Cefuroxime 750mg Powder for Solution for Injection

Cefuroxime 1.5g Powder for Solution for Injection or Infusion

PL 14894/0399

PL 14894/0400

UKPAR

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CEFUROXIME 750MG POWDER FOR SOLUTION FOR INJECTION

CEFUROXIME 1.5G POWDER FOR SOLUTION FOR INJECTION OR INFUSION

PL 14894/0399

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LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Marketing Authorisations (licences) for the medicinal products Cefuroxime 750mg Powder for Solution for Injection and Cefuroxime 1.5g Powder for Solution for Injection or Infusion (Product Licence numbers: 14894/0399-400).

Cefuroxime is an antibiotic which helps the body fight infections by destroying certain bacteria. Cefuroxime injection is used to treat many types of infection, including:

- Bronchitis, pneumonia and any other chest infections;
- Cystitis and kidney infections;
- Pelvic inflammatory diseases;
- Gonorrhoea;
- Ear, nose and throat infections;
- Skin, soft tissue, bone and joint infections;
- Meningitis.

Cefuroxime 750mg Powder for Solution for Injection and Cefuroxime 1.5g Powder for Solution for Injection or Infusion raised no clinically significant safety concerns and it was, therefore, judged that the benefits of using these products outweigh the risks; hence Marketing Authorisations have been granted.
CEFUROXIME 750MG POWDER FOR SOLUTION FOR INJECTION

CEFUROXIME 1.5G POWDER FOR SOLUTION FOR INJECTION OR INFUSION

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SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted Marketing Authorisations for the medicinal products Cefuroxime 750mg Powder for Solution for Injection and Cefuroxime 1.5g Powder for Solution for Injection or Infusion (PL 14894/0399-400) on 12 November 2009. These medicines are only available on prescription.

The applicant claims that Cefuroxime 750mg Powder for Solution for Injection and Cefuroxime 1.5g Powder for Solution for Injection or Infusion are generic versions of Zinacef (PL 00004/0263), which is available in vials of either 250mg, 750mg or 1.5g cefuroxime. Zinacef has been licensed to Glaxo Operations UK Limited since 7 April 1978, the ten year rule is, therefore, complied with and the legal basis of these applications is acceptable.

Cefuroxime 750mg Powder for Solution for Injection and Cefuroxime 1.5g Powder for Solution for Injection or Infusion are indicated for the treatment of infections before the infecting organism has been identified or when caused by sensitive bacteria. In addition, it is an effective prophylactic against post-operative infection in a variety of operations. Usually Cefuroxime will be effective alone, but when appropriate it may be used in combination with an aminoglycoside antibiotic, or in conjunction with metronidazole.
PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE
The method of manufacture of cefuroxime is appropriate.

The proposed drug substance specification and its justification, analytical procedures and their validation, batch analyses and reference standards used by the drug substance manufacturer are satisfactory.

Satisfactory certificates of analysis have been provided for working standards used by the active substance manufacturer and finished product manufacturer during validation studies.

Active cefuroxime is stored in appropriate packaging. The specifications and typical analytical test reports are provided and are satisfactory.

Appropriate stability data have been generated supporting the retest period.

DRUG PRODUCT
Other ingredients
The products are vials containing sterile cefuroxime sodium Ph Eur; there are no excipients.

Manufacture
A description and flow-chart of the manufacturing method has been provided.

In-process controls are appropriate considering the nature of the product and the method of manufacture. Process validation has been carried out on batches of each strength. The results are satisfactory.

Finished product specification
The finished product specification is satisfactory. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where appropriate, safety. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of analysis have been provided for any working standards used.

Container Closure System
The solution is stored in a type II transparent, colourless glass vial, with a bromobutyl stopper and either a blue (750mg product) or green (1.5g product) aluminum and polypropylene flip off cap with adhesive labels. Cefuroxime 750mg Powder for Injection is available in 10ml vials in packs of 1, 5 or 100 vials. Cefuroxime 1.5g Powder for Injection or Infusion is available in 20 and 100ml vial packs of 1, 10 or 20 vials. Not all pack sizes may be marketed.
**Stability**

Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 3 years for unopened dry powder has been set, which is satisfactory. Storage conditions are “do not store above 30°C” and “store in the original package”. When the solution is reconstituted it may be stored up to 24 hours when stored at 2 to 8°C, however, from a microbiological point of view, the product should be used immediately.

**Product literature**

All product literature (SPCs, PIL and labelling) are satisfactory. The package leaflet was submitted to the MHRA along with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

**Conclusion**

It is recommended that Marketing Authorisations are granted for these applications.
PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with these applications and none are required for applications of this type.
CLINICAL ASSESSMENT

INDICATIONS
The indications for these products are given in the SPC. These indications are appropriate.

DOSE & DOSE SCHEDULE
The recommend dosage and administration are outlined in detail in the SPCs. In addition, recommendations are included for the use of cefuroxime to treat specific infections such as meningitis, exacerbations of chronic bronchitis and impaired renal function.

The text is identical to that of the reference product and is satisfactory.

TOXICOLOGY
No data required.

CLINICAL PHARMACOLOGY

Pharmacokinetics.
In accordance with Note for Guidance on the investigation of bioavailability and bioequivalence (CPMP/EWP/QWP/1401/98), point 5.1.6, a bioequivalence study is not requested if the product is an aqueous intravenous solution containing the same active substance in the same concentration as the currently licensed product.

No pharmacokinetic studies are required.

EFFICACY
No efficacy studies are required. The efficacy of cefuroxime has been well described.

SAFETY
No safety studies are required for these applications. The safety of cefuroxime and the profile of its potential toxicity in humans have been well described. No new concerns that are not already known from the profile of cefuroxime have been raised.

PRODUCT LITERATURE
All product literature is medically satisfactory. The SPC is almost identical to that of the brand leader and complies with current information on cefuroxime.

DISCUSSION
These applications submitted meet the criteria for grant of a Marketing Authorisation in all respects.

CONCLUSIONS
Marketing Authorisations should be granted.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
The important quality characteristics of Cefuroxime 750mg Powder for Solution for Injection and Cefuroxime 1.5g Powder for Solution for Injection or Infusion are well defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL
No new preclinical data were submitted and none are required for applications of this type.

EFFICACY
The efficacy of cefuroxime is well established.
The SPCs, PIL and labelling are satisfactory and consistent with those for the cross-reference product.

RISK BENEFIT ASSESSMENT
The quality of the products is acceptable, no significant preclinical or clinical safety concerns were identified, and benefit has been shown to be associated with cefuroximel. The risk benefit is therefore considered to be positive.
# CEFUROXIME 750MG POWDER FOR SOLUTION FOR INJECTION

# CEFUROXIME 1.5G POWDER FOR SOLUTION FOR INJECTION OR INFUSION

**PL 14894/0399**

**PL 14894/0400**

## STEPS TAKEN FOR ASSESSMENT

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
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<tbody>
<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation application on 23 December 2004</td>
</tr>
<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the application valid on 28 January 2008.</td>
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<tr>
<td>3</td>
<td>Following assessment of the application the MHRA requested further information relating to the quality and clinical dossier on 18 April 2008</td>
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<tr>
<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information on the quality and clinical dossiers on 11 August 2008</td>
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<tr>
<td>5</td>
<td>Following assessment of the response the MHRA requested further information relating to the quality dossier on 1 October 2008</td>
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<tr>
<td>6</td>
<td>The applicant responded to the MHRA’s requests, providing further information on the quality dossier on 30 March 2009</td>
</tr>
<tr>
<td>7</td>
<td>The application was determined on 12 November 2009</td>
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SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Cefuroxime 750mg Powder for Solution for Injection.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Vials contain 750mg cefuroxime (as sodium salt).
For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM
Powder for solution for injection
White or off-white powder.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Cefuroxime 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. In addition, it is an effective prophylactic against post-operative infection in a variety of operations. Usually 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, (see Pharmaceutical precautions).

In situations where mixed aerobic and anaerobic infections are encountered or suspected (e.g. peritonitis, aspiration pneumonia, abscesses in the lung, pelvis and brain), or are likely to occur (e.g. in association with colorectal or gynaecological surgery) it is appropriate to administer Cefuroxime in combination with metronidazole.

Most of these infections will respond to an i.v. regimen of Cefuroxime (750mg) plus metronidazole injection (500mg/100ml) administered eight-hourly. In more severe or well established mixed infections, an i.v. regimen of Cefuroxime (1.5g) plus metronidazole injection (500mg/100ml) eight-hourly may be indicated. For the prophylaxis of infection in surgery (e.g. colorectal and gynaecological) a single dose of 1.5g Cefuroxime plus metronidazole injection (500mg/100ml) is appropriate.
Alternatively this may be followed by two 750mg doses of Cefuroxime plus metronidazole.

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 and pharyngitis.

Urinary tract infections for example acute and chronic pyelonephritis, cystitis and asymptomatic bacteriuria.

Soft-tissue infections for example cellulitis, erysipelas, peritonitis 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 such as meningitis.

Prophylaxis against infection in abdominal, pelvic, orthopaedic, cardiac, pulmonary, oesophageal and vascular surgery where there is increased risk from infection.

This permits the use of sequential therapy with the same antibiotic, when a change from parenteral to oral therapy is clinically indicated.

Where appropriate 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 Posology and method of administration

Route and method of administration

Cefuroxime 750mg may be administered by intravenous or intramuscular injection. For instructions on dilution of the product before administration, see section 6.6.

Normal dosage

Adults:

Many infections will respond to 750mg t.i.d. by i.m. or i.v. injection. For more severe infections, this dose should be increased to 1.5g t.i.d. i.v. The frequency of i.m. or i.v. injection can be increased to six-hourly if necessary, giving total doses of 3g to 6g daily.

Where clinically indicated, adults with pneumonia and acute exacerbations of chronic bronchitis have been shown to respond to 750mg or 1.5g b.d., followed by oral therapy with cefuroxime axetil (see Sequential therapy).
**Infants and Children:**
Doses of 30 to 100mg/kg/day given as three or four divided doses. A dose of 60mg/kg/day will be appropriate for most infections.

**Neonates:**
Doses of 30 to 100mg/kg/day given as two or three divided doses. In the first weeks of life the serum half-life of cefuroxime can be three to five times that in adults.

**Elderly:**
See dosage in adults.

**Other Recommendations**

**Gonorrhoea:**
1.5g should be given as a single dose. This may be given as 2 x 750mg injections into different sites e.g. each buttock.

**Meningitis:**
Cefuroxime is suitable for sole therapy of bacterial meningitis due to sensitive strains. The following dosages are recommended.

Infants and Children: 200 to 240mg/kg/day i.v. in three or four divided doses. This dosage may be reduced to 100mg/kg/day i.v. after three days or when clinical improvement occurs.

Neonates: The initial dosage should be 100mg/kg/day i.v. A reduction to 50mg/kg/day i.v. may be made when clinically indicated.

Adults: 3g i.v. every eight hours. Data are not yet sufficient to recommend a dose for intrathecal administration.

**Prophylaxis:**
The usual dose is 1.5g i.v. with induction of anaesthesia for abdominal, pelvic and orthopaedic operations, but may be supplemented with two 750mg i.m. doses eight and sixteen hours later. In cardiac pulmonary oesophageal and vascular operations, the usual dose is 1.5g i.v. with induction of anaesthesia continuing with 750mg i.m. t.d.s. for a further 24 to 48 hours.

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

**Sequential therapy**

**Pneumonia:**
1.5g b.d. (i.v. or i.m.) for 48-72 hours, followed by 500mg b.d. cefuroxime axetil oral therapy for 7 days.

**Acute exacerbations of chronic bronchitis:**
750mg b.d. (i.v. or i.m.) for 48-72 hours, followed by 500mg b.d. cefuroxime axetil oral therapy for 5-7 days.

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

**Dosage in 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 Cefuroxime should be reduced to compensate for its slower excretion. However, it is not necessary to reduce the dose until the creatinine clearance falls below 20ml/min. In adults with marked impairment (creatinine clearance 10-20ml/min) 750mg b.d. is recommended and with severe impairment (creatinine clearance <10ml/min) 750mg once daily is adequate. For patients on haemodialysis a further 750mg dose should be given at the end of each dialysis. When continuous peritoneal dialysis is being used, a suitable dosage is usually 750mg twice daily.

For patients in renal failure on continuous arteriovenous haemodialysis or high-flux haemofiltration in intensive therapy units a suitable dosage is 750mg 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 cefuroxime or to any of the cephalosporins. Previous immediate and/or severe hypersensitivity reaction to a penicillin or to any other type of beta-lactam drug.

### 4.4 Special warnings and precautions for use
Special care is indicated in patients who have experienced an allergic reaction to penicillins or beta-lactams.

There may be some variation on the results of biochemical tests of renal function, but these do not appear to be of clinical importance. As a precaution, renal function should be monitored if this is already impaired.

Delayed sterilisation of the CSF in patients with Haemophilus influenzae meningitis may result in an adverse outcome such as deafness and/or neurological sequelae. Persistence of positive CSF cultures of H. influenzae at 18-36 hours has been noted in some patients treated with cefuroxime sodium injection and, as with other therapeutic regimens used in the treatment of meningitis, hearing loss has been reported in some children.

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. The change to oral therapy should
only be made once there is a clear clinical improvement. If there has been no clinical improvement after 72 hours of parenteral treatment, then the patient's treatment should be reviewed. Please refer to the relevant prescribing information for cefuroxime axetil before initiating sequential therapy.

This medicinal product contains 36.75 mg sodium per dose. To be taken into consideration by patients on a controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

Cephalosporin antibiotics at high dosage should be given with caution to patients receiving concurrent treatment with potent diuretics such as furosemide and aminoglycosides, as these combinations are suspected of adversely affecting renal function. Clinical experience with Cefuroxime has shown that this is not likely to be a problem at the recommended dose levels.

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 Cefuroxime. This antibiotic does not interfere in the alkaline picrate assay for creatinine.

4.6 Pregnancy and lactation

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

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

4.7 Effects on ability to drive and use machines

None reported.

4.8 Undesirable effects

The following convention has been used for the classification of frequency:

Very common >1/10
Common >1/100 and <1/10
Uncommon >1/1000 and <1/100
Rare >1/10,000 and <1/1000
Very rare <1/10,000.

Infections and infestations

Rare: Candida overgrowth from prolonged use.

Blood and lymphatic system disorders

Common: Neutropenia, eosinophilia.
Uncommon: Leukopenia, decreased haemoglobin concentration, positive Coomb’s test.
Rare: Thrombocytopenia.
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.

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

**Gastrointestinal disorders**
Uncommon: Gastrointestinal disturbance.
Very rare: Pseudomembranous colitis.

**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 Section 4.4 Special Warnings and Precautions for use).

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.
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.

5 **PHARMACOLOGICAL PROPERTIES**

5.1 **Pharmacodynamic properties**
Pharmacotherapeutic group: cephalosporins and related substances, ATC-Code: J01D A06

**Mode of action**
Cefuroxime axetil owes its *in vivo* bactericidal activity to the parent compound cefuroxime. All cephalosporins (β-lactam antibiotics) inhibit cell wall production and are selective inhibitors of peptidoglycan synthesis. The initial step in drug action consists of binding of the drug to cell receptors, called Penicillin-Binding Proteins. After a β-lactam antibiotic has bound to these receptors, the transpeptidation reaction is inhibited and peptidoglycan synthesis is blocked. Bacterial lysis is the end result.

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

- hydrolysis by beta-lactamases. Cefuroxime may be efficiently hydrolysed by certain of the extended-spectrum beta-lactamases (ESBLs) and by the chromosomally-encoded (AmpC) enzyme 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 organisms
- drug efflux pumps

Methicillin-resistant staphylococci (MRS) are resistant to all currently available β-lactam antibiotics including cefuroxime. Penicillin-resistant *Streptococcus pneumoniae* are cross-resistant to cephalosporins such as cefuroxime through alteration of penicillin binding proteins. Beta-lactamase negative, ampicillin resistant (BLNAR) strains of *H. influenzae* should be considered resistant to cefuroxime despite apparent in vitro susceptibility. Strains of Enterobacteriaceae, in particular *Klebsiella* spp. and *Escherichia coli* that produce ESBLs (extended spectrum β-lactamase) may be clinically resistant to therapy with cephalosporins despite apparent in vitro susceptibility and should be considered as resistant.

**Breakpoints:**
According to the NCCLS (National Committee on Clinical Laboratory Standards) in 2001 the following breakpoints have been defined for cefuroxime:
Enterobacteriaceae: ≤ 4 µg/ml susceptible, ≥ 32 µg/ml resistant  
*Staphylococcus* spp.: ≤ 4 µg/ml susceptible, ≥ 32 µg/ml resistant  
*Haemophilus* spp.: ≤ 4 µg/ml susceptible; ≥ 16 µg/ml resistant  
*Streptococcus pneumoniae*: ≤ 1 µg/ml susceptible, ≥ 4 µg/ml resistant  
*Streptococcus* spp. other than *S. pneumoniae*: Streptococcal isolates susceptible to penicillin (MIC90 ≤ 0.12 µg/ml) may be considered susceptible to cefuroxime.

**Susceptibility:**
The prevalence of resistance may vary geographically and with time 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 such that the utility of the agent in at least some types of infections is questionable.

<table>
<thead>
<tr>
<th>Commonly susceptible species</th>
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<tbody>
<tr>
<td>Aerobes, Gram positive:</td>
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<tr>
<td><em>Staphylococcus aureus</em> (methicillin-susceptible)</td>
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<tr>
<td>Coagulase-negative staphylococci (methicillin-susceptible)</td>
</tr>
<tr>
<td><em>Streptococcus agalactiae</em></td>
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<tr>
<td><em>Streptococcus pneumoniae</em></td>
</tr>
<tr>
<td><em>Streptococcus pyogenes</em></td>
</tr>
<tr>
<td>Aerobes, Gram negative:</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
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<tr>
<td><em>Klebsiella</em> species</td>
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<tr>
<td><em>Moraxella catarrhalis</em></td>
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<tr>
<td><em>Proteus mirabilis</em></td>
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<tr>
<td><em>Proteus rettgeri</em></td>
</tr>
<tr>
<td>Anaerobes, Peptococcus species</td>
</tr>
<tr>
<td><em>Peptostreptococcus</em> species</td>
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<tr>
<td>Other organisms:</td>
</tr>
<tr>
<td><em>Borrelia burgdorferi.</em></td>
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<tr>
<td>Species for which resistance may be a problem</td>
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<tr>
<td><em>Acinetobacter</em> species</td>
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<tr>
<td><em>Citrobacter</em> species</td>
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<tr>
<td><em>Enterobacter</em> species</td>
</tr>
<tr>
<td><em>Morganella morganii</em></td>
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<tr>
<td>Resistant</td>
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<tr>
<td><em>Bacteroides fragilis</em></td>
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<tr>
<td><em>Clostridium difficile</em></td>
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<tr>
<td>Enterococci</td>
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<tr>
<td><em>Listeria monocytogenes</em></td>
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<tr>
<td><em>Proteus vulgaris</em></td>
</tr>
<tr>
<td><em>Pseudomonas</em> species</td>
</tr>
<tr>
<td><em>Serratia</em> species</td>
</tr>
</tbody>
</table>
5.2 Pharmacokinetic properties
Peak levels of cefuroxime are achieved within 30 to 45 minutes after intramuscular administration. The serum half-life after either intramuscular or intravenous injection is approximately 70 minutes. Concurrent administration of probenecid prolongs the excretion of the antibiotic and produces an elevated peak serum level. There is almost complete recovery of unchanged cefuroxime in the urine within 24 hours of administration, the major part being eliminated in the first six hours. Approximately 50% is excreted through the renal tubules and approximately 50% by glomerular filtration. Concentrations of cefuroxime in excess of the minimum inhibitory levels for common pathogens can be achieved in bone, synovial fluid and aqueous humor. Cefuroxime passes the blood-brain barrier when the meninges are inflamed.

5.3 Preclinical safety data
No additional data of relevance.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
None.

6.2 Incompatibilities
Cefuroxime is compatible with most commonly used intravenous fluids and electrolyte solutions.

The pH of 2.74% w/v sodium bicarbonate injection BP considerably affects the colour of solutions and therefore this solution is not recommended for the dilution of Cefuroxime. However, if required, for patients receiving sodium bicarbonate injection by infusion the Cefuroxime may be introduced into the tube of the giving set.

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

6.3 Shelf life
Un-opened dry powder: 3 years
Reconstituted solution: 24 hours stored in the conditions recommended in section 6.4.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless reconstitution/dilution (etc) has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage
Up-opened dry powder: Store below 30°C. Store in the original package.
Reconstituted solution: The reconstituted solution should be stored at 2-8°C for no longer than 24 hours.

Refer to section 6.3 for the storage of sterile products that have been opened, diluted or reconstituted.

6.5 Nature and contents of container
A type II transparent, colourless glass vial, with a bromobutyl stopper and a blue aluminum and polypropylene flip off cap with adhesive labels.

Cefuroxime 750mg Powder for Injection is available in 10ml vials in packs of 1, 5 or 100 vials. Not all pack sizes may be marketed.

6.6 Special precautions for disposal
Cefuroxime 750mg when dissolved in Water for Injections forms an off-white, opaque suspension for intramuscular use or a yellowish, clear solution for intravenous administration.

Intramuscular injection
750mg of Cefuroxime should be dissolved in 3ml of Water for Injections. Shake gently to produce an opaque suspension.

Intravenous injection
750mg of Cefuroxime should be dissolved in 6ml of Water for Injections. Shake gently to produce a clear solution. This solution may be given directly into the vein or introduced into the tubing of the giving set if the patient is receiving parenteral fluids.

On reconstitution, product must be mixed vigorously for at least 90 seconds prior to withdrawing into the syringe; and if not given immediately, again just prior to administration.

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

7 MARKETING AUTHORIZATION HOLDER
Ranbaxy (UK) Limited
20 Balderton Street,
London W1K 6TL
United Kingdom

8 MARKETING AUTHORIZATION NUMBER(S)
PL 14894 / 0399

9 DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION
12/11/2009
10 DATE OF REVISION OF THE TEXT
12/11/2009

1 NAME OF THE MEDICINAL PRODUCT
Cefuroxime 1.5g Powder for Solution for Injection or Infusion.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Vials contain 1.5g cefuroxime (as sodium salt).

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM
Powder for solution for injection or infusion.

White or off-white powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Cefuroxime 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. In addition, it is an effective prophylactic against post-operative infection in a variety of operations. Usually 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, (see Pharmaceutical precautions).

In situations where mixed aerobic and anaerobic infections are encountered or suspected (e.g. peritonitis, aspiration pneumonia, abscesses in the lung, pelvis and brain), or are likely to occur (e.g. in association with colorectal or gynaecological surgery) it is appropriate to administer Cefuroxime in combination with metronidazole.

Most of these infections will respond to an i.v. regimen of Cefuroxime (750mg) plus metronidazole injection (500mg/100ml) administered eight-hourly. In more severe or well established mixed infections, an i.v. regimen of Cefuroxime (1.5g) plus metronidazole injection (500mg/100ml) eight-hourly may be indicated. For the prophylaxis of infection in surgery (e.g. colorectal and gynaecological) a single dose of 1.5g Cefuroxime plus metronidazole injection (500mg/100ml) is appropriate.
Alternatively this may be followed by two 750mg doses of Cefuroxime plus metronidazole.
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 and pharyngitis.

Urinary tract infections for example acute and chronic pyelonephritis, cystitis and asymptomatic bacteriuria.

Soft-tissue infections for example cellulitis, erysipelas, peritonitis 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 such as meningitis.

Prophylaxis against infection in abdominal, pelvic, orthopaedic, cardiac, pulmonary, oesophageal and vascular surgery where there is increased risk from infection.

This permits the use of sequential therapy with the same antibiotic, when a change from parenteral to oral therapy is clinically indicated.

Where appropriate, 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 Posology and method of administration

Route and method of administration

Cefuroxime 1.5g may be administered by intravenous injection or infusion. For instructions on dilution of the product before administration, see section 6.6.

Normal dosage

Adults:
Many infections will respond to 750mg t.i.d. by i.m. or i.v. injection. For more severe infections, this dose should be increased to 1.5g t.i.d. i.v. The frequency of i.m. or i.v. injection can be increased to six-hourly if necessary, giving total doses of 3g to 6g daily.
Where clinically indicated, adults with pneumonia and acute exacerbations of chronic bronchitis have been shown to respond to 750mg or 1.5g b.d., followed by oral therapy with cefuroxime axetil (see Sequential therapy).

**Infants and Children:**
Doses of 30 to 100mg/kg/day given as three or four divided doses. A dose of 60mg/kg/day will be appropriate for most infections.

**Neonates:**
Doses of 30 to 100mg/kg/day given as two or three divided doses. In the first weeks of life the serum half-life of cefuroxime can be three to five times that in adults.

**Elderly:**
See dosage in adults.

**Other Recommendations**

**Gonorrhoea:**
1.5g should be given as a single dose. This may be given as 2 x 750mg injections into different sites e.g. each buttock.

**Meningitis:**
Cefuroxime is suitable for sole therapy of bacterial meningitis due to sensitive strains. The following dosages are recommended.

Infants and Children: 200 to 240mg/kg/day i.v. in three or four divided doses. This dosage may be reduced to 100mg/kg/day i.v. after three days or when clinical improvement occurs.

Neonates: The initial dosage should be 100mg/kg/day i.v. A reduction to 50mg/kg/day i.v. may be made when clinically indicated.

Adults: 3g i.v. every eight hours. Data are not yet sufficient to recommend a dose for intrathecal administration.

**Prophylaxis:**
The usual dose is 1.5g i.v. with induction of anaesthesia for abdominal, pelvic and orthopaedic operations, but may be supplemented with two 750mg i.m. doses eight and sixteen hours later. In cardiac pulmonary oesophageal and vascular operations, the usual dose is 1.5g i.v. with induction of anaesthesia continuing with 750mg i.m. t.d.s. for a further 24 to 48 hours.

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

**Sequential therapy**

**Pneumonia:**
1.5g b.d. (i.v. or i.m.) for 48-72 hours, followed by 500mg b.d. cefuroxime axetil oral therapy for 7 days.

**Acute exacerbations of chronic bronchitis:**
750mg b.d. (i.v. or i.m.) for 48-72 hours, followed by 500mg b.d. cefuroxime axetil oral therapy for 5-7 days.

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

**Dosage in 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 Cefuroxime should be reduced to compensate for its slower excretion. However, it is not necessary to reduce the dose until the creatinine clearance falls below 20ml/min. In adults with marked impairment (creatinine clearance 10-20ml/min) 750mg b.d. is recommended and with severe impairment (creatinine clearance <10ml/min) 750mg once daily is adequate. For patients on haemodialysis a further 750mg dose should be given at the end of each dialysis. When continuous peritoneal dialysis is being used, a suitable dosage is usually 750mg twice daily.

For patients in renal failure on continuous arteriovenous haemodialysis or high-flux haemofiltration in intensive therapy units a suitable dosage is 750mg 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 cefuroxime or to any of the cephalosporins. Previous immediate and/or severe hypersensitivity reaction to a penicillin or to any other type of beta-lactam drug.

**4.4 Special warnings and precautions for use**
Special care is indicated in patients who have experienced an allergic reaction to penicillins or beta-lactams.

There may be some variation on the results of biochemical tests of renal function, but these do not appear to be of clinical importance. As a precaution, renal function should be monitored if this is already impaired.

Delayed sterilisation of the CSF in patients with Haemophilus influenzae meningitis may result in an adverse outcome such as deafness and/or neurological sequelae. Persistence of positive CSF cultures of H. influenzae at 18-36 hours has been noted in some patients treated with cefuroxime sodium injection and, as with other therapeutic regimens used in the treatment of meningitis, hearing loss has been reported in some children.
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. The change to oral therapy should only be made once there is a clear clinical improvement. If there has been no clinical improvement after 72 hours of parenteral treatment, then the patient's treatment should be reviewed. Please refer to the relevant prescribing information for cefuroxime axetil before initiating sequential therapy.

This medicinal product contains 73.5 mg sodium per dose. To be taken into consideration by patients on a controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction
Cephalosporin antibiotics at high dosage should be given with caution to patients receiving concurrent treatment with potent diuretics such as furosemide and aminoglycosides, as these combinations are suspected of adversely affecting renal function. Clinical experience with Cefuroxime has shown that this is not likely to be a problem at the recommended dose levels.

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 Cefuroxime. This antibiotic does not interfere in the alkaline picrate assay for creatinine.

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

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

4.7 Effects on ability to drive and use machines
None reported.

4.8 Undesirable effects
The following convention has been used for the classification of frequency:
Very common >1/10
Common   >1/100 and <1/10
Uncommon  >1/1000 and <1/100
Rare      >1/10,000 and <1/1000
Very rare  <1/10,000.

Infections and infestations
Rare: Candida overgrowth from prolonged use.
Blood and lymphatic system disorders
Common: Neutropenia, eosinophilia.
Uncommon: Leukopenia, decreased haemoglobin concentration, positive Coomb’s test.
Rare: Thrombocytopenia.
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.

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

Gastrointestinal disorders
Uncommon: Gastrointestinal disturbance.
Very rare: Pseudomembranous colitis.

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 Section 4.4 Special Warnings and Precautions for use).

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.

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.

5 **PHARMACOLOGICAL PROPERTIES**

5.1 **Pharmacodynamic properties**
Pharmacotherapeutic group: cephalosporins and related substances, ATC-Code: J01D A06

**Mode of action**
Cefuroxime axetil owes its in vivo bactericidal activity to the parent compound cefuroxime. All cephalosporins (β-lactam antibiotics) inhibit cell wall production and are selective inhibitors of peptidoglycan synthesis. The initial step in drug action consists of binding of the drug to cell receptors, called Penicillin-Binding Proteins. After a β-lactam antibiotic has bound to these receptors, the transpeptidation reaction is inhibited and peptidoglycan synthesis is blocked. Bacterial lysis is the end result.

**Mechanism of resistance**
Bacterial resistance to cefuroxime may be due to one or more of the following mechanisms:
- hydrolysis by beta-lactamases. Cefuroxime may be efficiently hydrolysed by certain of the extended-spectrum beta-lactamases (ESBLs) and by the chromosomally-encoded (AmpC) enzyme 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 organisms
- drug efflux pumps

Methicillin-resistant staphylococci (MRS) are resistant to all currently available β-lactam antibiotics including cefuroxime. Penicillin-resistant *Streptococcus pneumoniae* are cross-resistant to cephalosporins such as cefuroxime through alteration of penicillin binding proteins.

Beta-lactamase negative, ampicillin resistant (BLNAR) strains of *H. influenzae* should be considered resistant to cefuroxime despite apparent in vitro susceptibility.

Strains of Enterobacteriaceae, in particular *Klebsiella* spp. and *Escherichia coli* that produce ESBLs (extended spectrum β-lactamase) may be clinically resistant to therapy with cephalosporins despite apparent in vitro susceptibility and should be considered as resistant.
**Breakpoints:**
According to the NCCLS (National Committee on Clinical Laboratory Standards) in 2001 the following breakpoints have been defined for cefuroxime:
- Enterobacteriaceae: ≤ 4 µg/ml susceptible, ≥ 32 µg/ml resistant
  - *Staphylococcus* spp.: ≤ 4 µg/ml susceptible, ≥ 32 µg/ml resistant
  - *Haemophilus* spp.: ≤ 4 µg/ml susceptible; ≥ 16 µg/ml resistant
- *Streptococcus pneumoniae*: ≤ 1 µg/ml susceptible, ≥ 4 µg/ml resistant
- *Streptococcus* spp. other than *S. pneumoniae*:
  - Streptococcal isolates susceptible to penicillin (MIC90 ≤ 0.12 µg/ml) may be considered susceptible to cefuroxime.

**Susceptibility:**
The prevalence of resistance may vary geographically and with time 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 such that the utility of the agent in at least some types of infections is questionable.

<table>
<thead>
<tr>
<th>Commonly susceptible species</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aerobes, Gram positive:</strong></td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em> (methicillin-susceptible)</td>
</tr>
<tr>
<td>Coagulase-negative staphylococci (methicillin-susceptible)</td>
</tr>
<tr>
<td><em>Streptococcus agalactiae</em></td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
</tr>
<tr>
<td><em>Streptococcus pyogenes</em></td>
</tr>
<tr>
<td><strong>Aerobes, Gram negative:</strong></td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
</tr>
<tr>
<td><em>Klebsiella</em> species</td>
</tr>
<tr>
<td><em>Moraxella catarrhalis</em></td>
</tr>
<tr>
<td><em>Proteus mirabilis</em></td>
</tr>
<tr>
<td><em>Proteus rettgeri</em></td>
</tr>
<tr>
<td><strong>Anaerobes,</strong></td>
</tr>
<tr>
<td><em>Peptococcus</em> species</td>
</tr>
<tr>
<td><em>Peptostreptococcus</em> species</td>
</tr>
<tr>
<td><strong>Other organisms:</strong></td>
</tr>
<tr>
<td><em>Borrelia burgdorferi.</em></td>
</tr>
<tr>
<td><strong>Species for which resistance may be a problem</strong></td>
</tr>
<tr>
<td><em>Acinetobacter</em> species</td>
</tr>
<tr>
<td><em>Citrobacter</em> species</td>
</tr>
<tr>
<td><em>Enterobacter</em> species</td>
</tr>
<tr>
<td><em>Morganella morganii</em></td>
</tr>
<tr>
<td><strong>Resistant</strong></td>
</tr>
<tr>
<td><em>Bacteroides fragilis</em></td>
</tr>
<tr>
<td><em>Clostridium difficile</em></td>
</tr>
<tr>
<td>Enterococci</td>
</tr>
<tr>
<td><em>Listeria monocytogenes</em></td>
</tr>
</tbody>
</table>
5.2 Pharmacokinetic properties
Peak levels of cefuroxime are achieved within 30 to 45 minutes after intramuscular administration. The serum half-life after either intramuscular or intravenous injection is approximately 70 minutes. Concurrent administration of probenecid prolongs the excretion of the antibiotic and produces an elevated peak serum level. There is almost complete recovery of unchanged cefuroxime in the urine within 24 hours of administration, the major part being eliminated in the first six hours. Approximately 50% is excreted through the renal tubules and approximately 50% by glomerular filtration. Concentrations of cefuroxime in excess of the minimum inhibitory levels for common pathogens can be achieved in bone, synovial fluid and aqueous humor. Cefuroxime passes the blood-brain barrier when the meninges are inflamed.

5.3 Preclinical safety data
No additional data of relevance.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
None.

6.2 Incompatibilities
Cefuroxime is compatible with most commonly used intravenous fluids and electrolyte solutions.

The pH of 2.74% w/v sodium bicarbonate injection BP considerably affects the colour of solutions and therefore this solution is not recommended for the dilution of Cefuroxime. However, if required, for patients receiving sodium bicarbonate injection by infusion the Cefuroxime may be introduced into the tube of the giving set.

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

6.3 Shelf life
Un-opened dry powder: 3 years
Reconstituted solution: 24 hours stored in the conditions recommended in section 6.4.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless reconstitution/dilution (etc) has taken place in controlled and validated aseptic conditions.
6.4 **Special precautions for storage**

Up-opened dry powder: Store below 30°C. Store in the original package.

Reconstituted solution: The reconstituted solution should be stored at 2-8°C for no longer than 24 hours.

Refer to section 6.3 for the storage of sterile products that have been opened, diluted or reconstituted.

6.5 **Nature and contents of container**

A type II transparent, colourless glass vial, with a bromobutyl stopper and a green aluminum and polypropylene flip off cap with adhesive labels.

Cefuroxime 1.5g Powder for Injection or Infusion is available in 20 and 100ml vial packs of 1, 10 or 20 vials. Not all pack sizes may be marketed.

6.6 **Special precautions for disposal**

Cefuroxime 1.5g when dissolved in Water for Injections forms a yellowish, clear solution for intravenous administration.

**Intravenous injection**

1.5g of Cefuroxime should be dissolved in 15ml of Water for Injections. Shake gently to produce a clear solution.

**Intravenous infusion**

1.5g of Cefuroxime should be dissolved in 50ml of Water for Injections. Shake gently to produce a clear solution. The reconstituted solution for infusion should be administered as a short time infusion over 30 minutes.

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.

On reconstitution, product must be mixed vigorously for at least 90 seconds prior to withdrawing into the syringe; and if not given immediately, again just prior to administration.

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

7 **MARKETING AUTHORISATION HOLDER**

Ranbaxy (UK) Limited  
20 Balderton Street  
London W1K 6TL  
United Kingdom

8 **MARKETING AUTHORISATION NUMBER(S)**

PL 14894 / 0400
9    DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
12/11/2009

10   DATE OF REVISION OF THE TEXT
12/11/2009
Cefuroxime 750mg powder for solution for injection.
Cefuroxime 1.5g powder for solution for injection or infusion (cefuroxime sodium)

Read all of this leaflet carefully before you start taking this medicine.
• Keep this leaflet. You may need to read it again.
• If you have further questions, ask your doctor or pharmacist.
• This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
• If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:
1. What Cefuroxime is and what it is used for
2. Before you use Cefuroxime
3. How to use Cefuroxime
4. Possible side effects
5. How to store Cefuroxime
6. Further information

The name of your medicine is Cefuroxime 750mg Powder for Injection or Cefuroxime 1.5g Powder for Injection or Infusion but will be referred to as Cefuroxime or as Cefuroxime injection throughout this leaflet.

1. WHAT CEFUROXIME IS AND WHAT IT IS USED FOR

Cefuroxime injection is an antibiotic which helps the body fight infections by destroying certain bacteria that causes them.

Cefuroxime injection is used to treat many different types of infections including:
• bronchitis, pneumonia and any other chest infections;
• cystitis and kidney infections;
• pelvic inflammatory diseases;
• gonorrhoea;
• ear, nose and throat infections;
• skin, soft tissue, bone and joint infections;
• meningitis.

Your doctor may also give it to you before an operation to protect you from infection.

2. BEFORE YOU USE CEFUROXIME

Your doctor or nurse will make sure it is safe for you to have Cefuroxime injection.

Do not take Cefuroxime if you:
• are allergic (hypersensitive) to Cefuroxime or any of the other ingredients of Cefuroxime listed in section 6;
• have ever had an allergic reaction to antibiotics such as penicillin or cephalosporins. An allergic reaction may include a rash, itching, swelling or breathing difficulties.

Take special care with Cefuroxime and tell your doctor if:
• you have kidney problems or are on dialysis;
• you have jaundice (yellowing of the skin and eyes), low blood protein;
• this injection is for a premature baby;
• you are on a low sodium diet because Cefuroxime injection contains significant quantities of sodium.

This medicine can alter the results of some blood tests e.g. blood cross-matching and blood sugar tests for diabetes. It is important to tell the doctor that you are taking this medicine if you have to have any of these tests.

Unlike certain cephalosporin antibiotics, Cefuroxime does not usually cause a false positive result when the urine is tested for sugar.

Taking other medicines
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Cefuroxime may interfere with:
• diuretics (water tablets), e.g. furosemide;
• aminoglycoside antibiotics e.g. gentamicin and neomycin;
• other antibiotics e.g. probenecid.

In some cases your doctor will arrange further monitoring, but this is routine and nothing to worry about.

Using Cefuroxime with food and drink
Cefuroxime injection can be used at any time of the day without regard to food intake.

Pregnancy and breast-feeding
Ask your doctor or pharmacist for advice before taking any medicine.

Cefuroxime is not known to harm the unborn child but, like all medicines, it will only be given to a pregnant woman if it is really needed. Your doctor will decide this.

Breast-feeding is not recommended whilst taking Cefuroxime as small amounts of Cefuroxime may enter the milk.

Driving and using machines
Cefuroxime is not known to affect the ability to drive or operate machinery.

Important information about some of the ingredients of Cefuroxime injection
Each 750mg vial contains 36.75mg sodium; each 1.5g vial contains 73.3mg sodium. To be taken into consideration by patients on a controlled sodium diet.

3. HOW TO USE CEFUROXIME

Your doctor will decide which dose you need. Year doctor or nurse will inject the Cefuroxime injection into a muscle or into a vein. In some cases, it may be added to a 'drip' intravenous infusion.

Cefuroxime injection is made up by adding the following amount of sterile water or other recommended diluents:

<table>
<thead>
<tr>
<th>Vial size</th>
<th>Intramuscular injection (suspension)</th>
<th>Intravenous injection (solution)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5g</td>
<td>X ml</td>
<td>X ml</td>
</tr>
<tr>
<td>750mg</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

On reconstitution, product must be mixed vigorously for at least 30 seconds prior to withdrawing into the syringe; and it given immediately, again just prior to administration.

Usual doses

Adults: Most adults need 750mg three or four times a day but for more severe infections this may be increased to 1.5g three or four times a day. If you have kidney trouble, you may be given the lower dose once or twice a day.

• Your doctor may give you 1.5g of Cefuroxime injection before surgery to protect you from infection. You may get further doses of 750mg of Cefuroxime injection after the operation.
• If you have a joint replacement operation, Cefuroxime may be mixed in the cement which is used.

Infants and children:
Most need 60mg for each kilogram of their body weight each day. This will be divided into three or four doses.

Newborn babies: Most need 30 to 100mg for each kilogram of their body weight each day. This will be divided into three or four doses.

MHRA PAR; CEFUROXIME 750MG POWDER FOR SOLUTION FOR INJECTION AND CEFUROXIME 1.5G POWDER FOR SOLUTION FOR INJECTION OR INFUSION, PL 14894/0399-400
If you or a child is being treated for meningitis, larger doses of Cefuroxime injection may be needed.

For the treatment of gonorrhoea:
- 1.5g should be given as a single dose. This may be given as 2 x 0.75g injections into different sites e.g. each buttok.

For the treatment of pneumonia:
- A twice daily dose of 1.5g injection should be given for 48-72 hours, followed by a twice daily dose of 500mg cefuroxime axetil oral therapy for 7 days.

For the treatment of acute exacerbations of chronic bronchitis:
- A twice daily dose of 750mg injection should be given for 48-72 hours, followed by a twice daily dose of 500mg cefuroxime axetil oral therapy for 5-7 days.

If you take more Cefuroxime than you should:
It is most unlikely that you will be given too much medicine by the nurse or doctor. Your doctor and nurse will be monitoring your progress, and checking the medicine that you are given. Always ask if you are not sure why you are getting a dose of medicine.

If you forget to take Cefuroxime:
Your doctor or nurse have instructions when to give you your medicine. It is most unlikely that you will not be given the medicine as it has been prescribed. If you think that you may have missed a dose then talk to your nurse or doctor. It is important that the course of treatment your doctor has prescribed is taken. You may start to feel better but it is important not to stop taking this medicine, until the doctor advises, otherwise your condition may get worse again.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS
Like all medicines, Cefuroxime can cause side effects, although not everybody gets them.

Some people may be allergic to antibiotics; if any of the following rare side effects occur soon after having your injection, tell your doctor immediately:
- Loss of consciousness
- Sudden wheezing and chest tightness or breathing difficulties
- Swelling of the eyelids, face or lips
- Severe skin rash that can peel or blister
- Fever

Other side effects are classified according to the following frequencies:
- Very common (in more than 1 in 10 patients)
- Common (in more than 1 in 100 but less than 1 in 10 patients)
- Uncommon (in more than 1 in 1000 but in less than 1 in 100 patients)
- Rare (in more than 1 in 10,000 but less than 1 in 1000 patients)
- Very rare (in less than 1 in 10,000 patients including reports of isolated cases)

Common:
- Changes in liver enzymes
- Inflammation or pain at the site of injection

Uncommon:
- Diarrhoea which contains blood or mucus

Rare:
- Infections
- Easy bruising (thrombocytopenia)
- Changes in how the liver and kidneys function

Very rare:
- Headache, joint pain, generally feeling unwell (Pseudomembranous colitis)
- Inflammation of the kidneys

Laboratory tests have shown that Cefuroxime can also cause changes in the blood, such as a decrease in blood haemoglobin concentrations (may result in anaemia), decreases in white blood cell counts (with an increased risk of infection), decreases in the very small blood cells called platelets (resulting in bruising and prolonged bleeding) and increases in the numbers of a type of white blood cells (eosinophils).

Like other medicines used to treat meningitis, Cefuroxime may take some time in clearing up the infection. As a result of this, hearing loss caused by meningitis has occurred in a few patients after using cefuroxime.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE CEFUROXIME
Keep out of the reach and sight of children.

The unopened dry powder should be stored below 30°C.

Store in the original package.

From a microbiological point of view, the reconstituted solution should be used immediately. If not used immediately, the reconstituted solution should be stored at 2-8°C for no longer than 24 hours.

Do not use Cefuroxime after the expiry date which is stated on the label and carton after EXP.

The expiry refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION
What Cefuroxime Injection contains
Cefuroxime injection contains the active ingredient Cefuroxime Sodium. There are no other ingredients.

What Cefuroxime looks like and contents of the pack
Cefuroxime 750 mg powder for injection is a white or off-white powder which forms:
- an off-white, opaque suspension for intramuscular use when reconstituted with 3ml of Water for Injections.
- a yellowish, clear solution for intravenous use when reconstituted with 6ml of Water for Injections.

Cefuroxime 1.5 g powder for injection or infusion is a white or off-white powder which forms:
- a yellowish, clear solution for intravenous injection when reconstituted with 15 ml of Water for Injection
- a yellowish, clear solution for intravenous infusion when reconstituted with 50 ml of Water for Injection

Cefuroxime 750 mg powder for injection is available in 10 ml vials in packs of 1, 5 or 10 vials.

Cefuroxime 1.5 g powder for injection or infusion is available in 20 and 100 ml vials in packs of 1, 10 or 20 vials.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Marketing authorisation holder:
Ranbaxy (UK) Limited,
20 Balderton Street,
W1K 6LJ, United Kingdom

Manufacturer:
Laboratory Delphic,
Gran Capilla, 10-08970 Sant Joan Despi, Barcelona, Spain

Date of PIL revision: September 2009
Cefuroxime 750mg powder for solution for injection.
Cefuroxime 1.5g powder for solution for injection or infusion (cefuroxime sodium)

Read all of this leaflet carefully before you start taking this medicine.
- Keep this leaflet. You may need to read it again.
- If you have further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:
1. What Cefuroxime is and what it is used for
2. Before you use Cefuroxime
3. How to use Cefuroxime
4. Possible side effects
5. How to store Cefuroxime
6. Further information

The name of your medicine is Cefuroxime 750mg Powder for Injection or Cefuroxime 1.5g Powder for Injection or Infusion but will be referred to as Cefuroxime throughout this leaflet.

1. WHAT CEFUROXIME IS AND WHAT IT IS USED FOR
Cefuroxime injection is an antibiotic which helps the body fight infections by destroying certain bacteria that causes them.

Cefuroxime injection is used to treat many different types of infections including:
- bronchitis, pneumonia and any other chest infections;
- cystitis and kidney infections;
- pelvic inflammatory diseases;
- gonorrhoea;
- ear, nose and throat infections;
- skin, soft tissue, bone and joint infections;
-_aspect.

Your doctor may also give it to you before an operation to prevent you from infection.

2. BEFORE YOU USE CEFUROXIME
Your doctor or nurse will make sure it is safe for you to have Cefuroxime injection.

Do not take Cefuroxime if you:
- are allergic (hypersensitive) to Cefuroxime or any of the other ingredients of Cefuroxime listed in section 6.
- have had an allergic reaction to antibiotics such as penicillin or cephalosporins. An allergic reaction may include a rash, itching, swelling or breathing difficulties.

Take special care with Cefuroxime and tell your doctor if:
- you have kidney problems or are on dialysis;
- you have jaundice (yellowing of the skin and eyes), low blood protein;
- this injection is for a premature baby;
- you are on a low sodium diet because Cefuroxime injection contains significant quantities of sodium;

This medicine can alter the results of some blood tests e.g. blood cross-matching and blood sugar tests for diabetes. It is important to tell the doctor that you are taking this medicine if you have to have any of these tests.

Unlike certain cephalosporin antibiotics, Cefuroxime does not usually cause a false positive result when the urine is tested for sugar.

Taking other medicines
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Cefuroxime may interfere with:
- diuretics (water tablets) e.g. frusemide;
- aminoglycoside antibiotics e.g. gentamicin and neomycin;
- other antibiotics e.g. premarin.

In some cases your doctor will arrange further monitoring, but this is routine and nothing to worry about.

Using Cefuroxime with food and drink
Cefuroxime injection can be given at any time of the day with regard to food intake.

Pregnancy and breast-feeding
Ask your doctor or pharmacist for advice before taking any medicine.

Cefuroxime is not known to harm the unborn child but, like all antibiotics, it will only be given to a pregnant woman if it is really needed. Your doctor will decide this.

Breast-feeding is not recommended whilst taking Cefuroxime as small amounts of Cefuroxime may enter the milk.

Driving and using machines
Cefuroxime is not known to affect the ability to drive or operate machinery.

Important Information about some of the ingredients of Cefuroxime injection
Each 750mg vial contains 36.75mg sodium; each 1.5g vial contains 73.5mg sodium. To be taken into consideration by patients on a controlled sodium diet.

3. HOW TO USE CEFUROXIME
Your doctor will decide which dose you need. Your doctor or nurse will inject the Cefuroxime injection into a muscle or into a vein. In some cases, it may be added to a ‘drip’ intravenous infusion.

Cefuroxime injection is made up by adding the following amount of sterile water or other recommended diluting solution:

<table>
<thead>
<tr>
<th>Vial size</th>
<th>Intramuscular injection (suspension)</th>
<th>Intramuscular injection (solution)</th>
<th>Intravenous infusion (solution)</th>
</tr>
</thead>
<tbody>
<tr>
<td>750mg</td>
<td>7.5 ml</td>
<td>7.5 ml</td>
<td>15 ml</td>
</tr>
<tr>
<td>1.5g</td>
<td>15 ml</td>
<td>15 ml</td>
<td>15 ml</td>
</tr>
</tbody>
</table>

On reconstitution, product must be mixed vigorously for at least 10 seconds prior to withdrawing into the syringe, and if not given immediately, again just prior to administration.

Usual doses

Adults: Most adults need 750mg three or four times a day but for more severe infections this may be increased to 1.5g three or four times a day. If you have kidney trouble, you may be given the lower dose just once or twice a day.

- Your doctor may give you 1.5g of Cefuroxime injection before surgery to protect you from infection. You may get further doses of 750mg at Cefuroxime injection after the operation.
- If you have a joint replacement operation, Cefuroxime may be mixed in the cement which is used.

Infants and children: Most need 60mg per kilogram of their body weight each day. This will be divided into three or four doses.

Newborn babies: Most need 30 to 100mg per kilogram of their body weight each day. This will be divided into three or four doses.
If you or a child is being treated for meningitis, larger doses of Cefuroxime injection may be needed.

For the treatment of gonorrhoea:
- 1.5g should be given as a single dose. This may be given as 2 x 750mg injections into different sites e.g. each buttock.

For the treatment of pneumonia:
- A twice daily dose of 1.5g injection should be given for 48-72 hours, followed by a twice daily dose of 500mg cefuroxime axetil oral therapy for 7 days.

For the treatment of acute exacerbations of chronic bronchitis:
- A twice daily dose of 750mg injection should be given for 48-72 hours, followed by a twice daily dose of 500mg cefuroxime axetil oral therapy for 5-7 days.

If you take more Cefuroxime than you should:
It is most unlikely that you will be given too much medicine by the nurse or doctor. Your doctor and nurse will be monitoring your progress, and checking the medication that you have been given. Always ask if you are sure why you are getting a dose of medicine.

If you forget to take Cefuroxime:
Your doctor or nurse have instructions on how to give you your medicine. It is most unlikely that you will not be given the medicine as it has been prescribed. If you think that you may have missed a dose then talk to your nurse or doctor. It is important that the course of treatment your doctor has prescribed is taken. You may start to feel better but it is important not to stop taking this medicine, until the doctor advises, otherwise your condition may get worse again.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Cefuroxime can cause side effects, although not everybody gets them.

Some people may be allergic to antibiotics; if any of the following rare side effects occur soon after having your injection, tell your doctor immediately:
- Loss of co-ordination
- Sudden wheezelessness and chest tightness or breathing difficulties
- Swelling of the eyelids, face or lips
- Severe skin rashes that can peel or blister
- Fever

Other side effects are listed below according to the following frequencies:
- Very common (in more than 1 in 10 patients)
- Common (in more than 1 in 100 but less than 1 in 10 patients)
- Uncommon (in more than 1 in 1000 but less than 1 in 100 patients)
- Rare (in more than 1 in 10,000 but less than 1 in 1000 patients)
- Very rare (in less than 1 in 10,000 patients including reports of isolated cases)

Common:
- Changes in liver enzymes
- Inflammation or pain at the site of injection

Uncommon:
- Diarrhoea which contains blood or mucus

Rare:
- Thrush infections
- Easy bruising (thrombocytopenia)
- Changes in how the liver and kidneys function

Very rare:
- Headache, joint pain, generally feeling unwell
- Pseudomembranous colitis
- Inflammation of the kidneys

Laboratory tests have shown that Cefuroxime can also cause changes in the blood, such as a decrease in blood haemoglobin concentrations (may result in anaemia), decreases in white blood cell counts (with an increased risk of infection), decreases in the very tiny blood cells called platelets (resulting in bruising and prolonged bleeding) and increases in the numbers of a type of white blood cells (eosinophils).

Like other medicines used to treat meningitis, Cefuroxime may take some time in clearing up the infection. As a result of this, hearing loss caused by meningitis has occurred in a few patients after using cefuroxime.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE CEFUROXIME

Keep out of the reach and sight of children.

The un-opened dry powder should be stored below 30°C. Store in the original package.

From a microbiological point of view, the reconstituted solution should be used immediately. If not used immediately, the reconstituted solution should be stored at 2-8°C for no longer than 24 hours.

Do not use Cefuroxime after the expiry date which is stated on the label and carton after EXP.

The expiry refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Cefuroxime injection contains
Cefuroxime injection contains the active ingredient Cefuroxime Sodium. There are no other ingredients.

What Cefuroxime looks like and contents of the pack
Cefuroxime 750 mg powder for injection is a white or off-white powder which forms:
- an off-white, opaque suspension for intramuscular use when reconstituted with 3ml of Water for Injections.

Cefuroxime 1.5 g powder for injection or infusion is a white or off-white powder which forms:
- a yellowish, clear solution for intravenous use when reconstituted with 5ml of Water for Injections.

Cefuroxime 1.5 g powder for injection or infusion is available in 10 ml vials in packs of 1, 5 or 100 vials.

Cefuroxime 1.5 g powder for injection or infusion is available in 20 and 100 ml vials in packs of 1, 10 or 20 vials.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Marketing authorisation holder:
Ranbaxy (UK) Limited,
20 Balderton Street,
WY1 6TL, United Kingdom

Manufacturers:
Laboratory Reig Jofre,
Gran Capita, 10-08930 Sant Joan Despi,
Barcelona, Spain

Date of PRL revision: September 2009
LABELLING

750mg:

Each vial contains Cefuroxime sodium 802 mg equivalent to 750 mg of cefuroxime.

**FOR I.V. OR I.M. INJECTION:**

Warning: Contains Penicillin

**FOR I.V. INJECTION:**

Solutions for injection are prepared by dissolving the dry substance in 6 ml of Water for Injection.

**FOR I.M. INJECTION:**

Solutions for injection are prepared by dissolving the dry substance in 5 ml of Water for Injection.

On reconstitution, product must be mixed vigorously for at least 90 seconds prior to withdrawing into the syringe; and if not given immediately, again just prior to administration.

Read the enclosed leaflet before use.

Use as directed by your doctor.

Each vial contains Cefuroxime sodium 802 mg equivalent to 750 mg of cefuroxime.

This medicinal product contains 36.75 mg sodium per dose.

To be taken into consideration by patients on a controlled sodium diet.

**KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.**

Store below 30°C. Store in the original package.

The reconstituted solution should be stored at 2 - 8°C for no longer than 24 hours.

**MA Holder:**

Ranbaxy (UK) Ltd,
20 Radcliff Court, London, W1K 6TL

United Kingdom. P.L. 14894/0399

MHRA PAR; CEFUROXIME 750MG POWDER FOR SOLUTION FOR INJECTION AND CEFUROXIME 1.5G POWDER FOR SOLUTION FOR INJECTION OR INFUSION, PL 14894/0399-400
Cefuroxime 750mg powder for solution for injection.

**FOR I.V. INJECTION**: Solutions for injection are prepared by dissolving the dry substance in 6 ml of Water for Injection.

**FOR I.M. INJECTION**: Solutions for injection are prepared by dissolving the dry substance in 5 ml of Water for Injection.

On reconstitution, protect must be mixed vigorously for at least 30 seconds prior to withdrawing into the syringe, and not given immediately, again just prior to administration. Pool the enclosed leaflet before use.

This medicinal product contains 36.75mg sodium per dose. To be taken into consideration by patients on a controlled sodium diet.

KEEPOUT OF THE REACH AND SIGHT OF CHILDREN.

Store below 30°C. Avoid the original package. The reconstituted solution should be stored at 2-8°C for no longer than 24 hours.

Use as directed by your doctor.
Cefuroxime 1.5 g
powder for solution for injection/infusion

Each vial contains Cefuroxime sodium 1.5 g equivalent to 1.5 g of cefuroxime.

This medicinal product contains 0.750 g sodium per dose.

To be taken into consideration by patients on a controlled sodium diet.

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.

Store below 30°C.

Keep in the original package.

The reconstituted solution should be stored at 2°C to 8°C for no longer than 24 hours.

Use as directed by your doctor.