CEFTUM TABLETS

Cefuroxime Axetil Tablets IP 125/250/500mg

QUALITATIVE AND QUANTITATIVE COMPOSITION

**CEFTUM TABLETS 125 mg**

Each film-coated tablet contains:
Cefuroxime Axetil IP equivalent to Cefuroxime 125 mg
Colour: Titanium Dioxide IP

**CEFTUM TABLETS 250 mg**

Each film-coated tablet contains:
Cefuroxime Axetil IP equivalent to Cefuroxime 250 mg
Colour: Titanium Dioxide IP

**CEFTUM TABLETS 500 mg**

Each film-coated tablet contains:
Cefuroxime Axetil IP equivalent to Cefuroxime 500 mg
Colour: Titanium Dioxide IP

PHARMACEUTICAL FORM

Film-coated tablets

CLINICAL PARTICULARS

Therapeutic Indications

*CEFTUM* is an oral prodrug of the bactericidal cephalosporin antibiotic cefuroxime, which is resistant to most β (beta)-lactamases and is active against a wide range of Gram-positive and Gram-negative organisms.

It is indicated for the treatment of infections caused by susceptible bacteria. Susceptibility to *CEFTUM* will vary with geography and time and local susceptibility data should be consulted where available (See Pharmacodynamic Properties).

**Indications include:**

- Upper respiratory tract infections (for example: ear, nose and throat infections, such as otitis media, sinusitis, tonsillitis and pharyngitis)
• Lower respiratory tract infections (for example: pneumonia, acute bronchitis, and acute exacerbations of chronic bronchitis)

• Genito-urinary tract infections (for example: pyelonephritis, cystitis and urethritis)

• Skin and soft tissue infections (for example: furunculosis, pyoderma and impetigo)

• Gonorrhoea, acute uncomplicated gonococcal urethritis, and cervicitis

Cefuroxime is also available as the sodium salt (SUPACEF) for parenteral administration. This permits the use of sequential therapy with the same antibiotic, when a change from parenteral to oral therapy is clinically indicated.

Where appropriate CEFTUM (cefuroxime axetil) is effective when used following initial parenteral SUPACEF (cefuroxime sodium) in the treatment of pneumonia and acute exacerbations of chronic bronchitis.

**Posology and Method of Administration**

The usual course of therapy is seven days (range five to ten days).

CEFTUM tablets should be taken after food for optimum absorption.

**Adults:**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most infections</td>
<td>250 mg twice daily</td>
</tr>
<tr>
<td>Urinary tract infections</td>
<td>250 mg twice daily</td>
</tr>
<tr>
<td>Mild to moderate lower respiratory tract infections e.g. bronchitis</td>
<td>250 mg twice daily</td>
</tr>
<tr>
<td>More severe lower respiratory tract infections, or if pneumonia is suspected</td>
<td>500 mg twice daily</td>
</tr>
<tr>
<td>Pyelonephritis</td>
<td>250 mg twice daily</td>
</tr>
<tr>
<td>Uncomplicated gonorrhoea</td>
<td>Single dose of 1 g</td>
</tr>
</tbody>
</table>

**Sequential therapy**

**Pneumonia**
1.5 g SUPACEF (cefuroxime sodium) three times a day or twice a day (intravenous (i.v.) or intramuscular (i.m.) for 48 to 72 hours, followed by 500 mg twice a day CEFTUM (cefuroxime axetil) oral therapy for 7 to 10 days.

**Acute exacerbations of chronic bronchitis**
750 mg SUPACEF (cefuroxime sodium) three times a day or twice a day (i.v. or i.m.) for 48 to 72 hours, followed by 500 mg twice a day CEFTUM (cefuroxime axetil) oral therapy for 5 to 10 days.
Duration of both parenteral and oral therapy is determined by the severity of the infection and the clinical status of the patient.

**Children:**

<table>
<thead>
<tr>
<th></th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most infections</td>
<td>125 mg (1 x 125 mg tablet) twice daily</td>
</tr>
<tr>
<td>Children with otitis media or, where appropriate, with more severe infections</td>
<td>250 mg (1 x 250 mg tablet or 2 x 125 mg tablets) twice daily</td>
</tr>
</tbody>
</table>

*CEFTUM* tablets should not be crushed or split and are therefore unsuitable for treatment of patients, such as younger children, who cannot swallow whole tablets.

There is no experience of using cefuroxime axetil formulations in children under the age of 3 months.

**Renal impairment:**

Cefuroxime is primarily excreted by the kidneys. In patients with markedly impaired renal function it is recommended that the dosage of cefuroxime be reduced to compensate for its slower excretion (see the table below).

<table>
<thead>
<tr>
<th>Creatinine Clearance</th>
<th>( T_{1/2} ) (hours)</th>
<th>Recommended Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \geq 30 ) ml/min</td>
<td>1.4 - 2.4</td>
<td>No dose adjustment necessary standard dose of 125 mg to 500 mg given twice daily</td>
</tr>
<tr>
<td>10-29 ml/min</td>
<td>4.6</td>
<td>Standard individual dose given every 24 hours</td>
</tr>
<tr>
<td>&lt;10 ml/min</td>
<td>16.8</td>
<td>Standard individual dose given every 48 hours</td>
</tr>
<tr>
<td>During haemodialysis</td>
<td>2 – 4</td>
<td>A single additional standard individual dose should be given at the end of each dialysis</td>
</tr>
</tbody>
</table>

**Contraindications**

Patients with known hypersensitivity to cephalosporin antibiotics.

**Special Warnings and Special Precautions for Use**

Special care is indicated in patients who have experienced an allergic reaction to penicillins or other beta-lactams.

As with other antibiotics, use of *CEFTUM* 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 has been reported with the use of antibiotics, and may range in severity from mild to life-threatening. Therefore, it is important to consider its diagnosis in patients who develop diarrhoea during or after antibiotic use. If prolonged or significant diarrhoea occurs or the patient experiences abdominal cramps, treatment should be discontinued immediately and the patient investigated further.

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.

Please refer to the relevant prescribing information for cefuroxime sodium before initiating sequential therapy.

**Interaction with Other Medicaments and Other Forms of Interaction**

Drugs which reduce gastric acidity may result in a lower bioavailability of *CEFTUM* compared with that of the fasting state and tend to cancel the effect of enhanced post-prandial absorption.

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

As a false negative result may occur in the ferricyanide test, it is recommended that either the glucose oxidase or hexokinase methods are used to determine blood/plasma glucose levels in patients receiving *CEFTUM*. This antibiotic does not interfere in the alkaline picrate assay for creatinine.

**Pregnancy and Lactation**

There is no experimental evidence of embryopathic or teratogenic effects attributable to Cefuroxime axetil 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 *CEFTUM* is administered to a nursing mother.

**Effects on Ability to Drive and Use Machines**

As this medicine may cause dizziness, patients should be warned to be cautious when driving or operating machinery.

**Undesirable Effects**

Adverse drug reactions to Cefuroxime axetil 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 example from placebo-controlled studies) for calculating incidence
were not available. In addition the incidence of adverse reactions associated with Cefuroxime axetil may vary according to the indication.

Data from large clinical studies 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 true frequency. Placebo-controlled trial data were not available. Where incidences have been calculated from clinical trial data, these were based on drug-related (investigator assessed) data.

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**
- Common: Overgrowth of Candida.

**Blood and lymphatic system disorders**
- Common: Eosinophilia
- Uncommon: Positive Coombs’ test, thrombocytopenia, leukopenia (sometimes profound)
- Very rare: Haemolytic anaemia

Cephalosporins as a class tend to be absorbed onto the surface of red cells membranes and react with antibodies directed against the drug to produce a positive Coombs’ test (which can interfere with cross-matching of blood) and very rarely haemolytic anaemia.

**Immune system disorders**
- Hypersensitivity reactions including
  - Uncommon: Skin rashes
  - Rare: Urticaria, pruritus
  - Very rare: Drug fever, serum sickness, anaphylaxis

**Nervous system disorders**
- Common: Headache, dizziness

**Gastrointestinal disorders**
- Common: Gastrointestinal disturbances including diarrhoea, nausea, abdominal pain
- Uncommon: Vomiting
Rare: Pseudomembranous colitis (See Special Warnings and Special Precautions for Use)

Hepatobiliary disorders
Common: Transient increases of hepatic enzyme levels, [ALT (SGPT), AST (SGOT), LDH]
Very rare: Jaundice (predominantly cholestatic), hepatitis

Skin and subcutaneous tissue disorders
Very rare: Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (exanthematic necrolysis)

See also Immune system disorders.

Overdose

Signs and Symptoms
Overdosage of cephalosporins can cause cerebral irritation leading to convulsions.

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

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties
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 axetil has been demonstrated in clinical trials this is indicated with an asterisk (*).</td>
</tr>
<tr>
<td><strong>Commonly Susceptible Species</strong></td>
</tr>
<tr>
<td>Gram-Positive Aerobes:</td>
</tr>
<tr>
<td><em>Staphylococcus aureus (methicillin susceptible)</em></td>
</tr>
<tr>
<td><em>Coagulase negative staphylococcus (methicillin susceptible)</em></td>
</tr>
<tr>
<td><em>Streptococcus pyogenes</em></td>
</tr>
<tr>
<td>Beta-hemolytic streptococci</td>
</tr>
<tr>
<td>Gram-Negative Aerobes:</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em> including ampicillin resistant strains</td>
</tr>
<tr>
<td><em>Haemophilus parainfluenzae</em></td>
</tr>
<tr>
<td>Moraxella catarrhalis*</td>
</tr>
<tr>
<td>Neisseria gonorrhoea* including penicillinase and non-penicillinase producing strains</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td><strong>Gram-Positive Anaerobes:</strong></td>
</tr>
<tr>
<td>Peptostreptococcus spp.</td>
</tr>
<tr>
<td>Propionibacterium spp.</td>
</tr>
<tr>
<td><strong>Spirochetes:</strong></td>
</tr>
<tr>
<td>Borrelia burgdorferi*</td>
</tr>
<tr>
<td><strong>Organisms for which acquired resistance may be a problem</strong></td>
</tr>
<tr>
<td><strong>Gram-Positive Aerobes:</strong></td>
</tr>
<tr>
<td>Streptococcus pneumoniae*</td>
</tr>
<tr>
<td><strong>Gram-Negative Aerobes:</strong></td>
</tr>
<tr>
<td>Citrobacter spp. not including <em>C. freundii</em></td>
</tr>
<tr>
<td>Enterobacter spp. not including <em>E. aerogenes</em> and <em>E. cloacae</em></td>
</tr>
<tr>
<td>Escherichia coli*</td>
</tr>
<tr>
<td>Klebsiella spp. including <em>Klebsiella pneumoniae</em>*</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
</tr>
<tr>
<td>Proteus spp. not including <em>P. penneri</em> and <em>P. vulgaris</em></td>
</tr>
<tr>
<td>Providencia spp.</td>
</tr>
<tr>
<td><strong>Gram-Positive Anaerobes:</strong></td>
</tr>
<tr>
<td>Clostridium spp. not including <em>C. difficile</em></td>
</tr>
<tr>
<td><strong>Gram-Negative Anaerobes:</strong></td>
</tr>
<tr>
<td>Bacteroides spp. not including <em>B. fragilis</em></td>
</tr>
<tr>
<td>Fusobacterium spp.</td>
</tr>
<tr>
<td><strong>Inherently resistant organisms</strong></td>
</tr>
<tr>
<td><strong>Gram-Positive Aerobes:</strong></td>
</tr>
<tr>
<td>Enterococcus spp. including <em>E. faecalis</em> and <em>E. faecium</em></td>
</tr>
<tr>
<td>Listeria monocytogenes</td>
</tr>
<tr>
<td><strong>Gram-Negative Aerobes:</strong></td>
</tr>
<tr>
<td>Acinetobacter spp.</td>
</tr>
<tr>
<td>Burkholderia cepacia</td>
</tr>
<tr>
<td>Campylobacter spp.</td>
</tr>
<tr>
<td>Citrobacter freundii</td>
</tr>
<tr>
<td>Enterobacter aerogenes</td>
</tr>
<tr>
<td>Enterobacter cloacae</td>
</tr>
</tbody>
</table>
Morganella morganii
Proteus penneri
Proteus vulgaris
Pseudomonas spp. including Pseudomonas aeruginosa
Serratia spp.
Stenotrophomonas maltophilia

Gram-Positive Anaerobes:
Clostridium difficile

Gram-Negative Anaerobes:
Bacteroides fragilis

Others:
Chlamydia species
Mycoplasma species
Legionella species

**Pharmacokinetic Properties**

**Absorption**

After oral administration Cefuroxime axetil is slowly absorbed from the gastrointestinal tract and rapidly hydrolysed in the intestinal mucosa and blood to release cefuroxime into the circulation.

Optimum absorption occurs when it is administered shortly after a meal. Following administration of Cefuroxime axetil tablets peak serum levels (2.1 mg/l for a 125 mg dose, 4.1 mg/l for a 250 mg dose, 7.0 mg/l for a 500 mg dose and 13.6 mg/l for a 1 g dose) occur approximately 2 to 3 hours after dosing when taken with food.

**Distribution**

Protein binding has been variously stated as 33 to 50% depending on the methodology used.

**Metabolism**

Cefuroxime is not metabolised.

**Elimination**

The serum half life is between 1 and 1.5 hours.
Cefuroxime is excreted by glomerular filtration and tubular secretion. Concurrent administration of probenecid increases the area under the mean serum concentrations time curve by 50%.

**Renal impairment:**

Cefuroxime pharmacokinetics have been investigated in patients with various degrees of renal impairment. Cefuroxime elimination half-life increases with decrease in renal function which serves as the basis for dosage adjustment recommendations in this group of patients (See Posology and Method of Administration). In patients undergoing haemodialysis, at least 60% of the total amount of cefuroxime present in the body at the start of dialysis will be removed during a 4-hour dialysis period. Therefore, an additional single dose of cefuroxime should be administered following the completion of haemodialysis.

**Preclinical Safety Data**

Animal toxicity studies indicated that cefuroxime axetil is of low toxicity with no significant findings.

**PHARMACEUTICAL PARTICULARS**

**List of Excipients**

Hydroxy Propyl Methyl Cellulose, Propylene Glycol, Methylparaben, Propylparaben, Opaspray White M-1-7120 J, Titanium Dioxide, Purified water.

**Incompatibilities**

No data available.

**Shelf Life**

The expiry date is indicated on the label and packaging.

**Special Precautions for Storage**

Store in a dry place at temperature not exceeding 30°C. Protect from light

Keep out of reach of children.

**Nature and Specification of Container**

Blister strips in a carton.

All presentations may not be marketed in the Country.

**Instructions for Use / Handling**

No relevant information.
For further information please contact:
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Mumbai 400 030, India.

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