

**OCEROXIME DRY SYRUP (Cefuroxime Axetil for Oral Suspension USP 125 mg / 5 ml)**  
**MODULE 1 (Administrative & Prescribing Information)**

**1.3 Product Information**

**1.3.1 Summary of Product Characteristics (SmPC)**

**SUMMARY OF PRODUCT CHARACTERISTICS**

**1. Name of the Medicinal Product**

**OCEROXIME DRY SYRUP**

(Cefuroxime Axetil for Oral Suspension USP 125 mg / 5 ml)

**2. Quality and Quantitative Composition**

**Qualitative Composition:**

Each 5 ml of Reconstitution suspension Contains:

Cefuroxime Axetil USP

Equivalent to Cefuroxime      125 mg

Excipients                              Q.S.

<b>Sr. No.</b>	<b>Ingredients</b>	<b>Standard</b>
1	Maltodextrin	BP
2	Purified Water	BP
3	Isopropyl Alcohol	BP
4	Sucrose	BP
5	Xanthan Gum	BP
6	Tutti Fruti Powder Flavour	In-House
7	Peppermint Powder flavour	In-House
8	Pineapple powder flavour	In-House
9	Aspartame	BP

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<b>10</b>	Acesulfame Potassium (Acesulfame -K)	BP
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**Quantitative Composition:**

Each 5 ml of Reconstitution suspension Contains:

Cefuroxime Axetil USP

Equivalent to Cefuroxime      125 mg

Excipients                              Q.S.

Sr. No.	Ingredients	Standard	Quantity / 5 ml
1	Maltodextrin	BP	504.00 mg
2	Purified Water	BP	158.00 mg
3	Isopropyl Alcohol	BP	504.00 mg
4	Sucrose	BP	2234.00 mg
5	Xanthan Gum	BP	4.00 mg
6	Tutti Fruti Powder Flavour	In-House	90.00 mg
7	Peppermint Powder flavour	In-House	30.00 mg
8	Pineapple powder flavour	In-House	30.00 mg
9	Aspartame	BP	27.00 mg
10	Acesulfame Potassium (Acesulfame -K)	BP	23.00 mg

**3. Pharmaceutical Form**

Liquid Dosage form (Oral Suspension)

White free flowing powder. It gives white coloured flavored suspension after reconstitution as per the label.

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#### **4. Clinical Particulars**

##### **4.1 Therapeutic indications**

Cefuroxime axetil 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.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

##### **4.2 Posology and method of administration**

###### Posology

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

*Table 1. Adults and children ( $\geq 40$  kg)*

Indication	Dosage
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

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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)

*Table 2. Children (<40 kg)*

Indication	Dosage
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)

There is no experience of using Cefuroxime axetil in children under the age of 3 months.

*Renal impairment*

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

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Cefuroxime is primarily excreted by the kidneys. 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.

*Table 3. Recommended doses for Cefuroxime axetil in renal impairment*

Creatinine clearance	T <sub>1/2</sub> (hrs)	Recommended dosage
≥30 mL/min/1.73 m <sup>2</sup>	1.4–2.4	no dose adjustment necessary (standard dose of 125 mg to 500 mg given twice daily)
10-29 mL/min/1.73 m <sup>2</sup>	4.6	standard individual dose given every 24 hours
<10 mL/min/1.73 m <sup>2</sup>	16.8	standard individual dose given every 48 hours
Patients on haemodialysis	2–4	a further 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

For optimal absorption cefuroxime axetil suspension should be taken with food.

Constitution/Administration instructions

The bottle should be shaken vigorously before the medication is taken.

The reconstituted suspension when refrigerated between 2 and 8°C can be kept for up to 10 days.

Depending on the dosage, there are other presentations available.

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**4.3 Contraindications**

Hypersensitivity to the active substance or to any of the excipients used.

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

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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 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.

**Important information about excipients**

The sucrose content of cefuroxime axetil suspension should be taken into account when treating diabetic patients and appropriate advice provided.

Contains 3 g of sucrose per 5 ml dose

Contains 6 mg of propylene glycol (E1520) per 5 ml dose.

Contains 4.5 mg benzyl alcohol (E1519) per 5 ml dose. Benzyl alcohol may cause allergic reactions

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Cefuroxime axetil suspension contains aspartame, which is a source of phenylalanine and so should be used with caution in patients with phenylketonuria. Neither non-clinical nor clinical data are available to assess aspartame use in infants below 12 weeks of age.

#### **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.

##### **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.

##### **Fertility**



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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**

The most common adverse reactions are *Candida* overgrowth, eosinophilia, headache, dizziness, gastrointestinal disturbances and transient rise in liver enzymes.

Common side effects of Cefuroxime Suspension includes:

- diarrhea
- dizziness
- headache
- drowsiness
- itching/swelling
- rash
- nausea
- vomiting
- abdominal pain
- stomach upset
- gas
- headache
- itching or rash
- hives
- cough

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- stuffy nose
- stiff or tight muscles
- muscle pain
- joint pain or swelling
- restlessness
- irritability
- hyperactivity
- vaginal itching or discharge
- unusual or unpleasant taste in the mouth
- white patches or sores in the mouth, and
- Diaper rash (in infants taking liquid cefuroxime).

#### **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 Pharmacodynamic 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.

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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 beta-lactamases (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 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.

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Following administration of cefuroxime axetil tablets peak serum levels (2.1 mcg/ml for a 125 mg dose, 4.1 mcg/ml for a 250 mg dose, 7.0 mcg/ml for a 500 mg dose and 13.6 mcg/ml for a 1000 mg dose) occur approximately 2 to 3 hours after dosing when taken with food. The rate of absorption of cefuroxime from the suspension is reduced compared with the tablets, leading to later, lower peak serum levels and reduced systemic bioavailability (4 to 17% less). Cefuroxime axetil oral suspension was not bioequivalent to cefuroxime axetil tablets when tested in healthy adults and therefore is not substitutable on a milligram-per-milligram basis. 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.

**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<sup>2</sup>.

**Special patient populations**

**Gender**

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

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**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.

There is no clinical trial data available on the use of cefuroxime axetil in children under the age of 3 months.

**Renal impairment**

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

Cefuroxime is primarily excreted by the kidneys. Therefore, as with all such antibiotics, in patients with markedly impaired renal function (i.e.  $Cl_{cr} < 30$  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**

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.

**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

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concentration remains above the minimum inhibitory concentration (MIC) of cefuroxime for individual target species (i.e. %T>MIC).

### 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. 0 Pharmaceutical Particulars

### 6.1 List of excipients

Sr. No.	Ingredients	Standard
1	Maltodextrin	BP
2	Purified Water	BP
3	Isopropyl Alcohol	BP
4	Sucrose	BP
5	Xanthan Gum	BP
6	Tutti Fruti Powder Flavour	In-House
7	Peppermint Powder flavour	In-House
8	Pineapple powder flavour	In-House
9	Aspartame	BP
10	Acesulfame Potassium (Acesulfame -K)	BP

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**6.2 Incompatibilities**

Not applicable.

**6.3 Shelf life**

36 months

**6.4 Special precautions for storage**

Store below 30°C protected from light.

**6.5 Nature and contents of container**

1 x 50 ml Amber glass Bottle packed in unit carton

1 x 100 ml Amber glass Bottle packed in unit carton

**6.6 Special precautions for disposal**

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Constitution/Administration instructions

The bottle should be shaken vigorously before the medication is taken.

The reconstituted suspension when refrigerated between 2 and 8°C can be kept for up to 10 days.

**7. Marketing Authorization Holder/ Applicant**

**SWISS PHARMA NIG. LTD**

5 Dopemu Road Agege Lagos

**8. Marketing Authorization Numbers**

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**9. Date of first authorization/renewal of the authorization**

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**10. Date of revision of the text**

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