For the use only of Registered Medical Practitioners or a Hospital or a Laboratory

CEFTUM TABLETS

1. GENERIC NAME

Cefuroxime Axetil Tablets IP 125/250/500 mg

2. 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

3. DOSAGE FORM AND STRENGTH

Film-coated tablets

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

4. CLINICAL PARTICULARS

4.1 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 it should be used in accordance with local official antibiotic prescribing guidelines and local susceptibility data (See *5.2 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 exacerbations of chronic obstructive pulmonary disease)

- 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 obstructive pulmonary disease.

4.2 Posology and Method of Administration

The usual course of therapy is seven days (range five to ten days). The dose of Cefuroxime that is selected to treat an individual infection should take into account:
• The expected pathogens and their likely susceptibility to Cefuroxime Axetil
• The severity and the site of the infection
• The age, weight and renal function of the patient; as shown below.
The duration of therapy should be determined by the type of infection and the response of the patient, and should generally not be longer than recommended.

CEFTUM tablets should be taken after food for optimum absorption.

Adults and Children weighing more than 40 kg:

Indication	**Dosage**
Acute tonsillitis and pharyngitis	250 mg twice daily
Acute otitis media	500 mg twice daily
Acute bacterial sinusitis	500 mg twice daily
Community acquired pneumonia	

Acute exacerbations of chronic obstructive pulmonary disease	
Urinary tract infections	250 mg – 500 mg twice daily
Uncomplicated gonorrhoea	single dose of 1 g
Skin and soft tissue infections	250 mg – 500 mg twice daily

Sequential therapy

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

Pneumonia
1.5 g *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 *CEFTUM* (Cefuroxime Axetil) 500 mg twice a day oral therapy for 7 to 10 days.

Acute exacerbations of chronic obstructive pulmonary disease
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 *CEFTUM* (Cefuroxime Axetil) 500 mg twice a day oral therapy for 5 to 10 days.

Children weighing between 20-40 kg:

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.

Indication	**Dosage**
Acute tonsillitis and pharyngitis	250 mg twice daily
Acute otitis media	250 mg twice daily to 500 mg twice daily
Acute bacterial sinusitis	
Community acquired pneumonia	
Urinary tract infections	
Skin and soft tissue infections	

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).

Creatinine Clearance	***$T_{1/2}$ (hours)***	***Recommended Dosage***
≥30 ml/min	1.4 - 2.4	No dose adjustment necessary standard dose of 125 mg to 500 mg given twice daily
10-29 ml/min	4.6	Standard individual dose given every 24 hours
<10 ml/min	16.8	Standard individual dose given every 48 hours
During haemodialysis	2 – 4	A single additional standard individual dose should be given at the end of each dialysis

4.3 Contraindications

Patients with known hypersensitivity to cephalosporin antibiotics.

4.4. Special Warnings and 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.

4.5 Drug Interactions

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.

4.6 Use in Special Populations (such as pregnant women, lactating women, pediatric patients, geriatric patients, etc.)

Children weighing more than 40 kg:

Indication	**Dosage**
Acute tonsillitis and pharyngitis	250 mg twice daily
Acute otitis media	500 mg twice daily
Acute bacterial sinusitis	500 mg twice daily
Community acquired pneumonia	
Acute exacerbations of chronic obstructive pulmonary disease	
Urinary tract infections	250 mg – 500 mg twice daily
Uncomplicated gonorrhoea	single dose of 1 g
Skin and soft tissue infections	250 mg – 500 mg twice daily

Children weighing between 20-40 kg:

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.

Indication	Dosage
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Acute otitis media	250 mg twice daily to 500 mg twice daily
Acute bacterial sinusitis	
Community acquired pneumonia	
Urinary tract infections	
Skin and soft tissue infections	

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).

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Pregnancy and Lactation

Pregnancy

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.

Lactation

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

4.7 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.

4.8 Undesirable Effects

Adverse drug reactions to *CEFTUM* 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 *CEFTUM* 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.

B*lood 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 *4.4 Special Warnings and 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.

4.9 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of Action

Cefuroxime axetil owes its *in vivo* bactericidal activity to the parent compound cefuroxime.

Cefuroxime is a well characterised and effective antibacterial agent which has bactericidal activity against a wide range of common pathogens, including beta-lactamase producing strains.

Cefuroxime has good stability to bacterial beta-lactamase, and consequently is active against many ampicillin-resistant or amoxycillin-resistant strains. The bactericidal action of cefuroxime results from inhibition of cell wall synthesis by binding to essential target proteins.

5.2 Pharmacodynamic Properties

Pharmacotherapeutic Group - Antiinfectives for Systemic Use
ATC code - J01DC02

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.

In vitro **susceptibility of micro-organisms to Cefuroxime** Where clinical efficacy of Cefuroxime Axetil has been demonstrated in clinical trials this is indicated with an asterisk (*).
Commonly Susceptible Species
Gram-Positive Aerobes: *Staphylococcus aureus (methicillin susceptible)** *Coagulase negative staphylococcus (methicillin susceptible)* *Streptococcus pyogenes** Beta-hemolytic streptococci
Gram-Negative Aerobes: *Haemophilus influenzae** including ampicillin resistant strains *Haemophilus parainfluenzae** *Moraxella catarrhalis** *Neisseria gonorrhoea** including penicillinase and non-penicillinase producing strains

Gram-Positive Anaerobes: *Peptostreptococcus* spp. *Propionibacterium* spp.
Spirochetes: *Borrelia burgdorferi**
Organisms for which acquired resistance may be a problem
Gram-Positive Aerobes: *Streptococcus pneumoniae**
Gram-Negative Aerobes: *Citrobacter* spp. not including *C. freundii* *Enterobacter* spp. not including *E. aerogenes* and *E. cloacae* *Escherichia coli** *Klebsiella* spp. including *Klebsiella pneumoniae** *Proteus mirabilis* *Proteus* spp. not including *P. penneri* and *P. vul*garis *Providencia* spp.
Gram-Positive Anaerobes: *Clostridium* spp.
Gram-Negative Anaerobes: *Bacteroides* spp. not including *B. fragilis* *Fusobacterium* spp.
Inherently resistant organisms
Gram-Positive Aerobes: E*nterococcus* spp. including *E. faecalis* and *E. faecium* *Listeria* monocytogenes
Gram-Negative Aerobes: *Acinetobacter* spp. *Burkholderia cepacia* *Campylobacter* spp. *Citrobacter freundii* *Enterobacter aerogenes* *Enterobacter cloacae* *Morganella morganii* *Proteus penneri* *Proteus vulgaris* *Pseudomonas* spp. including *Pseudomonas aeruginosa* *Serratia* spp. *Stenotrophomonas maltophilia*
Gram-Positive Anaerobes: *Clostridioides difficile*
Gram-Negative Anaerobes: *Bacteroides fragilis*
Others: *Chlamydia* species *Mycoplasma* species *Legionella* species

5.3 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 *4.2 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.

6. NONCLINICAL PROPERTIES

6.1 Animal Toxicology and Pharmacology

Animal toxicity studies indicated that Cefuroxime Axetil is of low toxicity with no significant findings.

7. DESCRIPTION

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

Film-coated tablets

List of Excipients

Citric Acid Anhydrous, Sodium Hydrogen Carbonate, Crospovidone, Croscarmellose Sodium, Sodium Lauryl Sulfate, silica colloidal anhydrous, Cellulose Microcristilline, Talc, Opadry, Purified Water.

8. PHARMACEUTICAL PARTICULARS

8.1 Incompatibilities

In the absence of compatibility studies Cefuroxime Axetil must not be mixed with other medicinal products.

8.2 Shelf Life

The expiry date is indicated on the label and packaging.

8.3 Packaging Information

Blister strips in a carton.

All presentations may not be marketed in India.

8.4 Storage and Handling Information

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

Keep out of reach of children.

9. PATIENT COUNSELLING INFORMATION

Registered Medical Practitioners may counsel their patients (and/or patient's caregiver as applicable) about the special warnings and precautions for use, drug interactions, undesirable effects, and any relevant contra-indications of *CEFTUM*. Patients (and/or patient's caregiver) may also be informed about posology, method of administration and storage/handling information as applicable.

10. DETAILS OF MANUFACTURER

The Manufacturing Site details are mentioned on the label and packaging.

For further information please contact:

GlaxoSmithKline Pharmaceuticals Limited.
Registered Office:
Dr. Annie Besant Road, Worli
Mumbai 400 030, India.

11. DETAILS OF PERMISSION OR LICENCE NUMBER WITH DATE

Manufacturing License number is indicated on the label and packaging.

12. DATE OF REVISION

03-JAN-2022

Trade marks are owned by or licensed to the GSK group of companies.

Version: CEF/PI/IN/2022/01

Adapted from Cefuroxime Axetil VGDS 30/IPI 10 dated 09 October 2020.