).

Interference with serological testing

Interference with Coombs tests may occur, as Ceftriaxone 1000 Injection Resmed may lead to false-positive test results. Ceftriaxone 1000 Injection Resmed can also lead to false-positive test results for galactosaemia (see section 4.8).

Non-enzymatic methods for the glucose determination in urine may give false-positive results. Urine glucose determination during therapy with Ceftriaxone 1000 Injection Resmed should be done enzymatically (see section 4.8).

The presence of ceftriaxone may falsely lower estimated blood glucose values obtained with some blood glucose monitoring systems. Please refer to instructions for use for each system. Alternative testing methods should be used if necessary.

Antibacterial spectrum

Ceftriaxone has a limited spectrum of antibacterial activity and may not be suitable for use as a single medicine for the treatment of some types of infections unless the pathogen has already been confirmed (see section 4.2). In polymicrobial infections, where suspected pathogens include organisms resistant to ceftriaxone, administration of an additional antibiotic should be considered.

Use of lidocaine

In case a lidocaine solution is used as a solvent, ceftriaxone solutions must only be used for intramuscular injection. Contraindications to lidocaine, warnings and other relevant information as detailed in the Professional information of lidocaine must be considered before use (see section 4.3). The lidocaine solution should never be administered intravenously.

Renal lithiasis

Cases of renal lithiasis have been reported, which is reversible upon discontinuation of ceftriaxone (see section 4.8). In symptomatic cases, sonography should be performed. Use in patients with history of renal lithiasis or with hypercalciuria should be considered by the medical practitioner based on specific benefit risk assessment.

Jarisch-Herxheimer reaction (JHR)

Some patients with spirochete infections may experience a Jarisch-Herxheimer reaction (JHR) shortly after Ceftriaxone 1000 Injection Resmed treatment is started. JHR is usually a self - limiting condition or can be managed by symptomatic treatment. The antibiotic treatment should not be discontinued if such reaction occurs.

Sodium content

Ceftriaxone 1000 Injection Resmed powder for solution for injection or infusion contains approximately 83 mg sodium per 1g vial, equivalent to approximately 4% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Precautions

Pseudomembranous enterocolitis and coagulation disorders have been reported with Ceftriaxone 1000 Injection Resmed. It is important to consider pseudomembranous enterocolitis in patients who present with diarrhoea subsequent to the administration of Ceftriaxone 1000 Injection Resmed.

Superinfections with non-susceptible micro-organisms may occur. Shadows, which have been mistaken for gallstones have been detected on sonograms of the gallbladder, usually following doses higher than the standard recommended dose.

These shadows are, however, precipitates of calcium ceftriaxone, which disappear on completion or discontinuation of Ceftriaxone 1000 Injection Resmed therapy. In symptomatic cases, conservative non-surgical management is recommended.

Cases of pancreatitis, possibly of biliary obstruction aetiology, have been reported in patients treated with Ceftriaxone 1000 Injection Resmed. Most patients presented with risk factors for biliary stasis and biliary sludge, e.g., severe illness and total parenteral nutrition.

Ceftriaxone displaces bilirubin from serum albumin.

Caution should be exercised when considering Ceftriaxone 1000 Injection Resmed treatment in hyperbilirubinaemic neonates.

Ceftriaxone 1000 Injection Resmed is not recommended for use in neonates (especially premature) at risk of developing bilirubin encephalopathy.

4.5 Interaction with other medicines and other forms of interaction

Calcium-containing diluents, such as Ringer's solution or Hartmann's solution, should not be used to reconstitute Ceftriaxone 1000 Injection Resmed vials or to further dilute a reconstituted vial for intravenous administration because a precipitate can form. Precipitation of ceftriaxone-calcium can also occur when ceftriaxone is mixed with calcium-containing solutions in the same intravenous administration line. Ceftriaxone must not be administered simultaneously with calcium-containing intravenous solutions, including continuous calcium-containing infusions such as parenteral nutrition via a Y-site. However, in patients other than neonates, ceftriaxone and calcium-containing solutions may be administered sequentially of one another if the infusion lines are thoroughly flushed between infusions with a compatible fluid. *In vitro* studies using adult and neonatal plasma from umbilical cord blood demonstrated that neonates have an increased risk of precipitation of ceftriaxone-calcium (see sections 4.2, 4.3, 4.4, and 4.8).

Concomitant use with oral anticoagulants may increase the anti-vitamin K effect and the risk of bleeding. It is recommended that the International Normalised Ratio (INR) is

monitored frequently and the posology of the anti-vitamin K medicine adjusted accordingly, both during and after treatment with Ceftriaxone 1000 Injection Resmed (see section 4.8).

There is conflicting evidence regarding a potential increase in renal toxicity of aminoglycosides when used with cephalosporins. The recommended monitoring of aminoglycoside levels (and renal function) in clinical practice should be closely adhered to in such cases.

In an *in-vitro* study antagonistic effects have been observed with the combination of chloramphenicol and ceftriaxone. The clinical relevance of this finding is unknown.

There have been no reports of an interaction between ceftriaxone and oral calcium-containing products or interaction between intramuscular ceftriaxone and calcium-containing products (intravenous or oral).

In patients treated with ceftriaxone, the Coombs test may lead to false-positive test results.

Ceftriaxone may result in false-positive tests for galactosaemia.

Likewise, non-enzymatic methods for glucose determination in urine may yield false-positive results. For this reason, glucose level determination in urine during therapy with ceftriaxone should be carried out enzymatically.

No impairment of renal function has been observed after concurrent administration of large doses of ceftriaxone and potent diuretics (e.g., furosemide).

Simultaneous administration of probenecid does not reduce the elimination of ceftriaxone.

4.6 Fertility, pregnancy and lactation

Safety in pregnancy and lactation has not been established.

Ceftriaxone crosses the placental barrier and is excreted into breast milk; therefore, caution is advised in nursing mothers.

4.7 Effects on ability to drive and use machines

During treatment with Ceftriaxone 1000 Injection Resmed, undesirable effects such as dizziness may occur, which may influence the ability to drive and use machines (see section 4.8). Patients should be cautious when driving or operating machinery.

4.8 Undesirable effects

The most frequently reported adverse reactions for ceftriaxone are eosinophilia, leucopoenia, thrombocytopenia, diarrhoea, rash, and hepatic enzymes increased.

The following undesirable effects may occur with frequencies:

System Organ Class	Frequent	Less frequent	Frequency unknown
Infections and infestations		Genital fungal infection Pseudomembranous colitis	Superinfection
Blood and lymphatic system disorders	Eosinophilia Leucopenia Thrombocytopenia	Granulocytopenia Anaemia Coagulopathy	Haemolytic anaemia Agranulocytosis*
Immune system disorders			Anaphylactic shock Anaphylactic reaction Anaphylactoid reaction Hypersensitivity Jarisch-Herxheimer reaction
Nervous system disorders		Headache Dizziness Encephalopathy	Convulsion
Ear and labyrinth disorders			Vertigo
Respiratory, thoracic and mediastinal disorders		Bronchospasm	
Gastrointestinal disorders	Diarrhoea Loose stools	Nausea Vomiting	Pancreatitis Stomatitis Glossitis

Hepatobiliary disorders	Hepatic enzyme increased		Gall bladder precipitation Kernicterus
Skin and subcutaneous tissue disorders	Rash	Pruritus Urticaria	Stevens Johnson Syndrome Toxic epidermal necrolysis Erythema multiforme Acute generalised exanthematous pustulosis Drug reaction with eosinophilia and systemic symptoms (DRESS)
Renal and urinary disorders		Haematuria Glycosuria	Oliguria Renal precipitation (reversible)**
General disorders and administration site conditions		Phlebitis Injection site pain*** Pyrexia Oedema Chills	
Investigations		Blood creatinine increased	Coombs test false positive Galactosaemia test false positive Non enzymatic methods for glucose determination false positive

* Isolated cases of agranulocytosis (<500/mm^3) have been reported, most of them following total doses of 20 g or more.

** Cases of medicine precipitation in the kidneys have been reported, mostly in children older than 3 years and who have been treated with either high daily doses (e.g., ≥ 80 mg/kg/day) or total doses exceeding 10 g and presenting with other risk factors (e.g., fluid restrictions, confinement to bed, etc.). This event may lead to renal insufficiency and is usually reversible upon discontinuation of Ceftriaxone 1000 Injection Resmed.

*** Phlebitic reactions may occur after i.v. administration. These may be minimized by slow (2 – 4 minutes) injection of the medicine.

Intramuscular injection ***without*** lignocaine solution is painful.

4.9 Overdose

In the case of overdosage, plasma concentration would not be reduced by haemodialysis or peritoneal dialysis. There is no specific antidote.

Treatment of overdosage is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 20.1.1 Broad and medium spectrum antibiotics.

The bactericidal activity of ceftriaxone results from inhibition of bacterial cell wall synthesis. Ceftriaxone exerts *in vitro* activity against a wide range of gram-negative and gram-positive micro-organisms.

Ceftriaxone is stable to most β-lactamases, both penicillinases and cephalosporinases, of gram-positive and gram-negative bacteria.

Gram-positive aerobes

Methicillin-resistant *Staphylococcus* spp. is resistant to ceftriaxone. *Enterococcus faecalis, Enterococcus faecium,* and *Listeria monocytogenes* are resistant.

Gram-negative aerobes

Acinetobacter anitratus (mostly *A. baumanii*)* *Citrobacter freundii*, Enterobacter aerogenes*, Enterobacter cloacae*, Enterobacter* spp, (other*)*, Klebsiella pneumoniae**, Proteus penneri*, Proteus vulgaris*, Pseudomonas fluorescens*, Pseudomonas* spp. (other)*, Providentia rettgeri*, Providentia* spp. (other)*, Serratia marcescens*, Serratia* spp. (other)*,

*Some isolates of these species are resistant to ceftriaxone, mainly due to the production of the chromosomally encoded β–lactamase.

** Some isolates of these species are resistant due to production of extended spectrum, plasmid-mediated β-lactamase.

With a few exceptions clinical *P. aeruginosa* isolates are resistant to ceftriaxone. *Ureaplasma urealyticum*, *Mycoplasma* sp., *Mycobacterium* sp. and fungi are resistant to ceftriaxone

Anaerobic organisms

Bacteroides spp. (bile sensitive)*,

*Some isolates of these species are resistant to ceftriaxone due to β-lactamase-production.

Note: Many strains of β-lactamase-producing *Bacteroides* spp (notably *B. fragilis*) are resistant.

Clostridium difficile is resistant.

5.2 Pharmacokinetic properties

The pharmacokinetics of ceftriaxone are non-linear and all basic pharmacokinetic parameters, except the elimination half-life, are dose dependent if based on total medicine concentrations.

Absorption

The maximum plasma concentration after a single intramuscular (i.m) dose of 1.0 g is about 81 mg/litre and is reached within 2 – 3 hours after administration.

The area under the plasma concentration versus time curve (AUC) after intramuscular administration is equivalent to that after intravenous (i.v) administration of an equivalent dose, indicating 100% bioavailability of intravenous (i.v) administered ceftriaxone.

Distribution

The apparent volume of distribution of ceftriaxone is 7 -12 litres.

Ceftriaxone shows good tissue penetration and body fluid distribution after a dose of 1 – 2 g; concentrations well above the minimum inhibitory concentrations of most pathogens responsible for infection are detectable for more than 24 hours in body fluids or tissues including lung, heart, biliary tract/liver, tonsil, middle ear and nasal mucosa, bone as well as cerebrospinal, pleural, prostatic and synovial fluids.

On intravenous administration, ceftriaxone diffuses into the interstitial fluid, where if it is given in the recommended dosage range, bactericidal concentrations lasting 24 hours may be maintained.

Protein binding

Ceftriaxone is reversibly bound to albumin. There is proportionally decreased albumin binding with an increase in plasma concentration of ceftriaxone.

Penetration into particular tissues:

Paediatrics

Ceftriaxone penetrates the inflamed meninges of neonates, infants and children.

Ceftriaxone concentrations exceed 1.4 mg/litre in the cerebrospinal fluid (CSF) 24 hours after i.v. injection in doses of 50 mg/kg in neonates to 100 mg/kg in infants.

Peak concentration in CSF with a mean of 18 mg/litre is reached about 4 hours after intravenous injection.

Mean CSF concentrations are 17% of plasma concentrations in patients with bacterial meningitis and 4% in patients with aseptic meningitis.

The mean values of maximum plasma concentration, elimination half-life, plasma clearance and volume of distribution after a 50 mg/kg i.v dose and after a 75 mg/kg i.v

dose in paediatric patients suffering from bacterial meningitis are shown in the table below.

Mean pharmacokinetic parameters of ceftriaxone in paediatric patients with meningitis:

	50mg/kg i.v	75mg/kg i.v
Maximum Plasma Concentrations (µg/ml)	216	275
Elimination Half-life (hr)	4.6	4.3
Plasma Clearance (ml/hr/kg)	49	60
Volume of Distribution (ml/kg)	338	373
CSF Concentration–inflamed meninges (µg/ml)	5.6	6.4
Range (µg/ml)	1.3 – 18.5	1.3 – 44
Time after dose (hr)	3.7 (± 1.6)	3.3 (± 1.4)

Adults

In meningitis in adults, administration of 50 mg/kg leads within 2 – 24 hours to CSF concentrations several times higher than the minimum *in vitro* inhibitory concentrations required for the most common meningitis pathogens.

Ceftriaxone crosses the placental barrier and is excreted in the breast milk in low concentrations (See Fertility, pregnancy and lactation).

Metabolism

Ceftriaxone is not metabolised systemically but is converted to inactive metabolites by the gut flora.

Elimination

In healthy, young adult volunteers the total plasma clearance is 10 – 22 ml/min.

The renal clearance is 5 - 12 ml/min. 50 - 60% of ceftriaxone is excreted unchanged in the urine, while 40 - 50% is excreted unchanged in the bile. The elimination half-life in adults is about 8 hours.

Pharmacokinetics in special clinical situations

Neonates – urinary recovery accounts for about 70% of the dose.

Infants less than eight days old and elderly persons aged over 75 years – average elimination half-life is usually 2 – 3 times that in young adults.

Patients with renal or hepatic dysfunction – the pharmacokinetics of ceftriaxone are only minimally altered and the elimination half-life is only slightly increased.

Impaired kidney function alone – biliary elimination of ceftriaxone is increased.

Impaired liver function alone – renal elimination of ceftriaxone is increased.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

No excipients.

6.2 Incompatibilities

Ceftriaxone 1000 Injection Resmed should not be added to solutions containing calcium, such as Hartmann's solution and Ringer's solution. Ceftriaxone is incompatible with vancomycin, fluconazole and aminoglycosides.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store at or below 30^0 C. Keep product in outer container until required for use.

Protect from light.

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

10 ml clear glass vials sealed with rubber stopper and blue flip off aluminum seal.

Each 10ml vial is packed into a printed monocarton.

6.6 Special precautions for disposal and other handling

Reconstituted solutions retain their physical and chemical stability for 6 hours at room temperature or 24 hours in the refrigerator at +5^{o}C. As a general rule, however, the solutions should be used immediately after preparation. The solutions range in colour from pale yellow to amber, depending on the concentration and length of

storage. The colouration of the solutions is of no significance for the efficacy or tolerance of the medicine.

Calcium containing solutions are not among the appropriate solutions described for reconstitution, due to possible incompatibility. Do not use diluents containing calcium, such as Ringer's solutions or Hartman's solution to reconstitute Ceftriaxone 1000 Injection Resmed. Particulate formation can result. Ceftriaxone 1000 Injection Resmed and calcium-containing solutions, including continuous calcium-containing infusions such as parenteral nutrition, should not be mixed or co-administered to any patient irrespective of age even via different infusion lines at different sites (see Contraindications and Special warnings).

Intramuscular injection

For i.m. injection, Ceftriaxone 1000 Injection Resmed is dissolved in 3.5 ml of water for injection. Ceftriaxone 1000 Injection Resmed dissolved in a 1% lignocaine solution instead of water for injection can reduce pain at the site of injection.

It is recommended that not more than 1 g be injected at one site.

Reconstitution with 1% lignocaine (without adrenaline) has no effect on the absorption or the elimination of Ceftriaxone 1000 Injection Resmed.

Intravenous injection

The lignocaine solution must never be administered intravenously.

For i.v. injection, Ceftriaxone 1000 Injection Resmed is dissolved in 10 ml sterile water for injection. The intravenous administration should be given over 2 to 4 minutes.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Resmed Healthcare

71 Rochdale Road, Springfield Park, Durban, 4051.

8. REGISTRATION NUMBER

53/20.1.1/0171

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization:

Date of latest renewal:

10. DATE OF REVISION OF THE TEXT