SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Cefuroxime Axetil Tablets USP 250 mg & 500 mg

2. QUALITATIVE AND QUANTITAVE COMPOSITION

Cefuroxime Axetil Tablets USP 250 mg:

Each film coated tablet contains: Cefuroxime Axetil USP equivalent to Cefuroxime 250 mg

Cefuroxime Axetil Tablets USP 500 mg:

Each film coated tablet contains: Cefuroxime Axetil USP equivalent to Cefuroxime 500 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film- Coated Tablets

Cefuroxime Axetil Tablets USP 250 mg:

White to off-white coloured, oval shaped film coated tablets, engraved with "250" on one side and plain on other side.

Cefuroxime Axetil Tablets USP 500 mg:

White to off -white coloured, oval shaped, biconvex, film coated tablets with "500" engraved on one side and plain on other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Cefuroxime Axetil Tablets 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 Cefuroxime Axetil Tablets will vary with geography and time and it should be used in

accordance with local official antibiotic prescribing guidelines and local susceptibility data (*See Pharmacological properties, Pharmacodynamics*).

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
- treatment of early Lyme disease and subsequent prevention of late Lyme disease.

Cefuroxime is also available as the sodium salt 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 Cefuroxime Axetil Tablets is effective when used following initial parenteral cefuroxime sodium in the treatment of pneumonia and acute exacerbations of chronic obstructive pulmonary disease.

4.2 Posology and method of administration

Pharmaceutical Form: Coated tablet.

The usual course of therapy is seven days (range 5 to 10 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.

Cefuroxime Axetil 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
Lyme disease in adults and children over the age of 12 years	500 mg twice daily for 14 days (range of 10-21 days)

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 sodium salt three times a day or twice a day (intravenous (i.v.) or intramuscular (i.m)) for 48 to 72 hours, followed by Cefuroxime Axetil Tablets (cefuroxime axetil) oral therapy 500 mg twice a day for 7 to10 days.

Acute exacerbations of chronic obstructive pulmonary disease

750 mg sodium salt three times a day or twice a day (i.v. or i.m.) for 48 to 72 hours, followed by Cefuroxime Axetil Tablets (cefuroxime axetil) oral therapy 500 mg twice a day for 5 to 10 days.

- Children weighing between 20-40 kg

Cefuroxime Axetil Tablets should not be crushed or split and are therefore unsuitable for treatment of patients, such as younger children, who cannot swallow whole tablets. Therefore, cefuroxime axetil suspension is recommended for patients 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	
Lyme Disease in children under the age of 12 years	250 mg twice daily to 500 mg twice daily for 14 days (range of 10 to 21 days)

- **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 Cefuroxime Axetil Tablets 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.

The Jarisch-Herxheimer reaction has been seen following Cefuroxime Axetil Tablets treatment of Lyme disease. It results directly from the bactericidal activity of Cefuroxime Axetil Tablets on the causative organism of Lyme disease, the spirochaete Borrelia burgdorferi. Patients should be reassured that this is a common and usually self-limiting consequence of antibiotic treatment of Lyme disease.

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 Interaction with other medicinal products and other forms of interaction.

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

In common with other antibiotics, Cefuroxime Axetil Tablets 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 Cefuroxime Axetil Tablets. This antibiotic does not interfere in the alkaline picrate assay for creatinine.

4.6 Pregnancy and lactation

Pregnancy

There is no experimental evidence of embryopathic or teratogenic effects attributable to Cefuroxime Axetil Tablets 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 Cefuroxime Axetil Tablets 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 Cefuroxime Axetil Tablets 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 Tablets 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 <1/1000) 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 Warnings and Precautions*)

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 Pharmacodynamic properties

Pharmacodynamics

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. vulgaris*

Providencia spp.
Gram-Positive Anaerobes*:* *Clostridium spp.*
Gram-Negative Anaerobes*:* *Bacteroides spp.* not including *B. fragilis* *Fusobacterium spp.*
Inherently resistant organisms
Gram-Positive Aerobes: *Enterococcus 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

5.2 Pharmacokinetic properties

Absorption

After oral administration Cefuroxime Axetil Tablets 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 after 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%.

<u>Renal impairment:</u>

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 Dosage and 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.

5.3 Preclinical safety data

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Lauryl Sulphate
Croscarmellose Sodium (Primellose)
Hydrogenated Castor Oil (Boricin Pharma)
Microcrystalline Cellulose (Avicel PH102)
Colloidal Silicon Dioxide (Aerosil 200)
Methylene Chloride
Isopropyl Alcohol
Tab Coat TC - 1004 / 3100 White

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store below 30°C Keep out from the reach of children.

6.5 Nature and contents of container

Alu-Alu Strip pack of 10 tablets

6.6 Special precautions for disposal and other handling

There is no special requirement for disposal.

6.7 Inclusion in the list of poisonous substances

List I

7. **APPLICANT**

Geneith Pharmaceuticals Limited
12, Adewale Crescent, Off Ewenla
Street, Off Oshodi-Apapa
Expressway, Oshodi, Lagos.

8. MANUFACTURER

MICRO LABS LIMITED
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Bommasandra Industrial Area,
4th Phase, Anekal Taluk,
Bengaluru - 560 099