m-Cefuroxime
powder for injection 750mg and 1.5g

1. PRODUCT NAME
m-Cefuroxime powder for injection 750mg and 1.5g.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
m-Cefuroxime injection contains 750mg or 1.5g of cefuroxime powder (as cefuroxime sodium) for injection or infusion.

3. PHARMACEUTICAL FORM
Powder for injection. 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 yellow 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.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
Cefuroxime is a bactericidal cephalosporin antibiotic which is resistant to most β-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 cefuroxime sodium will vary with geography and time and local susceptibility data should be consulted where available (see Further Information, Pharmacodynamic Effects).

Indications include
- Respiratory tract infections for example, acute and 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 m-Cefuroxime 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 (see Pharmaceutical Precautions).
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Where appropriate m-Cefuroxime is effective when used prior to oral therapy with cefuroxime axetil in the treatment of pneumonia and acute exacerbations of chronic bronchitis.

4.2 Dose and method of administration

m-Cefuroxime Injection for intravenous (IV) and/or intramuscular (IM) administration.

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

General Recommendations

Adults
Many infections respond to 750 mg three times daily by intramuscular or intravenous injection. For more severe infections the dose should be increased to 1.5 g three times daily given intravenously. 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 (intravenously or intramuscularly) followed by oral therapy with cefuroxime axetil.

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 Pharmacokinetic Properties).

Gonorrhoea

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

Meningitis
m-Cefuroxime is suitable for sole therapy of bacterial meningitis due to sensitive strains.

Adults
3 g given intravenously every eight hours.

Infants and Children
150 to 250 mg/kg/day given intravenously in 3 or 4 divided doses.

Neonates
The dosage should be 100 mg/kg/day given intravenously.

Prophylaxis

Adults
The usual dose is 1.5 g given intravenously with induction of anaesthesia for abdominal, pelvic and orthopaedic operations. This may be supplemented with two 750 mg intramuscular doses eight and sixteen hours later.
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In cardiac, pulmonary, oesophageal and vascular operations, the usual dose is 1.5 g given intravenously with induction of anaesthesia, continuing with 750 mg given intramuscularly three times daily for a further 24 to 48 hours.

In total joint replacement, 1.5 g cefuroxime 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 m-Cefuroxime three times daily or twice daily (given intravenously or intramuscularly) for 48 to 72 hours, followed by 500 mg twice daily Cefuroxime axetil oral therapy for 7 to 10 days.

Acute exacerbations of chronic bronchitis: 750 mg m-Cefuroxime three times daily or twice daily (given intravenously or intramuscularly) for 48 to 72 hours, followed by 500 mg twice daily Cefuroxime axetil oral therapy for 5 to 10 days.

**Impaired Renal Function**

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 m-Cefuroxime 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 intravenously or intramuscularly at the end of each dialysis. In addition to parenteral use, cefuroxime 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.

Cefuroxime is also available as the axetil ester for oral administration. This permits parenteral therapy with cefuroxime to be followed by oral therapy in situations where a change from parenteral to oral is clinically indicated.

### 4.3 Contraindications

Hypersensitivity to cephalosporin antibiotics.

m-Cefuroxime is contraindicated in patients who have had previous experience of a major allergy or anaphylaxis to a cephalosporin or penicillin.
4.4 Special warnings and precautions for use

Special care is indicated in patients who have experienced an allergic reaction to penicillins or other β-lactams. m-Cefuroxime should be given with caution to patients who have experienced symptoms of allergy associated with a cephalosporin or penicillin.

Cephalosporin antibiotics at high dosage should be given with caution to patients receiving concurrent treatment with potent diuretics such as furosemide or aminoglycosides, as renal impairment has been reported with these combinations. Renal function should be monitored in these patients, the elderly, and those with pre-existing renal impairment (see Dosage and Administration).

As with other therapeutic regimens used in the treatment of meningitis, mild-to-moderate hearing loss has been reported in a few paediatric patients treated with cefuroxime sodium. Persistence of positive cerebral spinal fluid (CSF) cultures of Haemophilus influenzae at 18 to 36 hours has also been noted with cefuroxime sodium injection, as well as with other antibiotic therapies; however, the clinical relevance of this is unknown.

As with other antibiotics, use of cefuroxime 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.

Pseudomembranous colitis and delaying peristalsis – Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics. It is important to consider this diagnosis in patients who develop diarrhoea in association with the use of m-Cefuroxime. Drugs which delay peristalsis may prolong and/or worsen the condition and should not be used.

With a sequential therapy regime the timing of change to oral therapy is determined by severity of the infection, clinical status of the patient and susceptibility of the pathogens involved. If there is no clinical improvement within 72 hours, then the parenteral course of treatment must be continued.

Refer to the relevant prescribing information for Cefuroxime axetil before initiating sequential therapy.

Prothrombin time - Prolonged prothrombin time may occur in patients receiving protracted antimicrobial therapy.

4.5 Interaction with other medicines and other forms of interaction

In common with other antibiotics m-Cefuroxime may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral contraceptives.

m-Cefuroxime does not interfere in enzyme-based tests for glycosuria.

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.

It is recommended that either the glucose oxidase or hexokinase methods are used to determine blood/plasma glucose levels in patients receiving m-Cefuroxime.
This antibiotic does not interfere in the alkaline picrate assay for creatinine.

4.6 Fertility, pregnancy and lactation

Pregnancy
There is no experimental evidence of embryopathic or teratogenic effects attributable to cefuroxime, but, as with all medicines, it should be administered with caution during the early months of pregnancy.

Lactation
Cefuroxime is excreted in human milk, and consequently caution should be exercised when m-Cefuroxime is administered to a nursing mother.

4.7 Effects on ability to drive and use machines
During treatment with m-Cefuroxime, undesirable effects may occur (e.g. dizziness), which may influence the ability to drive and use machines. Patients should be cautious when driving or operating machinery.

4.8 Undesirable effects
Adverse drug reactions are very rare (<1/10,000) and are generally mild and transient in nature.

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 undesirable effects. 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.

The following convention has been used for the classification of frequency:
Very common ≥1/10,
Common ≥1/100 to <1/10,
Uncommon ≥1/1000 to <1/100,
Rare ≥1/10,000 to <1/1000,
Very rare <1/10,000.

Infections and infestations
Rare: Candida overgrowth.

Blood and lymphatic system disorders
Common: Neutropenia, eosinophilia.
Uncommon: Leukopenia, decreased haemoglobin concentration, positive Coomb’s test.
Rare: Thrombocytopenia.
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Very rare: Haemolytic anaemia.

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.

**Immune system disorders**

Hypersensitivity reactions including:

Uncommon: Skin rash, urticaria and pruritus.
Rare: Drug fever.
Very rare: Interstitial nephritis, anaphylaxis, cutaneous vasculitis.

See also Skin and subcutaneous tissue disorders and Renal and urinary disorders.

**Vascular disorders**

Common: Thrombophlebitis may follow intravenous injection.

**Gastrointestinal disorders**

Uncommon: Gastrointestinal disturbance.
Very rare: Pseudomembranous colitis (see Warnings and Precautions).

**Hepatobiliary disorders**

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

Transient rises in serum liver enzymes or bilirubin occur, particularly in patients with pre-existing liver disease, but there is no evidence of harm to the liver.

**Skin and subcutaneous tissue disorders**

Very rare: Erythema multiforme, toxic epidermal necrolysis and Stevens Johnson Syndrome.

See also Immune system disorders.

**Renal and urinary disorders**

Very rare: Elevations in serum creatinine, elevations in blood urea nitrogen and decreased creatinine clearance (See Warnings and Precautions).

See also Immune system disorders.

**General disorders and administration site conditions**

Common: Injection site reactions which may include pain and thrombophlebitis.
Pain at the intramuscular injection site is more likely at higher doses. However it is unlikely to be a cause for discontinuation of treatment.

**Reporting of suspected adverse reactions**
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions [https://nzphvc.otago.ac.nz/reporting/](https://nzphvc.otago.ac.nz/reporting/)

**4.9 Overdose**

Overdosage of cephalosporins can cause cerebral irritation leading to convulsions. Serum levels of cefuroxime can be reduced by haemodialysis or peritoneal dialysis.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

**5 PHARMACOLOGICAL PROPERTIES**

**5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: antibacterials for systemic use, second generation cephalosporins,
ATC code: J01DC02

**Mechanism of Action**
Cefuroxime is a well characterised and effective antibacterial agent which has bactericidal activity against a wide range of common pathogens, including β-lactamase producing strains.
Cefuroxime has good stability to bacterial β-lactamase, and consequently is active against many ampicillin-resistant or amoxycillin-resistant strains.
The bactericidal action of cefuroxime results from inhibition of cell wall synthesis by binding to essential target proteins.

**Pharmacodynamic Effects**
The prevalence of acquired resistance is geographically and time dependent and for select species may be very high. Local information on resistance is desirable, particularly when treating severe infections.

<table>
<thead>
<tr>
<th>In vitro susceptibility of micro-organisms to Cefuroxime</th>
</tr>
</thead>
<tbody>
<tr>
<td>Where clinical efficacy of cefuroxime has been demonstrated in clinical trials this is indicated with an asterisk (*).</td>
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</tbody>
</table>

**Commonly Susceptible Species**

<table>
<thead>
<tr>
<th>Gram-Positive Aerobes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus (methicillin susceptible)*</td>
</tr>
<tr>
<td>Coagulase negative staphylococcus (methicillin susceptible)</td>
</tr>
<tr>
<td>Streptococcus pyogenes*</td>
</tr>
<tr>
<td>Beta-hemolytic streptococci</td>
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</tbody>
</table>

| Gram-Negative Aerobes: |
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<table>
<thead>
<tr>
<th>Gram-Positive Anaerobes:</th>
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<tbody>
<tr>
<td>Peptostreptococcus spp.</td>
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<tr>
<td>Propionibacterium spp.</td>
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<table>
<thead>
<tr>
<th>Spirochetes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Borrelia burgdorferi*</td>
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<table>
<thead>
<tr>
<th>Organisms for which acquired resistance may be a problem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-Positive Aerobes:</td>
</tr>
<tr>
<td>Streptococcus pneumoniae*</td>
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<tr>
<td>Viridans group streptococcus</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Gram-Negative Aerobes:</th>
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</thead>
<tbody>
<tr>
<td>Bordetella pertussis</td>
</tr>
<tr>
<td>Citrobacter spp. not including C. freundii</td>
</tr>
<tr>
<td>Enterobacter spp. not including E. aerogenes and E. cloacae</td>
</tr>
<tr>
<td>Escherichia coli*</td>
</tr>
<tr>
<td>Klebsiella spp. including K. pneumoniae*</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
</tr>
<tr>
<td>Proteus spp. not including P. penneri and P. vulgaris</td>
</tr>
<tr>
<td>Providencia spp.</td>
</tr>
<tr>
<td>Salmonella spp.</td>
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<table>
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<tr>
<th>Gram-Positive Anaerobes:</th>
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<tbody>
<tr>
<td>Clostridium spp. not including C. difficile</td>
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</table>

<table>
<thead>
<tr>
<th>Gram-Negative Anaerobes:</th>
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<tbody>
<tr>
<td>Bacteroides spp. not including B. fragilis</td>
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<tr>
<td>Fusobacterium spp.</td>
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</table>

**Inherrently resistant organisms**

<table>
<thead>
<tr>
<th>Gram-Positive Aerobes:</th>
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</thead>
<tbody>
<tr>
<td>Enterococcus spp. including E. faecalis and E. faecium</td>
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<tr>
<td>Listeria monocytogenes</td>
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</table>

<table>
<thead>
<tr>
<th>Gram-Negative Aerobes:</th>
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<tbody>
<tr>
<td>Acinetobacter spp.</td>
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<tr>
<td>Burkholderia cepacia</td>
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<tr>
<td>Campylobacter spp.</td>
</tr>
<tr>
<td>Citrobacter freundii</td>
</tr>
<tr>
<td>Enterobacter aerogenes</td>
</tr>
<tr>
<td>Enterobacter cloacae</td>
</tr>
<tr>
<td>Morganella morganii</td>
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<tr>
<td>Proteus penneri</td>
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<tr>
<td>Proteus vulgaris</td>
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</tbody>
</table>
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| Pseudomonas spp. including P. aeruginosa  
Serratia spp.  
Stenotrophomonas maltophilia  
**Gram-Positive Anaerobes:**  
Clostridium difficile  
**Gram-Negative Anaerobes:**  
Bacteroides fragilis  
**Others:**  
Chlamydia species  
Mycoplasma species  
Legionella species |

### 5.2 Pharmacokinetic properties

#### Absorption
Peak levels of cefuroxime are achieved within 30 to 45 minutes after intramuscular administration.

#### Distribution
Protein binding has been variously stated as 33 to 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.

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

#### Elimination
The serum half-life after either intramuscular or intravenous 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 (85-90%) of unchanged cefuroxime in urine within 24 hours of administration. The major part is excreted in the first six hours. Serum levels of cefuroxime are reduced by dialysis.

### 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, carcinogenic potential and toxicity to reproduction and development.
6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

None.

6.2 Incompatibilities

m-Cefuroxime 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 m-Cefuroxime. However, if required, for patients receiving Sodium Bicarbonate Injection by infusion the m-Cefuroxime may be introduced into the tube of the giving set.

6.3 Shelf life

24 months from date of manufacture stored at or below 25°C.

750mg

5 hours reconstituted stored at or below 25°C.
24 hours reconstituted stored at 2° to 8° C (Refrigerate, do not freeze).

1.5g

5 hours reconstituted stored at or below 25° C.
24 hours reconstituted stored at 2° to 8° C (Refrigerate, do not freeze).

Instructions for Handling

Intramuscular

Add 3 mL Water for Injections to 750 mg m-Cefuroxime. Shake gently to produce an opaque suspension.

Intravenous

Dissolve m-Cefuroxime in Water for Injections using at least 6 mL for 750mg, or at least 15 mL for 1.5 g.

Intravenous infusion

Dissolve 1.5 g of cefuroxime sodium in 15 ml of Water for Injections. Add the reconstituted solution of cefuroxime sodium to 50 or 100 ml of a compatible infusion fluid (see Compatibility). 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

1.5 g m-Cefuroxime constituted with 15mL Water for Injections may be added to metronidazole injection (500 mg/100 mL) and both retain their activity for up to 24 hours below 25°C.
1.5 g m-Cefuroxime is compatible with azlocillin 1 g (in 15 mL) or 5 g (in 50 mL) for up to 24 hours at 4°C or 6 hours below 25°C.

m-Cefuroxime (5 mg/mL) in 5% w/v or 10% w/v xylitol injection may be stored for up to 24 hours at 25°C.

m-Cefuroxime is compatible with aqueous solutions containing up to 1% lignocaine hydrochloride.

m-Cefuroxime is compatible with the more commonly used intravenous 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 m-Cefuroxime in Sodium Chloride Injection BP 0.9% w/v and in 5% Dextrose Injection is not affected by the presence of hydrocortisone sodium phosphate.

m-Cefuroxime has also been found compatible for 24 hours at room temperature when admixed in intravenous infusion with:

- Heparin (10 and 50 units/mL) in 0.9% Sodium Chloride Injection; Potassium Chloride (10 and 40 mEq/L) in 0.9% Sodium Chloride Injection.

6.4 Special precautions for storage

Store at or below 25°C. Protect from light

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

Glass type II transparent vial with grey bromobutyl stopper, green aluminium and polypropylene flip-off cap (1 vial pack size 750mg or 5 vial pack size 750mg) or (1 vial size 1.5g).

Not all pack sizes may be marketed.
6.6 Special precautions for disposal <and other handling>

No special requirements.

7. MEDICINE SCHEDULE

Prescription medicine

8. SPONSOR

Multichem NZ Ltd
8 Apollo Drive
Mairangi Bay
Private Bag 93527
Takapuna 0740
AUCKLAND

Telephone: (09) 488 0330

9. DATE OF FIRST APPROVAL

26 October 2006

10. DATE OF REVISION OF THE TEXT

25 October 2017

SUMMARY TABLE OF CHANGES

<table>
<thead>
<tr>
<th>DATE</th>
<th>CHANGE</th>
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<tbody>
<tr>
<td>25 October 2017</td>
<td>Updated data sheet to be in line with a current source data sheet. Updated to fit the SPC-style format and to include the Cephalosporins and β-lactams cross-reactivity warnings provided by Medsafe 16/02/2016.</td>
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