1.3.1 Summary of Product Characteristics (SmPC)

1. Name of Medicinal Product

CEFUROXIME AXETIL TABLETS USP 500 MG

2. Qualitative and Quantitative Composition

2.1. Qualitative declaration:

Composition of the Drug product:

Each Film coated tablet contains:

Cefuroxime Axetil USP

Eq. to Cefuroxime 500 mg

Excipients Q.S.

Colour: Titanium Dioxide BP

Qualitative & Quantitative Composition Formula:

Batch size: 1,00,000 Tablets

Sr. No	Name of Raw Material	Spec	Label claim / tab	Qty per tablet	% Overage	Qty per tablet with Overages	Std. Qty for 1.0 Lac
GRANULATION-1							
1.	Cefuroxime Axetil eq to Cefuroxime	USP	500.00	500.00 MG		620.00	62.00
2.	Cross Carmosine Sodium	BP		32.00	2 %	32.00	3.20
3.	MCCP	BP		158.00		158.00	15.80
4.	Sodium Benzoate	BP		1.00		1.00	0.100
5.	Indion – 234	BP		50.00		50.00	5.00
6.	Cross Carmosine Sodium	BP		24.00		24.00	2.40
7.	Magnesium Stearate	BP		5.00		5.00	0.500
8.	Talcum	BP		10.00		10.00	1.00
9.	Aerosil	BP		30.00		30.00	3.00

	FINAL TOTAL			930.00		930.00	93.00
Coating							
10.	Iso propyl alcohol	BP		0.189		0.189	18.90
11.	MDC	BP		0.284		0.284	28.40
12.	Pure coat WT 1001 White	BP		27.9		27.9	2.790
	Avg. wt of tablet		**Total**	958.00		958.00	143.09

Calculation of Active material =

$$\frac{\text{Label Claim}}{\text{Assay}} \times \frac{100}{100} \times \frac{100}{(100-\text{Water})} \times \frac{\text{Batch size}}{(1000 \times 1000)} \times \frac{(100+\%\text{O.A})}{100}$$

3. Pharmaceutical form

Tablets

White coloured, oblong shaped, biconvex bisected on one side film coated 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

Posology

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

For Adults and children (≥40 kg)

- Acute tonsillitis and pharyngitis, acute bacterial sinusitis- 250 mg twice daily.
- Acute otitis media- 500 mg twice daily.
- Acute exacerbations of chronic bronchitis- 500 mg twice daily.
- Cystitis- 250 mg twice daily.
- Pyelonephritis- 250 mg twice daily.
- Uncomplicated skin and soft tissue infections- 250 mg twice daily.
- Lyme disease- 500 mg twice daily for 14 days (range of 10 to 21 days)

For Children (< 40 Kg)

- Acute tonsillitis and pharyngitis, acute bacterial sinusitis- 10 mg/kg twice daily to a maximum of 125 mg twice daily.
- Children aged two years or older with otitis media or, where appropriate, with more severe infections- 15 mg/kg twice daily to a maximum of 250 mg twice daily.
- Cystitis- 15 mg/kg twice daily to a maximum of 250 mg twice daily.
- Pyelonephritis- 15 mg/kg twice daily to a maximum of 250 mg twice daily for 10 to 14 days.
- Uncomplicated skin and soft tissue infections- 15 mg/kg twice daily to a maximum of 250 mg twice daily.
- Lyme disease- 15 mg/kg twice daily to a maximum of 250 mg twice daily for 14 days (10 to 21 days).

Renal impairment

The safety and efficacy of cefuroxime axetil in patients with renal failure have not been established. Cefuroxime is primarily excreted by the kidney. In patients with markedly impaired renal function it is recommended that the dosage of cefuroxime should be reduced to compensate for its slower excretion. Cefuroxime is effectively removed by dialysis.

- ≥30 ml/min/1.73 m2 (T1/2 1.4–2.4 hrs.)- No dose adjustment necessary (standard dose of 125 mg to 500 mg given twice daily).
- 10-29 ml/min/1.73 m2 (T1/2 4.6 hrs.)- Standard individual dose given every 24 hours.
- < 10 ml/min/1.73 m2 (T1/2 16.8 hrs.)- Standard individual dose given every 48 hours.

- During haemodialysis (T1/2 16.8 hrs.)- A single additional standard individual dose should be given at the end of each dialysis.

Hepatic impairment

There are no data available for patients with hepatic impairment. Since cefuroxime is primarily eliminated by the kidney, the presence of hepatic dysfunction is expected to have no effect on the pharmacokinetics of cefuroxime.

Method of Administration

Oral use

Should be taken after food for optimum absorption.

Should not be crushed and are therefore unsuitable for treatment of patients who cannot swallow tablets.

4.3 Contraindications

Hypersensitivity to cefuroxime or to any of the excipients used in formulation.

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 warning 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 betalactam agent. Caution should be used if cefuroxime is given to patients with a history of nonsevere 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. Medicinal products that inhibit peristalsis should not be given.

Interference with diagnostic tests

The development of a positive Coomb's Test associated with the use of cefuroxime may interfere with cross matching of blood.

4.5 Interaction with other medicinal products and other forms of interactions:

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 axetil may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral contraceptives.

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.

4.6. Use in pregnancy and lactation:

Pregnancy

The Studies have shown no harmful effects on pregnancy, embryonal or foetal development, parturition or postnatal development. Cefuroxime should be prescribed to pregnant women only if the benefit outweighs the risk.

Breastfeeding

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.

4.7. Effects on ability to drive and operate machine: ---

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

4.8. Undesirable effects:

Adverse reactions have been ranked under headings of frequency using the following convention:

Very common (≥1/10)

Common (≥1/100 to <1/10)

Uncommon (≥1/1,000 to <1/100)

Rare (≥1/10,000 to <1/1,000)

Very rare (<1/10,000)

Not known (cannot be estimated from available data).

Common: Candida overgrowth, eosinophilia, headache, dizziness, diarrhoea, nausea, abdominal pain, transient increases of hepatic enzyme levels.

Uncommon: positive Coomb's test, thrombocytopenia, leukopenia (sometimes profound), vomiting, skin rashes.

Not known: Clostridium difficile overgrowth, haemolytic anaemia, drug fever, serum sickness, anaphylaxis, Jarisch-Herxheimer reaction, pseudomembranous colitis, jaundice (predominantly cholestatic), hepatitis, urticaria, pruritus, erythema multiforme, StevensJohnson 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. Pharmaco-dynamic 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.

Mechanism of resistance

Bacterial resistance to cefuroxime may be due to one or more of the following mechanisms:

• Hydrolysis by beta-lactamases; including (but not limited to) by extended-spectrum betalactamases (ESBLs), and AmpC enzymes that may be induced or stably derepressed in certain aerobic Gram-negative bacteria species;

• Reduced affinity of penicillin-binding proteins for cefuroxime;

• Outer membrane impermeability, which restricts access of cefuroxime to penicillin binding proteins in Gram-negative bacteria;

• Bacterial efflux pumps.

Organisms that have acquired resistance to other injectable cephalosporins are expected to be resistant to cefuroxime.

Depending on the mechanism of resistance, organisms with acquired resistance to penicillins may demonstrate reduced susceptibility or resistance to cefuroxime

5.2. Pharmaco-kinetic 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.

Distribution

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

Biotransformation

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.

Special patient populations

Gender

No differences in the pharmacokinetics of cefuroxime were observed between males and females.

Elderly

No special precaution is necessary in the elderly patients with normal renal function at dosages up to the normal maximum of 1 g per day. Elderly patients are more likely to have decreased renal function; therefore, the dose should be adjusted in accordance with the renal function in the elderly.

Paediatrics

In older infants (aged >3 months) and in children, the pharmacokinetics of cefuroxime are similar to that observed in adults.

Renal impairment

The safety and efficacy of cefuroxime axetil in patients with renal failure have not been established.

Cefuroxime is primarily excreted by the kidney. Therefore, as with all such antibiotics, in patients with markedly impaired renal function (i.e. C1cr< 30 ml/minute) it is recommended that the dosage of cefuroxime should be reduced to compensate for its slower excretion. Cefuroxime is effectively removed by dialysis.

Hepatic impairment

Since cefuroxime is primarily eliminated by the kidney, the presence of hepatic dysfunction is expected to have no effect on the pharmacokinetics of cefuroxime.

Pharmacokinetic/Pharmacodynamic relationship

For cephalosporins, the most important pharmacokinetic-Pharmacodynamic index correlating with in vivo efficacy has been shown to be the percentage of the dosing interval (%T) that the unbound concentration remains above the minimum inhibitory concentration (MIC) of cefuroxime for individual target species (i.e. %T>MIC).

5.3. Pre-clinical 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.

6. Pharmaceutical Particulars

6.1 List of Excipients:

Cross Carmosine Sodium	BP
MCCP	BP
Sodium Benzoate	BP
Indion – 234	BP
Cross Carmosine Sodium	BP
Magnesium Stearate	BP
Talcum	BP

Aerosil	BP
Iso propyl alcohol	BP
MDC	BP
Pure coat WT 1001 White	BP

6.2 Incompatibilities: Not Applicable

6.3 Shelf-life: 24 Months

6.4 Special precautions for storage:

Store at temperature not exceeding 30°C, protect from light and moisture.

6.5 Nature and contents of container:

Primary Packing: 10 Tablets in Alu-Alu blister,

Secondary Packing: 1 Alu-Alu blister in a carton with package insert.

Such 10 cartons are packed in outer carton.

6.6 Special precautions for disposal and other handling

No special instructions for use/handling

7- Marketing Authorization Holder:

SONYDONS & SONS PHARMACEUTICAL NIG LTD

No. 126 Egbe Road, Ejigbo, Lagos,Nigeria.

8- Marketing Authorization Number (s):

Product license / registration Number (s)

9- Manufacturer Name:

M/S SWISS PHARMA PVT.LTD

3709,G.I.D.C.,PHASE IV, Valva, Ahmedabad-382 445,Gujarat India.

10- Date of first authorization/renewal of the authorization:

11- Date of revision of the text:
