Brand Name: GORBACEF 125

Generic Name: Cefuroxime Axetil For Oral Suspension USP

SUMMARY OF PRODUCT CHARACTERISTIC (SMPC)

1. NAME OF THE MEDICINAL PRODUCT

1.1 Invented Name of the Medicinal Product

GORBACEF 125 POWDER FOR ORAL SUSPENSION

Cefuroxime Axetil for Oral Suspension USP

1.2 Strength

Cefuroxime Axetil USP 125 mg .

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml of reconstituted suspension contains :

Cefuroxime Axetil USP

Equivalent to Cefuroxime ……..125 mg.

Excipients…….……..q.s.

Colour : Approved colour used

3. PHARMACEUTICAL FORM

Powder for Oral Suspension.

An off white colour granular powder .

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

GORBACEF 125 Powder for Oral Suspension 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:

1. Pharyngitis/Tonsillitis caused by Streptococcus pyogenes.
2. 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.
3. Acute Bacterial Maxillary Sinusitis caused by Streptococcus pneumoniae or Haemophilus influenzae (non-beta-lactamase-producing strains only).
4. Impetigo caused by Staphylococcus aureus (including beta-lactamase-producing strains) or Streptococcus pyogenes.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

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

Table 1. Adults and children (≥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
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 Gorbacef 125 powder for oral suspension in children under the age of 3 months.

Cefuroxime axetil tablets and cefuroxime axetil granules for oral suspension are not bioequivalent and are not substitutable on a milligram-per-milligram basis.

In infants (from the age of 3 months) and children with a body mass of less than 40 kg, it may be preferable to adjust dosage according to weight or age. The dose in infants and children 3 months to 18 years is 10 mg/kg twice daily for most infections, to a maximum of 250 mg daily. In otitis media or more severe infections the recommended dose is 15 mg/kg twice daily to a maximum of 500 mg daily.

The following two tables, divided by age group, serve as a guideline for simplified administration, e.g measuring spoon (5 ml) for the 125 mg/5 ml or the 250 mg/5 ml multi-dose suspension if provided.

Table 3. 10 mg/kg dosage for most infections

Age	Dose (mg) twice daily	Volume per dose (ml)	
		125 mg	250 mg
3 to 6 months	40 to 60	2.5	-
6 months to 2 years	60 to 120	2.5 to 5	-
2 to 18 years	125	5	2.5

Table 4. 15 mg/kg dosage for otitis media and more serious infections

Age	**Dose (mg) twice daily**	**Volume per dose (ml)**	
		125 mg	250 mg
3 to 6 months	60 to 90	2.5	-
6 months to 2 years	90 to 180	5 to 7.5	2.5
2 to 18 years	180 to 250	7.5 to 10	2.5 to 5

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. 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 5. Recommended doses for Gorbacef 125 powder for oral suspension in renal impairment

Creatinine clearance	**$T_{1/2}$ (hrs)**	**Recommended dosage**
≥30 ml/min/1.73 m^2	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^2	4.6	standard individual dose given every 24 hours
<10 ml/min/1.73 m^2	16.8	standard individual dose given every 48 hours
During haemodialysis	2–4	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

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

For instructions on reconstitution of the medicinal product before administration

Depending on the dosage, there are other presentations available.

Directions for reconstituting suspension in multidose bottles

1. Shake the bottle to loosen the content. All the granules should be free-flowing in the bottle. Remove the cap and the heat-seal membrane. If the latter is damaged or not present, the product should be returned to the pharmacist.

2. Add the total amount of cold water as stated on the label or up to the volume line on the cup provided (if supplied). If the water was previously boiled it must be allowed to cool to room temperature before adding. Do not mix Gorbacef 125 powder for oral suspension with hot or warm liquids. Cold water must be used to prevent the suspension becoming too thick.

3. Replace the cap. Allow the bottle to stand to allow the water to fully soak through the granules; this should take about one minute.

4. Invert the bottle and shake well (for at least 15 seconds) until all the granules have mixed with the water.

5. Turn the bottle into an upright position and shake well for one minute until all the granules have blended with the water.

Store the Gorbacef 125 powder for oral suspension immediately at between 2 and 8°C (do not freeze) and let it rest for at least one hour before taking the first dose. The reconstituted suspension when refrigerated between 2 and 8°C can be kept for up to 10 days.

Always shake the bottle well before taking the medication.

The reconstituted suspension or granules should not be mixed with hot liquids.

Brand Name: GORBACEF 125

Generic Name: Cefuroxime Axetil For Oral Suspension USP

4.3 CONTRAINDICATIONS

GORBACEF 125 powder for oral suspension is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

4.4 WARNING AND PRECAUTION

Hypersensitivity reactions special care is indicated in patients who have experienced an allergic reaction to penicillins or other beta-lactum antibiotics because there is a risk of cross-sensitivity. As with all beta-lactum 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-lactum agent. Caution should be used if cefuroxime is given to patients with a history of non-severe hypersensitivity to other beta-lactum 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.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Concomitant administration of probenecid with cefuroxime axetil suspension 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).

Drugs that reduce gastric acidity may result in a lower bioavailability of Viktinoxx compared with that of fasting state and tend to cancel the effect of postprandial absorption. 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 contraceptives.

Brand Name: GORBACEF 125

Generic Name: Cefuroxime Axetil For Oral Suspension USP

4.6 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. GORBACEF 125 powder for oral suspension 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 USE MACHINES

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

4.8 UNDESIRABLE EFFECTS

The most common adverse reactions that may be associated with cefuroxime axetil include gastro- intestinal events, such as nausea, vomiting, diarrhea, abdominal pain, flatulence. The gastrointestinal adverse events increase with the higher recommended doses.

4.9 OVERDOSE

Overdosage of cephalosporin can cause cerebral irritation leading to convulsions. Serum levels of cefuroxime can be reduced by hemodialysis and peritoneal dialysis

Brand Name: GORBACEF 125

Generic Name: Cefuroxime Axetil For Oral Suspension USP

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.

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.

Brand Name: GORBACEF 125

Generic Name: Cefuroxime Axetil For Oral Suspension USP

5.2 Pharmacokinetic properties

The preferred analytical Method is by bioassay, using agar diffusion and a Gram-negative organism as indicator, with the usual lower limit of sensitivity around 0.06 mg.1-1. Cefuroxime has a plasma half-life of approximately 75 min in subjects with normal renal function. It is about 33 % bound to serum. The volume of distribution after a 1 g dose is 11.1-13.71 per 1.73 m2. There were wide variations in absorption of cefuroxime axetil in early studies and some early papers refer to formulations not now used. The final formulation developed gives peak serum concentrations of 7-10 mg.1-1 if taken before food. Cefuroxime axetil is completely hydrolyzed in the intestine to cefuroxime; Its pharmacokinetics are then the same as cefuroxime sodium, but the serum level is much closer to the MIC of important pathogens that the parent form. The drug is primarily eliminated by the kidneys, with urinary recovery about 35% and an elimination half-life of 1.5 h. The drug crosses the placenta and can also be detected in breast milk.

Oral absorption	
Cefuroxime	not relevant
Cefuroxime axetil	good
Presystemic metabolism	
Cefuroxime	not relevant
Cefuroxime axetil	hydrolyzed to Cefuroxime
Plasma half-life	
Cefuroxime	75 min
Volume of distribution	11.-
(both drugs)	13.7I.173 m-2
Plasma protein binding	
(both drugs)	30%

Concentration –effect relationship

The therapeutic effect of cefuroxime sodium, as with all antibiotics, depends on achieving a level of antibiotic in excess of the MIC of the causative organism. This is relatively easily achieved with an infection in urine or blood, but is more difficult at enclosed sites such as abscesses or gallbladder infections. Fewer data are available for cefuroxime axetil. Serum levels are in excess of the MIC of many pathogens, but information on its penetration into sputum and other sites is still needed.

Metabolism

Cefuroxime is rapidly excreted in high concentration through the kidney with over 90 % of the given dose recovered in the urine within 6 h of injection. Renal clearance is equally divided between clearance through tubules and glomerular filtration ; mean drug: creatinine clearance rations were 1:1 to 1:3 suggesting half the drug is filtered and half is actively secreted by the kidney tubules.

Virtually all cefuroxime is excreted in the urine, with no detectable enterohepatic circulation. High pressure liquid chromatobgtraphy studies of cefuroxime in urine samples showed that over 95% is excreted as unchanged cefuroxime. There are no known pharmacologically active metabolites.

Cefuroxime axetil is better absorbed if taken after food, when 50% can be recovered in the urine. No unhydrolyzed ester is detected in serum.

5.3 Preclinical safety data

TOXICOLOGICAL DATA

Cefuroxime, like many other β-lactam antibiotics shows little evidence of human or animal toxicity. There are no reports of toxicological results in animals that are of human significance. There was no evidence of nephrotoxicity in mice given up to 6 g.kg-1 cefuroxime subcutaneously. There was no evidence of teratological effects in mice or rabbits. Long term carcinogenicity tests have not been carried out. Cefuroxime axetil has a similar toxicology profile to the parent drug.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Xanthan gum

Acesulfame potassium

Povidone K30

Stearic Acid

Sucrose

Tutti Frutti Flavour (containing propylene glycol)

Benzyl alcohol

Purified Water

6.2 Incompatibilities

A positive Coombs' test has been reported during treatment with cephalosporins - this phenomenon can interfere with cross-matching of blood.

6.3 Shelf life

Two years.

6.4 Special precautions for storage

Store below 30°C. Protected from light.

6.5 Nature and contents of container

Gorbacef 125 powder for oral suspension is provided as a dry, white to off-white, tutti-frutti flavoured granule. When reconstituted as directed, it provides the equivalent of 125 mg of cefuroxime (as cefuroxime axetil) per 5 ml of suspension.

It is supplied in plastic bottles of 100ml.

6.6 Special precautions for disposal and other handling

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

7. Marketing authorisation holder

CHIROS PHARMA

VILL.: LOHARON, P.O.: GHATTI,

DIST. SOLAN-173 211 (H.P), INDIA

Tel.: 01792 – 227307

Email: info@chirospharma.com

8. MARKETING AUTHORISATION NUMBER

Not Applicable

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

Not Applicable

10. DATE OF (PARTIAL) REVISION OF THE TEXT

To be given after approval of the product