

APPROVED PACKAGE INSERT

SCHEDULING STATUS

S4

PROPRIETARY NAME AND DOSAGE FORM

Ceroxim® 250 Tablets

Ceroxim® 500 Tablets

Ceroxim® Suspension

Ceroxim® Forte Suspension

COMPOSITION

Ceroxim 250 Tablets

Each tablet contains:

Cefuroxime axetil equivalent to cefuroxime 250 mg

Contains sugar: Sucrose 40 mg.

Ceroxim 500 Tablets

Each tablet contains:

Cefuroxime axetil equivalent to cefuroxime 500 mg

Contains sugar: Sucrose 80 mg.

Ceroxim Tablets also contain the following excipients: calcium carbonate, colloidal anhydrous silica (Aerosil-200), croscarmellose sodium, microcrystalline cellulose, monosodium citrate, povidone (K-30), purified water, sodium lauryl sulphate, stearic acid and sucrose.

Ceroxim Suspension

Each 5 ml of constituted suspension contains:

Cefuroxime axetil equivalent to cefuroxime 125 mg

Contains sugar: Sucrose 2,8 g.

Preservative: Sodium benzoate 0,2 % m/v

Ceroxim Forte Suspension

Each 5 ml of constituted suspension contains:

Cefuroxime axetil equivalent to cefuroxime 250 mg

Contains sugar: Sucrose 2,5 g.

Preservative: Sodium benzoate 0,2 % m/v

Ceroxim / Ceroxim Forte Suspension also contain the following excipients: aspartame, flavour peppermint, flavour tutti frutti, mannitol, mono sodium citrate, silica colloidal hydrated, sodium chloride and xanthan gum.

PHARMACOLOGICAL CLASSIFICATION

A 20.1.1 Broad and medium spectrum antibiotics

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

Cefuroxime is a bactericidal second-generation cephalosporin. The antibacterial action of cefuroxime results from inhibition of bacterial cell wall synthesis by binding to essential target proteins in bacterial cytoplasmic membranes. Cefuroxime has bactericidal activity against a wide range of bacterial organisms, including beta-lactamase producing strains.

Microbiological susceptibility:

The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of cefuroxime axetil in at least some types of infections is questionable.

Cefuroxime is usually active against the following microorganisms *in vitro*.

Microorganisms for which acquired resistance may be a problem

Gram-positive aerobes:

Streptococcus pneumonia

Gram-negative aerobes:

Citrobacter freundii

Enterobacter aerogenes

Enterobacter cloacae

Escherichia coli

Klebsiella pneumoniae

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.

Pharmacokinetic properties

Cefuroxime axetil is an oral prodrug of cefuroxime. After oral absorption, cefuroxime axetil is hydrolysed in the intestinal mucosa and blood to release cefuroxime into the plasma. Oral absorption is optimal when administered with food. Peak serum levels of cefuroxime occur approximately two to three hours after oral dosing when taken with food. Protein binding is approximately 33 % to 50 %. Cefuroxime is not metabolised and is excreted unchanged in the urine by glomerular filtration and tubular secretion. The elimination half-life is between 1 and 1,5 hours after oral dosing. The elimination half-life is prolonged with renal impairment and in neonates. Serum levels of cefuroxime are reduced by dialysis.

INDICATIONS

Ceroxim is indicated for the treatment of infections caused by susceptible organisms in the following infections:

- Pharyngitis and tonsillitis caused by *Streptococcus pyogenes*. Penicillin is the usual medicine of choice in the treatment and prevention of streptococcal infections including the prophylaxis of rheumatic fever. **Ceroxim** is generally effective in the eradication of streptococci from the oral pharynx. **Ceroxim** is not indicated for the prophylaxis of subsequent rheumatic fever due to insufficient data available to support such use.
- Otitis media caused by *Streptococcus pneumoniae*, *Haemophilus influenzae* (methicillin-

sensitive strains), *Moraxella (Branhamella) catarrhalis*, and *Streptococcus pyogenes*.

- Sinusitis caused by *Streptococcus pneumoniae* and *Haemophilus influenzae*.
- Bronchitis caused by *Streptococcus pneumoniae*, *Haemophilus influenzae* (methicillin-sensitive strains) and *Haemophilus parainfluenzae* (ampicillin-sensitive strains).
- Acute uncomplicated cystitis caused by *Escherichia coli* and *Klebsiella pneumoniae*.
- Lyme disease caused by *Borrelia burgdorferi*. **Ceroxim** is indicated for the treatment of early Lyme disease and subsequent prevention of late Lyme disease in adults and children over the age of 12 years.

CONTRAINDICATIONS

Hypersensitivity to cephalosporin antibiotics, cefuroxime or to any component of **Ceroxim**.

Hypersensitivity to penicillin and other beta-lactam antibiotics.

WARNINGS AND SPECIAL PRECAUTIONS

Ceroxim should be used with caution in patients with:

- a history of gastro-intestinal disease, especially ulcerative colitis, regional enteritis or pseudomembranous colitis.
- renal function impairment – A reduced dose may be required.
- porphyria, as safety has not been established.

Pseudomembranous colitis may occur. Patients who develop abdominal or stomach cramps, abdominal tenderness, severe and watery diarrhoea (which may be bloody) and fever should be investigated for this diagnosis. If the diagnosis of pseudomembranous colitis is suspected, **Ceroxim** should be stopped immediately and appropriate therapy initiated.

Patients who experience anaphylactoid reactions to penicillins may experience a similar reaction to cephalosporins (such as **Ceroxim**). Should anaphylaxis occur, **Ceroxim** should be discontinued and the patient treated with the appropriate medicines.

Use of **Ceroxim** may result in the overgrowth of candida. Prolonged use may also cause overgrowth of other non-susceptible organisms (e.g. Enterococci or *Clostridium difficile*), which may require discontinuation of treatment.

The Jarisch-Herxheimer reaction has been reported following treatment with **Ceroxim** for Lyme disease. This reaction is a common and usually self-limiting consequence of antibiotic treatment for Lyme disease.

Ceroxim Suspension contains 2,8 g of sucrose per 5 ml and **Ceroxim Forte Suspension** contains 2,5 g of sucrose per 5 ml. The sucrose content of **Ceroxim** should be taken into account when treating diabetic patients. Appropriate advice should be provided. Patients with rare hereditary problems of fructose intolerance or sucrase isomaltase insufficiency should not take **Ceroxim**.

Ceroxim and Ceroxim Forte suspensions contain aspartame, which is a source of phenylalanine and should be used with caution in patients with phenylketonuria.

Ceroxim and Ceroxim Forte suspensions contain mannitol which may have a mild laxative effect.

Ability to drive and operate machinery:

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

INTERACTIONS

Concurrent administration of probenecid increases the area under the mean serum concentration time-curve by 50 %.

Concomitant use of **Ceroxim** and furosemide should be avoided when possible, due to enhanced nephrotoxicity.

The combined use of cephalosporins and aminoglycosides should be undertaken with caution, due to nephrotoxicity.

The efficacy of combined oral contraceptives may be decreased by concomitant use with **Ceroxim**.

Interactions with Laboratory Tests

It is recommended that either glucose oxidase or hexokinase methods be used to determine blood/plasma glucose levels in patients receiving **Ceroxim**. **Ceroxim** may give false-negative test results with ferricyanide blood glucose test. **Ceroxim** does not interfere in the alkaline picrate assay for creatinine. A false-positive Coombs reaction may appear in patients who receive large doses of **Ceroxim** (see **WARNINGS AND SPECIAL PRECAUTIONS**).

PREGNANCY AND LACTATION

Safety and efficacy in pregnancy and lactation have not been established.

DOSAGE AND DIRECTIONS FOR USE

Adults

Pharyngitis and tonsillitis: 250 mg twice daily for seven days (range 5-10 days).

Otitis media: 500 mg twice daily for seven days (range 5-10 days).

Sinusitis and bronchitis: 250 mg twice daily for seven days (range 5-10 days).

Acute, uncomplicated cystitis: 250 mg twice daily for seven days (range 5-10 days).

Lyme disease: Adults and children over 12 years of age: 500 mg twice daily for 14 days (range 10-21 days).

Children

Usual dose: 125 mg twice daily for 7 days (range 5-10 days).

There is no experience with **Ceroxim** in children under 3 months of age.

Pharyngitis and tonsillitis: 10 mg/kg twice daily to a maximum of 125 mg twice daily for seven days (range 5-10 days).

For otitis media in children 3 months to 2 years of age the usual dose is: 10 mg/kg twice daily to a maximum of 125 mg twice daily (range 5-10 days).

For otitis media in children over 2 years of age the usual dose is: 15 mg/kg twice daily to a maximum of 250 mg twice daily for seven days (range 5-10 days).

Sinusitis and bronchitis: 10 mg/kg twice daily to a maximum of 125 mg twice daily for seven days (range 5-10 days).

Acute, uncomplicated cystitis: 15 mg/kg twice daily to a maximum of 250 mg twice daily for seven days (range 5-10 days).

Because of the bitter taste of cefuroxime axetil, tablets should not be crushed. **Ceroxim** should be taken half an hour after food for optimum absorption.

Directions for use of the **Ceroxim** and **Ceroxim Forte Suspensions**:

1. Shake the bottle to loosen the granules and remove the cap.
2. Use the measure cup to add water to the bottle (23 or 22 ml water for the 50 ml pack of **Ceroxim Suspension** or **Ceroxim Forte Suspension** respectively; and 44 or 43 ml water for the 100 ml pack of **Ceroxim Suspension** or **Ceroxim Forte Suspension** respectively)_and replace the cap.
3. Invert and shake the bottle vigorously until the sound of granules in the bottle disappear.
4. Turn the bottle into an upright position and shake vigorously.
5. Patient Instructions:

SHAKE THE BOTTLE BEFORE USE.

SIDE EFFECTS

Infections and infestations

Frequent: Candida overgrowth, oral thrush, vaginitis.

Blood and lymphatic system disorders

Frequent: Eosinophilia.

Less frequent: Thrombocytopenia, leucopenia, haemolytic anaemia, neutropenia.

Immune system disorders

Less frequent: Hypersensitivity reactions including skin rashes, urticaria, pruritus, cutaneous vasculitis, bronchospasm, drug fever, serum sickness and anaphylaxis.

Nervous system disorders

Frequency unknown: Headache, convulsions.

Gastro-intestinal disorders

Frequent: Nausea, diarrhoea, abdominal pain.

Less frequent: A particular form of enterocolitis (pseudomembranous colitis) (see **WARNINGS AND SPECIAL PRECAUTIONS**).

Frequency unknown: Vomiting, diarrhoea accompanied by blood in the stools which may be a symptom of enterocolitis.

Ear and labyrinth disorders

Less frequent: Hearing loss in children with meningitis.

Hepato-biliary disorders

Frequency unknown: Transient increases in hepatic enzyme levels, alanine aminotransferase (serum glutamic pyruvic acid transaminase), aspartate aminotransferase (serum glutamic oxaloacetic transaminase), LDH (lactate dehydrogenase) levels, cholestatic jaundice, hepatitis, rise in bilirubin.

Skin and subcutaneous tissue disorders

Less frequent: Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, porphyria.

Renal and urinary disorders

Less frequent: Acute interstitial nephritis, nephrotoxicity when **Ceroxim** is used in combination with aminoglycosides or furosemide.

Reproductive system and breast disorders

Frequency unknown: Vaginal candidiasis.

Investigations

Positive antiglobulin (Coombs') test.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

See **SIDE EFFECTS**.

Symptoms of overdose

Seizures have been reported.

Treatment of overdose

Treatment is symptomatic and supportive. Serum levels of **Ceroxim** can be reduced by haemodialysis or peritoneal dialysis.

IDENTIFICATION

Ceroxim® 250 Tablets: White coloured, uncoated caplets, engraved with 'RX751' on one side and plain on the other.

Ceroxim® 500 Tablets: White coloured, uncoated caplets, engraved with 'RX752' on one side and plain on the other.

Ceroxim® Suspension and **Ceroxim® Forte Suspension:** White to cream-colored granular powder forming white to cream coloured suspension on constitution with water. The resulting suspension has a sweet taste and fruity flavor.

PRESENTATION

Ceroxim 250 / 500 Tablets: Cartons containing PVC/Aclar Blister strips of 10 or 5x10 tablets.

Ceroxim and **Ceroxim Forte Suspensions** are packed in 50 ml and 100 ml HDPE bottle packs, that comprise of natural translucent HDPE bottles with Child resistant closure caps. Each packet also contains a measuring cup with graduated markings. Bottles are labelled and packed in cartons.

STORAGE INSTRUCTIONS

Ceroxim 250 / 500 Tablets:

Store at or below 25 °C, protected from moisture.

Ceroxim and Ceroxim Forte Suspension:

The unconstituted suspension is stored at or below 25 °C, protected from moisture.

Keep the container tightly closed.

The constituted suspension is stored in a refrigerator at 2 to 8 °C for 10 days.

Discard the unused portion of reconstituted suspension after 10 days.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS

Ceroxim® 250 Tablets: 34/20.1.1/0349

Ceroxim® 500 Tablets: 34/20.1.1/0350

Ceroxim® Suspension: 45/20.1.1/0965

Ceroxim® Forte Suspension: 45/20.1.1/0966

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

RANBAXY PHARMACEUTICALS (PTY) LTD

14 Lautre Road, Stormill, Ext.1,

Roodepoort, 1724

South Africa

DATE OF PUBLICATION OF THE PACKAGE INSERT

26 November 2015

Ceroxim® 250 mg Tablets

Namibia: NS2 Reg.No.: 05/20.1.1/0191

Botswana: S2 Reg.No.: BOT 0801204

Ceroxim® 500 mg Tablets

Namibia: NS2 Reg.No.: 05/20.1.1/0192

Botswana: S2 Reg.No.: BOT 0801205