1. Name of the medicinal product

CEFUROXIME AXETIL TABLETS USP 500 MG

2. Qualitative and quantitative composition

SR. NO.	NAME OF THE INGREDIENTS	PHARMACOPEIAL SPECIFICATION	LABEL CLAIM	OVERAGES %	QTY. / TABLET	PURPOSE
ACTIVE INGREDIENTS						
1.	Cefuroxime (As Cefuroxime Axetil)*	USP	500 mg (601.419 mg)	1.50 %	610.440 mg	API
INACTIVE INGREDIENTS						
2.	Colloidal Silicon Dioxide	USP	-	0.00 %	12.000 mg	Glidant
3.	Micro Crystalline Cellulose	BP	-	0.00 %	195.560 mg	Diluent
4.	Sodium Lauryl Sulphate	BP	-	0.00 %	6.000 mg	Surfactant
5.	Croscarmellose Sodium	BP	-	0.00 %	60.000 mg	Disintegrant
6.	Hydroxy Propyl Methyl Cellulose (E-15)	BP	-	0.00 %	2.000 mg	Polymer
7.	Colloidal Silicon Dioxide	USP	-	0.00 %	7.000 mg	Glidant
8.	Sodium Lauryl Sulphate	BP	-	0.00 %	9.000 mg	Surfactant
9.	Croscarmellose Sodium	BP	-	0.00 %	38.000 mg	Disintegrant
10.	Titanium Dioxide	BP	-	0.00 %	1.450 mg	Colour
11.	Hydroxy Propyl Methyl Cellulose (E-15)	BP	-	0.00 %	6.300 mg	Polymer
12.	Purified Talc	BP	-	0.00 %	0.450 mg	Polisher
13.	Polyethylene Glycol (Macrogol) 6000	BP	-	0.00 %	1.800 mg	Plasticizer
14.	Isopropyl Alcohol**	BP	-	0.00 %	0.100 ml	Solvent
15.	Dichloromethane**	BP	-	0.00 %	0.160 ml	Solvent

*1.50 % Overages are added on label claim due to water content present in API

*Evaporates during manufacturing and does not remain in final product

3. Pharmaceutical form

Tablet

4. Clinical particulars

4.1 Therapeutic indications

- Cefuroxime is indicated for the treatment of the infections listed below in adults and children from the age of 3 months.
- Acute streptococcal tonsillitis and pharyngitis.
- Acute bacterial sinusitis.
- Acute otitis media.
- Acute exacerbations of chronic bronchitis.
- Cystitis
- Pyelonephritis.
- Uncomplicated skin and soft tissue infections.
- Treatment of early Lyme disease

4.2 Posology and method of administration

Adults:
Tablet: Most infections: 250 mg twice daily.
Urinary tract infections: 250 mg twice daily
Mild to moderate lower respiratory tract infections e.g. bronchitis: 250 mg twice daily.
More severe lower respiratory tract infections, or if pneumonia is suspected: 500 mg twice daily.
Pyelonephritis: 250 mg twice daily.
Children:
Children with otitis media or, appropriate, with more severe infections: 250 mg twice daily.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed.
- Patients with known hypersensitivity to cephalosporin antibiotics.
- History of severe hypersensitivity (e.g. anaphylactic reaction) to any other type of betalactam antibacterial agent (penicillins, monobactams and carbapenems).

4.4 Special warnings and precautions for use

Hypersensitivity reactions: Special care is indicated in patients who have experienced an allergic reaction to penicillins or other beta-lactam antibiotics because there is a risk of cross-sensitivity. As with all beta-lactam antibacterial agents, serious and occasionally fatal hypersensitivity reactions have been reported. In case of severe hypersensitivity reactions, treatment with cefuroxime must be discontinued immediately and adequate emergency measures must be initiated. Before beginning treatment, it should be established whether the patient has a history of severe hypersensitivity reactions to cefuroxime, to other cephalosporins or to any other type of beta-lactam agent. Caution should be used if cefuroxime is given to patients with a history of non-severe hypersensitivity to other beta-lactam agents.
Jarisch-Herxheimer reaction: The Jarisch-Herxheimer reaction has been seen following cefuroxime axetil treatment of Lyme disease. It results directly from the bactericidal activity of cefuroxime axetil on the causative bacteria 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.

Overgrowth of non-susceptible microorganisms: As with other antibiotics, use of cefuroxime axetil may result in the overgrowth of Candida. Prolonged use may also result in the overgrowth of other non-susceptible microorganisms (e.g. enterococci and Clostridium difficile), which may require interruption of treatment. Antibacterial agent–associated pseudomembranous colitis have been reported with nearly all antibacterial agents, including cefuroxime and may range in severity from mild to life threatening. This diagnosis should be considered in patients with diarrhoea during or subsequent to the administration of cefuroxime. Discontinuation of therapy with cefuroxime and the administration of specific treatment for Clostridium difficile should be considered.

Interference with diagnostic tests: The development of a positive Coombs' Test associated with the use of cefuroxime may interfere with cross matching of blood. 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.

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 compared with that of the fasting state and tend to cancel the effect of enhanced absorption after food. Cefuroxime is excreted by glomerular filtration and tubular secretion. Concomitant use of probenecid is not recommended. Concurrent administration of probenecid significantly increases the peak concentration, area under the serum concentration time curve and elimination half-life of cefuroxime. Concomitant use with oral anticoagulants may give rise to increased INR.

4.6 Fertility, pregnancy and lactation

Pregnancy: There are limited data from the use of cefuroxime in pregnant women. Studies in animals have shown no harmful effects on pregnancy, embryonal or foetal development, parturition or postnatal development. Cefuroxime axetil should be prescribed to pregnant women only if the benefit outweighs the risk.

Lactation: Cefuroxime is excreted in human milk in small quantities. Adverse effects at therapeutic doses are not expected, although a risk of diarrhoea and fungus infection of the mucous membranes cannot be excluded. Breastfeeding might have to be discontinued due to these effects. The possibility of sensitisation should be taken into account. Cefuroxime should only be used during breastfeeding after benefit/risk assessment by the physician in charge.

Fertility: There are no data on the effects of cefuroxime axetil on fertility in humans. Reproductive studies in animals have shown no effects on fertility.

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

4.8 Undesirable effects

Blood and lymphatic system disorders: Common: eosinophilia **Uncommon:** positive Coombs' test, thrombocytopenia, leukopenia **Not known:** haemolytic anaemia.

Immune system disorders: Not known: drug fever, serum sickness, anaphylaxis, Jarisch-Herxheimer reaction.
Nervous system disorders: Common: headache, dizziness.
Gastrointestinal disorders: Common: diarrhoea, nausea, abdominal pain **Uncommon:** vomiting **Not known:** pseudomembranous colitis.
Hepatobiliary disorders: Common: transient increases of hepatic enzyme levels, **Not known:** jaundice (predominantly cholestatic), hepatitis.
Skin and subcutaneous tissue disorders: Uncommon: skin rashes **Not known:** urticaria, pruritus, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (exanthematic necrolysis), angioneurotic oedema.

4.9 Overdose

- Overdose can lead to neurological sequelae including encephalopathy, convulsions and coma. Symptoms of overdose can occur if the dose is not reduced appropriately in patients with renal impairment.
- Serum levels of cefuroxime can be reduced by haemodialysis and peritoneal dialysis.

5. Pharmacological properties

5.1 Pharmacodynamics properties

Pharmacotherapeutic group: antibacterials for systemic use, second-generation cephalosporins.
ATC-Code: J01DC02
Mechanism of action: Cefuroxime axetil undergoes hydrolysis by esterase enzymes to the active antibiotic, cefuroxime. Cefuroxime inhibits bacterial cell wall synthesis following attachment to penicillin binding proteins (PBPs). This results in the interruption of cell wall (peptidoglycan) biosynthesis, which leads to bacterial cell lysis and death.

5.2 Pharmacokinetic properties

Absorption: After oral administration cefuroxime axetil is 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 (2.9 µg/mL for a 125 mg dose, 4.4 µg/mL for a 250 mg dose, 7.7 µg/mL for a 500 mg dose and 13.6 µg/mL for a 1000 mg dose) occur approximately 2.4 hours after dosing when taken with food. The pharmacokinetics of cefuroxime is linear over the oral dosage range of 125 to 1000 mg. No accumulation of cefuroxime occurred following repeat oral doses of 250 to 500 mg.
Distribution: Protein binding has been stated as 33 to 50% depending on the methodology used. Following a single dose of cefuroxime axetil 500 mg tablet to 12 healthy volunteers, the apparent volume of distribution was 50 L (CV%=28%). Concentrations of cefuroxime in excess of the minimum inhibitory levels for common pathogens can be achieved in the tonsilla, sinus tissues, bronchial mucosa, bone, pleural fluid, joint fluid, synovial fluid, interstitial fluid, bile, sputum and aqueous humor. Cefuroxime passes the blood-brain barrier when the meninges are inflamed.
Metabolisam: 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. The renal clearance is in the region of 125 to 148 mL/min/1.73 m^2.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on studies of safety pharmacology, repeated dose toxicity, genotoxicity and toxicity to reproduction and development. No carcinogenicity studies have been performed; however, there is no evidence to suggest carcinogenic potential. Gamma glutamyl transpeptidase activity in rat urine is inhibited by various cephalosporins, however the level of inhibition is less with cefuroxime. This may have significance in the interference in clinical laboratory tests in humans.

6. Pharmaceutical particulars

6.1 List of excipients

- Colloidal Silicon Dioxide
- Micro Crystalline Cellulose
- Sodium Lauryl Sulphate
- Croscarmellose Sodium
- Hydroxy Propyl Methyl Cellulose (E-15)
- Titanium Dioxide
- Purified Talc
- Polyethylene Glycol (Macrogol) 6000
- Isopropyl Alcohol
- Dichloromethane

6.2 Incompatibilities

None

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store in a dry place at a temperature below 30°C.

6.5 Nature and contents of container

10 x 1 x 10 Tablets Alu-Alu Pack, packed in printed and laminated carton.

6.6 Special precautions for disposal and other handling

Not Applicable

7. Marketing authorization holder

West Coast Pharmaceutical Works LTD, Ahmedabad

8. Marketing authorization number(s)

Not Applicable

9. Date of first authorization/renewal of the authorization

Not Applicable

10. Date of revision of the text

August, 2019