PULMOCEF DR SYRUP
(Cefuroxime Axetil for Oral Suspension USP 125 mg)

1.3 Product Information

1.3.1 Summary of Product Characteristics (SmPC)

1. Name of the medicinal product:

PULMOCEF DRY SYRUP

(Cefuroxime Axetil for Oral Suspension USP 125 mg)

Each 5 ml of reconstitution suspension contains:

Cefuroxime Axetil USP

Eq. to Cefuroxime 125 mg

2. Qualitative and quantitative composition:

Sr. No.	Ingredients	Reference	Label Claim (mg)	Quantity/ Unit Dose (mg)	Quantity/ Bottle (gm)	Active / Inactive
1	Cefuroxime Axetil Taste Masked Granules *	IH	125.00	518.70= 125	10.374	Active
2	Aerosil (Colloidal Silicon Dioxide)	BP	--	15.27	0.305	Inactive
3	Sodium Carboxy Methyl Cellulose	BP	--	3.00	0.060	Inactive
4	Citric Acid Mohohydrate	BP	--	4.05	0.081	Inactive
5	Aspartame	BP	--	33.00	0.660	Inactive
6	Banana D.C. Flavour	IH	--	39.00	0.780	Inactive
7	Saccharine Sodium	USP	--	24.00	0.480	Inactive
8	Sucrose (Pharma Grade Sugar)	BP	--	2363.00	47.260	Inactive
Total Weight				**3000 mg**	**60 gm/ 100 ml**	

*518.70 mg of Cefuroxime Axetil Eq. to 125 mg of Cefuroxime.

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3. Pharmaceutical form:
Dry Powder for Oral Suspension.

4. Clinical particulars:
4.1 Therapeutic indications:
CEFUROXIME Suspension is an antibiotic used in children. It is indicated for the treatment of mild to moderate severe infection caused by micro-organism such as:
- Upper respiratory tract infection: Acute otitis media, sinusitis, tonsillitis and pharyngitis
- Acute bronchitis, acute exacerbation of chronic bronchitis
- Lower uncomplicated urinary tract infection: cystitis
- Skin and soft tissue infections: furunculosis, pyoiderma and impetigo
- Treatment of early stage Lyme disease (an infection spread by parasites called ticks).

4.2 Posology and method of administration:
DOSE:
Always take this medicine exactly as your doctor or pharmacist has told you to.
Children: The usual dose of CEFUROXIME suspension is 10 mg/kg (to a maximum of 25 mg) to 15 mg/kg (to a maximum of 250 mg) twice daily depending on the severity and type of infection.
DIRECTION FOR RECONSTITUTION: Add boiled and cooled water using the dispensing cup on the bottle. Shake vigorously to bring the level to the engraved ring mark. Add more water up to the 70 ml mark and shake well.
If you take too much CEFUROXIME Suspension
Have fits (seizures). Don't delay. Contact your doctor or your nearest hospital emergency department immediately.
If you forget to take CEFUROXIME Suspension
The usual time. Don't stop CEFUROXIME Suspension without advice.
It is important that you take the full course of CEFUROXIME Suspension. Don't stop unless your doctor advise you to –even if you are feeling better. If you don't complete the full course of treatment, the infection may come back.
: You may have neurological disorder, in particular you may be more likely to
: Don't take an extra dose to make up for a missed dose. Just take you next dose.

4.3 Contraindications:
A) Medicines used to reduce the amount of acid in your stomach (e.g. antacids used to treat heartburn) can affect how CEFUROXIME Suspension works
- Probenecid
- Oral anticoagulants

CEFUROXIME suspension is not recommended for children aged under 3 months, as the safety and effectiveness are not known in this age group.
Patients with Kidney problems: if you have a kidney problem, your doctor may change your dose. Talk to your doctor if this applies to you.

4.4 Special warnings and precautions:
Don't take CEFUROXIME Suspension
- If you are allergic (hypersensitive) to any cephalosporin antibiotics or any of the other ingredients of CEFUROXIME suspension
- If you have ever had a severe allergic (hypersensitive) reaction to any other type of betalactum antibiotic (penicillin, monobactams and carbapenems).
- If you think this applies to you, don't take CEFUROXIME Suspension until you have checked with your doctor.

Take special care with CEFUROXIME Suspension
CEFUROXIME Suspension is not recommended for children aged under 3 months. As the safety and effectiveness are not known in this age group.
You must look out for certain symptoms, such as allergic reaction, fungal infection (such as candida) and severe diahorrea (pseudomembranous colitis) while you are taking CEFUROXIME Suspension. This will reduce the brisk of any problems.

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 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 probenicid 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 Pregnancy and lactation
Pregnancy: 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 sensitization 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 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:
POSSIBLE SIDE EFFECTS:
Like all medicines, this medicine can cause side effects, although not everybody gets them.
Allergic Reaction: A small number of people taking CEFUROXIME Suspension get an allergic reaction or potentially serious skin reaction. Symptoms of these reaction include:
-Raised and itchy rash, swelling, sometimes of the face or mouth causing difficulty in breathing
- Skin rash, which may blister
- A wide spread rash with blister and peeling skin. (These may be signs of Stevens-Johnson syndrome or toxic epidermal necrolysis).
Fungal infections: Medicines like CEFUROXIME Suspension can cause an overgrowth of yeast (Candida) in the body which can leads to fungal infection (Such as thrust). This side effect is more likely if you take CEFUROXIME Suspension for a long time.
Severe diarrhoea: (Pseudomembranous colitis): Medicines like CEFUROXIME Suspension can cause inflammation of the colon (large intestine), causing severe diarrhoea, usually with blood and mucus, stomach pain, fever.
Jarisch-Herxheimer reaction: Some patients may get a high temperature (fever), chills, headache, and muscle pain and skin rash while being treated with CEFUROXIME Suspension.
Symptoms suually last a few hours or up to one day.
For Lyme disease. This is known as the Jarisch-Herxheimer reaction.
Contact a doctor or nurse immediately if you get any of these symptoms.
Common Side Effects: Fungal Infection (Candida), headache, dizziness, diarrhoea, feeling sick, stomach pain.
Uncommon Side Effects: Being sick, skin rashes.

4.9 Over dosage:
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 cephalosporin's

ATC code: J01DC02

Mechanism of action

The active substance, cefuroxime axetil, owes its in vivo bactericidal activity to the parent compound cefuroxime. Cefuroxime, like the penicillin, is a beta-lactam antibiotic. By binding to specific penicillin –binding proteins (PBPs) locate inside the bacterial cell wall, it inhibits the third and last stage of bacterial cell wall synthesis. Cell lysis is then mediated by bacterial cell wall autolytic enzyme such as autolysins.

It is resistance to β-lactamases and active in great number of Gram-positive and Gram-negative microbes.

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 depressed 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.

Microbiological susceptibility

Commonly susceptible species

Gram-positive aerobes: *Staphylococcus aureus* (methicillin susceptible)*, *Coagulase negative staphylococcus (methicillin susceptible), Streptococcus pyogenes, Streptococcus agalactiae*.

Gram-negative aerobes: *Haemophilus influenza, Haemophilus parainfluenzae, Moraxella catarrhalis.*

Spirochaetes: *Borrelia burgdorferi*

Microorganisms for which acquired resistance may be a problem

Gram-positive aerobes: *Streptococcus pneumoniae*
Gram-negative aerobes: *Citrobacter freundii, Enterobacter aerogenes, Enterobacter cloacae, Escherichia coli, Klebsiella pneumonia, Proteus mirabilis, Proteus spp.* (other than *P. vulgaris*), *Providencia spp.*
Gram-positive anaerobes: *Peptostreptococcus* spp. *Propionibacterium* spp.
Gram-negative anaerobes: *Fusobacterium* spp., *Bacteroides* spp.

Inherently resistant microorganisms
Gram-positive aerobes: *Enterococcus faecalis, Enterococcus faecium*
Gram-negative aerobes: *Acinetobacter* spp., *Campylobacter* spp., *Morganella morganii, Proteus vulgaris, Pseudomonas aeruginosa, Serratia marcescens.*
Gram-negative anaerobes: *Bacteroides fragilis*
Others: *Chlamydia* spp., *Mycoplasma* spp., *Legionella* spp.
* All *methicillin*-resistant *S. aureus* are resistant 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.
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 (see section 4.2).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^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.
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. 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
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 concentration remains above the minimum inhibitory concentration (MIC) of cefuroxime for individual target species (i.e. %T>MIC).

5.3 Preclinical safety data

Reported non-clinical data reveals that 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
Sodium Carboxy Methyl Cellulose
Citric Acid Monohydrate
Aspartame
Banana D.C. Flavor
Saccharin Sodium
Sucrose (Pharma Grade Sugar)

6.2 Incompatibilities:

Not Applicable

6.3 Shelf life:

24 months

6.4 Special precautions for storage:

Store in cool and dry place Below 30°C. Protect from light.

6.5 Nature and contents of container

60 gm /100 mL bottle.

6.6 Instructions for use and handling

Constitution/Administration instructions

Add 20 ml of Boiled and cooled water using the dispensing cup on the bottle. Shake vigorously to bring mark. Add more Water up to the 100 ml mark and shake well.

7. Marketing Authorization Holder

Manufactured by :
Zim Laboratories Limited
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