SUMMARY PRODUCT CHARACTERISTICS (SPC)

1.1 Name of medicinal product

Cefuroxime with Potassium Clavulanate for Oral Suspension

1.2 Strength

Cefuroxime Axetil BP Eq. to Cefuroxime……125 mg

Diluted Potassium Clavulanate BP Eq. to Clavulanic acid … 31.25 mg

1.3 Pharmaceutical Dosage form

Powder for Oral (For oral administration)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml reconstituted suspension contains:

Cefuroxime Axetil BP eq. to Cefuroxime…….. 125 mg

Clavulanate Potassium Diluted BP eq. to Clavulanic Acid…….31.25 mg

Excipients…… Q.S.

Colour: Tartrazine

3. PHARMACEUTICAL FORM

Powder for Oral Suspension

Light orange coloured granular powder which becomes yellow coloured suspension on addition of water.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

It is indicated for the treatment of pediatric patients 3 months to 12 years of age with mild to moderate infections caused by susceptible strains of the designated microorganisms in the conditions listed below.

- **Pharyngitis/Tonsillitis** caused by Streptococcus pyogenes.

• **Acute Bacterial Otitis Media** caused by Streptococcus pneumoniae, Haemophilus influenzae (including beta-lactamase–producing strains), Moraxella catarrhalis (including beta-lactamase–producing strains), or Streptococcus pyogenes.

Impetigo caused by Staphylococcus aureus (including beta-lactamase–producing strains) or Streptococcus pyogenes.

4.2 Posology and method of administration

Cefuroxime with Potassium Clavulanate for Oral Suspension may be administered to pediatric patients ranging in age from 3 months to 12 years, according to dosages in Table 2.

TABLE 2: Indications & dosage for CEFUROXIME-CLAV Oral Suspension (Must be administered with food. Shake well each time before using.)

Population/Infection	Dosage	Daily Maximum Dose	Duration (days)
Pediatric Patients (3 months to 12 years)			
Pharyngitis/tonsillitis	20 mg/kg/day divided b.i.d.	500 mg	10
Acute otitis media	30 mg/kg/day divided b.i.d.	1,000 mg	10
Acute bacterial maxillary sinusitis	30 mg/kg/day divided b.i.d.	1,000 mg	10
Impetigo	30 mg/kg/day divided b.i.d.	1,000 mg	10

4.3 Contraindications

Hypersensitivity to cephalosporin antibiotics.

4.4 Special warnings and special precautions for use

- Before therapy with Cefuroxime Axetil & Potassium Clavulanate is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cephalosporins, penicillins or other drugs.
- Because cefuroxime is excreted in human milk, consideration should be given to discontinuing nursing temporarily during treatment with cefuroxime.
- Prescribing Cefuroxime Axetil & Potassium Clavulanate in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.
- Cephalosporins, including cefuroxime, should be given with caution to patients receiving concurrent treatment with potent diuretics because these diuretics are suspected of adversely affecting renal function.

Cefuroxime, as with other broad-spectrum antibiotics, should be prescribed with caution in individuals with a history of colitis.

4.5 Interaction with other medicinal products and other forms of Interaction

Probenecid: Concomitant administration of probenecid with cefuroxime axetil tablets increases the area under the serum concentration versus time curve by 50%. The peak serum cefuroxime concentration after a 1.5-g single dose is greater when taken with 1 g of probenecid (mean = 14.8 mcg/mL) than without probenecid (mean = 12.2 mcg/mL).

Antacids: Drugs that reduce gastric acidity may result in a lower bioavailability of Cefuroxime Axetil & Potassium Clavulanate compared with that of fasting state and tend to cancel the effect of postprandial absorption.

Oral contraceptives: In common with other antibiotics, cefuroxime axetil may affect the gut flora, leading to lower estrogen reabsorption and reduced efficacy of combined oral estrogen/progesterone.

4.6 Pregnancy and lactation

Pregnancy Category B:

Reproduction studies have been performed in rats and mice at doses up to 3,200 mg/kg per day (23 times the recommended maximum human dose based on mg/m^2) and have revealed no evidence of harm to the fetus due to cefuroxime axetil. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Labor and Delivery: Cefuroxime axetil has not been studies for use during labor and delivery.

Nursing Mothers: Because cefuroxime is excreted in human milk, consideration should be given to discontinuing nursing temporarily during treatment with cefuroxime axetil.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects

Undesirable effects to cefuroxime axetil have been generally mild and transient in nature. The following undesirable effects to cefuroxime axetil have been reported. However, the possibility of the occurrence of other adverse reactions, seen with the cephalosporin class of antibiotics, should be borne in mind.

- Major undesirable effects which may occur are diarrhea/loose motions, Nausea/vomiting, transient elevation in AST, ALT, LDH, Eosinophilia.
- Other undesirable effects that may occur are abdominal pain, abdominal cramps, flatulence, indigestion, headache, vaginitis, vulvar itch, rash, hives, itch, dysuria, chills, chest pain, shortness of breath, mouth ulcers, swollen tongue, sleepiness, thirst, anorexia.

4.9 Overdose

Overdosage of cephalosporins can cause cerebral irritancy leading to convulsions.

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

The in vivo bactericidal activity of cefuroxime axetil is due to cefuroxime's binding to essential target proteins and the resultant inhibition of cell-wall synthesis.

Cefuroxime has bactericidal activity against a wide range of common pathogens, including many beta-lactamase–producing strains. Cefuroxime is stable to many bacterial beta-lactamases, especially plasmid-mediated enzymes that are commonly found in enterobacteriaceae.

Cefuroxime has been demonstrated to be active against most strains of the following microorganisms:

Aerobic Gram-Positive Microorganisms:
Staphylococcus aureus (including beta-lactamase–producing strains)
Streptococcus pneumoniae
Streptococcus pyogenes

Aerobic Gram-negative Microorganisms:
Escherichia coli
Haemophilus influenzae (including beta-lactamase–producing strains
Haemophilus parainfluenzae
Klebsiella pneumoniae
Moraxella catarrhalis (including beta-lactamase–producing strains)
Neisseria gonorrhoeae (including beta-lactamase–producing strains)

Spirochetes:
Borrelia burgdorferi

Cefuroxime has been shown to be active in vitro against most strains of the

following microorganisms; however, the clinical significance of these findings is unknown.

Cefuroxime exhibits in vitro minimum inhibitory concentrations (MICs) of 4.0 mcg/mL or less (systemic susceptible breakpoint) against most (≥90%) strains of the following microorganisms; however, the safety and effectiveness of cefuroxime in treating clinical infections due to these microorganisms have not been established in adequate and well-controlled trials.

Aerobic Gram-negative Microorganisms:
Aerobic Gram-Positive Microorganisms:
Staphylococcus epidermidis
Staphylococcus saprophyticus
Streptococcus agalactiae

Anaerobic Gram-positive Microorganisms:
Morganella morganii
Proteus inconstans
Proteus mirabilis
Providencia rettgeri

Anaerobic Microorganisms:
Peptococcus niger

5.2 Pharmacokinetic properties

After oral administration cefuroxime axetil is absorbed from the gastrointestinal tract and rapidly hydrolysed in the body to release cefuroxime into the circulation. Approximately 60% of an administered dose is absorbed. Optimum absorption occurs when it is administered after a light meal. Absorption is not decreased by drugs which affect gastrointestinal motility e.g. loperamide, diphenoxylate or castor oil. However, absorption is decreased by concurrent administration of drugs such as ranitidine.

The mean peak serum level of cefuroxime following a 250 mg dose in normal healthy adults, after food, was 4.1 mg/L and occurred two to three hours after dosing. Serum levels were significantly higher in the elderly, apparently due to slower excretion. Unhydrolysed drug was not detected in the serum but 1-2% of the administered dose is excreted in the urine in a form which indicates that small amounts of the intact ester are absorbed into circulation. The mean serum half-life of cefuroxime is approximately 1.2 hours. Protein binding has been variously stated as 33-50% depending on the methodology used. Cefuroxime is not metabolized to any significant extent.

Excretion occurs mainly through the kidney both by glomerular filtration and tubular secretion. Approximately 49% of an administered dose, after food, is recovered in the urine in 24 hours; urinary recovery is significantly reduced if the drug is taken on an empty stomach.

After 250 mg dose urinary concentrations at 0-6 and 6-12 hours were 227 mcg/mL (range 92-515) and 35.3 mcg/mL (range 7.6-102) respectively.

Concurrent administration of probenecid prolongs the terminal half-life of cefuroxime. Serum levels of cefuroxime are reduced by haemodialysis.

5.3 Preclinical safety data

Preclinical effects were observed in dosages far above the maximal human dosage which are therefore hardly relevant for the clinical use of Cefuroxime Axetil.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Each 5 ml reconstituted suspension contains: Cefuroxime Axetil BP, Potassium Clavulanate BP. Inactive Ingredients**:** Mannitol BP, , Colloidal Silicon Dioxide BP, Aspartame BP, Essence Dry Pippermint, Citric Acid Anhydrous BP, Xanthan Gum BP, Tartrazine IH.

6.2 Incompatibilities

Not Applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Powder for Oral Suspension: Store below 25°C, Protected from light & moisture.

Oral Suspension: After reconstitution, keep the suspension in the refrigerator when not in use.

6.5 Nature and contents of container

100 ml ring white HDPE bottle with 25 mm white cap with induction seal and measuring cup in a carton along with pack insert.

6.6 Special precautions for disposal

No special requirements. Any unused product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorization Holder

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9. Date of revision of the text

Not Applicable