Cefia®
(Cefixime)

Highnoon

COMPOSITION:
Cefia 200mg Capsule:
Each capsule contains: Cefixime (as trihydrate) 200mg
Cefia 400mg Capsule:
Each capsule contains: Cefixime (as trihydrate) 400mg
Cefia 100mg/5mL Suspension:
Each reconstituted 5mL contains: Cefixime (as trihydrate) 100mg
Cefia DS 200mg/5mL Suspension:
Each reconstituted 5mL contains: Cefixime (as trihydrate) 200mg

DESCRIPTION:
Cefia (Cefixime) capsules/suspension is a semisynthetic, cephalosporin antibiotic for oral administration.

MODE OF ACTION
Cefixime is an antibiotic belonging to the third-generation cephalosporin group. Like other cephalosporins, cefixime exerts antibacterial activity by binding to and inhibiting the action of penicillin-binding proteins involved in the synthesis of bacterial cell walls. This leads to bacterial cell lysis and cell death.
Bacterial resistance to cefixime may be due to one or more of the following mechanisms:
- Hydrolysis by extended-spectrum beta-lactamases and/or by chromosomally-encoded (AmpC) enzymes that may be induced or de-repressed in certain aerobic gram negative bacterial species
- Reduced affinity of penicillin-binding proteins
- Reduced permeability of the outer membrane of certain gram-negative organisms restricting access to penicillin-binding proteins
- Drug efflux pumps

More than one of these mechanisms of resistance may co-exist in a single bacterial cell. Depending on the mechanism(s) present, bacteria may express cross-resistance to several or all beta-lactams and/or antibacterial drugs of other classes.

Resistance
Resistance to cefixime in isolates of Haemophilus influenzae and Neisseria gonorrhoeae is most often associated with alterations in penicillin-binding proteins (PBPs). Cefixime may have limited activity against Enterobacteriaceae producing extended spectrum beta-lactamases (ESBLs). Pseudomonas species, Enterococcus species, strains of Group D streptococci, Listeria monocytogenes, most strains of staphylococci (including methicillin-resistant strains), most strains of Enterobacter species, most strains of Bacteroides fragilis, and most strains of Clostridium species are resistant to cefixime.

Antimicrobial Activity
Cefixime has been shown to be active against most isolates of the following microorganisms, both in vitro and in clinical infections.

Gram-positive Bacteria
Streptococcus pneumoniae, Streptococcus pyogenes

Gram-negative Bacteria
Escherichia coli, Haemophilus influenzae, Moraxella catarrhalis, Neisseria gonorrhoeae, Proteus mirabilis
The following in vitro data are available, but their clinical significance is unknown. At least 90 percent of the following bacteria exhibit an in vitro minimum inhibitory concentration (MIC) less than or equal to the susceptible breakpoint for cefixime against isolates of similar genus or organism group.

Gram-positive Bacteria
Streptococcus agalactiae

Gram-negative Bacteria
Citrobacter amalonaticus, Citrobacter diversus, Haemophilus parainfluenzae, Klebsiella oxytoca, Klebsiella pneumoniae, Pasteurella multocida, Proteus vulgaris, Providencia species Salmonella species, Serratia marcescens, Shigella species.

PHARMACOKINETICS
Only 40 to 50% of an oral dose of cefixime is absorbed from the gastrointestinal tract, whether taken before or after meals, although the rate of absorption may be decreased in the presence of food. Cefixime is better absorbed from oral suspension than from tablets. Absorption is fairly slow; peak plasma concentrations of 2 to 3 micrograms/mL and 3.7 to 4.6 micrograms/mL have been reported between 2 and 6 hours after single doses of 200 and 400 mg, respectively. The plasma half-life is usually about 3 to 4 hours and may be prolonged when there is renal impairment. About 65% of cefixime is bound to plasma proteins. Information on the distribution of cefixime in body tissues and fluids is limited. It crosses the placenta. Relatively high concentrations may occur in bile and urine. About 20% of an oral dose for 50% of an absorbed dose) is excreted unchanged in the urine within 24 hours. Up to 60% may be eliminated by non-renal mechanisms; there is no evidence of metabolism but some is probably excreted into the faeces from bile. It is not substantially removed by dialysis.

INDICATIONS
It is indicated for the treatment of the following infections when caused by susceptible organisms
- Acute exacerbations of chronic bronchitis (caused by Streptococcus pneumoniae and Haemophilus influenzae)
- Community-acquired Pneumonia
- Uncomplicated urinary tract infections (caused by Escherichia coli and Proteus mirabilis).
- Pyelonephritis
- In the treatment of: Otitis media (caused by Haemophilus influenzae, Moraxella catarrhalis, and Streptococcus pyogenes), Sinusitis, Pharyngitis and Tonsillitis (caused by Streptococcus pyogenes)
- Uncomplicated gonorrhea (cervical/urethral) caused by Neisseria gonorrhoeae (penicillinase and nonpenicillinase producing isolates)

The use of cefixime should be reserved for infections where the causative organism is known or suspected to be resistant to other commonly used antibiotics, or where treatment failure may carry significant risk.

DOSAGE AND ADMINISTRATION
The usual course of treatment is 7 days. In severe cases, this can be extended to 14 days.

Adults and children over 10 years of age (body weight is greater than 50 kg)
The recommended dose is 200-400 mg daily according to the severity of the infection, given either as a 400 mg single dose or as 200 mg in two divided doses.

Elderly patients
Elderly patients may be given the same dose as recommended for adults. Renal function should be assessed and dosage should be adjusted in severe impairment.

Children younger than 10 years of age (body weight is lower than 50 kg) – Paediatric Oral Suspension

The recommended dosage for children is 8 mg/kg/day administered as a single dose or in two divided doses. The following table describes a range of pediatric dosage according to the weight of the child:

Child's weight	Daily dose	Daily dose according to syringe graduations
5 kg	40 mg	2 mL (once daily) or 1 mL (twice daily)
10 kg	80 mg	4 mL (once daily) or 2 mL (twice daily)
12.5 kg	100 mg	5 mL (once daily) or 2.5 mL (twice daily)
15 kg	120 mg	6 mL (once daily) or 3 mL (twice daily)
17.5 kg	140 mg	7 mL (once daily) or 3.5 mL (twice daily)
20 kg	160 mg	8 mL (once daily) or 4 mL (twice daily)
22.5 kg	180 mg	9 mL (once daily) or 4.5 mL (twice daily)
25 kg	200 mg	10 mL (once daily) or 5 mL (twice daily)

Children weighing more than 50 kg or older than 10 years should be treated with the recommended adult dose (200-400 mg daily), depending on the severity of the infection.

Children younger than 6 months of age
The safety and efficacy in children aged less than 6 months has not been established.
The absorption of cefixime is not significantly affected by the presence of food. Hence it can be administered with or without food.

Renal impairment
It may be administered in the presence of impaired renal function. Normal dose and schedule may be given in patients with creatinine clearance of 20mL/ min or greater. In patients whose creatinine clearance is less than 20 mL/min, it is recommended that a dose of 200 mg once daily should not be exceeded. The dose and regimen for patients who are maintained on chronic ambulatory dialysis or hemodialysis should follow the same recommendation as that for patients with creatinine clearance of less than 20 mL/min.

CONTRAINDICATIONS:
- Hypersensitivity to the active substance, any of the excipients, or to other cephalosporin antibiotics.
- It is also contraindicated in patients with previous, immediate and/or severe hypersensitivity to penicillin or any beta-lactam antibiotics and preterm and term newborn infants (0-27 days).

PRECAUTIONS AND WARNING
Severe Cutaneous Adverse Reactions
Severe cutaneous adverse reactions such as toxic epidermal necrolysis, Stevens-Johnson syndrome and drug rash with eosinophilia and systemic symptoms (DRESS) have been reported in some patients on cefixime. When severe cutaneous adverse reactions occur, cefixime should be discontinued and appropriate therapy and/ormeasures should be taken. It should be given with caution to patients who have shown hypersensitivity to other drugs.

Hypersensitivity to Penicillin's
Cephalosporins should be given with caution to patients with a history of mild to moderate hypersensitivity to penicillin as there is some evidence of partial cross-allerginicitybetween penicillin and cephalosporins. Patients have had severe reactions (including anaphylaxis) to both classes of drugs. Special care is indicated in patients who have experienced any allergic reaction to penicillins or any beta-lactam antibiotics as cross-reactions may occur. If severe hypersensitivity reactions or anaphylactic reactions occur after administration of cefixime, the medicine should be discontinued immediately and appropriate emergency measures should be initiated.

Hemolytic Anemia
Drug-induced hemolytic anemia, including severe cases with a fatal outcome, has been described for cephalosporins (as a class). The recurrence of hemolytic anemia after re-administration of cephalosporins in a patient with a history of cephalosporin (including cefixime) - associated hemolytic anemia has also been reported.

Renal failure Acute
As with other cephalosporins, cefixime may cause acute renal failure including tubulointerstitial nephritis as an underlying pathological condition. When acute renal failure occurs, cefixime should be discontinued and appropriate therapy and/or measures should be taken.

Dose Adjustment in Renal Impairment
The dose of cefixime for oral suspension, should be adjusted in patients with renal impairment as well as those undergoing continuous ambulatory peritoneal dialysis (CAPD) and hemodialysis (HD). Patients on dialysis should be monitored carefully. There are insufficient data regarding use of cefixime in the paediatric and adolescent age group in the presence of renal insufficiency. The use of cefixime in these patient-groups is not recommended.

Clostridium Difficile Associated Diarrhoea
Clostridium difficile associated diarrhoea (CDAD) has been reported with use of nearly all antibacterial agents, including cefixime for oral suspension, and may range in severity from mild diarrhoea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C.difficile. C.difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing isolates of C.difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents. If CDAD is suspected or confirmed, ongoing antibiotic use not directed against C.difficile may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of C.difficile, and surgical evaluation should be instituted as clinically indicated.

Coagulation Effects
Cephalosporins, including cefixime, may be associated with a fall in prothrombin activity. Those at risk include patients with renal or hepatic impairment, or poor nutritional state, as well as patients receiving a protracted course of antimicrobial therapy, and patients previously stabilized on anticoagulant therapy. Prothrombin time should be monitored in patients at risk and exogenous vitamin K administered as indicated.

Development of Drug-Resistant Bacteria
Prescribing cefixime, in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of the development of drug resistant bacteria.

Pediatric Population
Safety of cefixime in premature or newborn infants has not been established.

Sucrose
Cefia contains sucrose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

DRUG INTERACTION
- The administration of cephalosporins may interfere with the results of some laboratory tests. A false positive reaction for glucose in the urine may occur with the Benedict's or Fehling's solutions or with copper sulphate test tablets, but not with tests based on enzymatic glucose oxidase reactions. A false positive direct Coombs' test has been reported during treatment with cephalosporin antibiotics, therefore it should be recognized that a positive Coombs' test may be due to the drug.
- Increased prothrombin time, with or without clinical bleeding, has been reported when cefixime is administered concomitantly.
- Care should therefore be taken in patients receiving anticoagulation therapy. Cefixime should be administered with caution to patients receiving coumarin-type anticoagulants, e.g. warfarin potassium. Since cefixime may enhance effects of the anticoagulants, prolonged prothrombin time with or without bleeding may occur.
- Nifedipine, a calcium channel blocker, may increase bioavailability of cefixime up to70%.
- Elevated carbamazepine levels have been reported when cefixime is administered concomitantly. Drug monitoring may be of assistance in detecting alterations in carbamazepine plasma concentrations.

USE IN SPECIFIC POPULATION
Pregnancy
There are no adequate and well controlled studies in pregnant women. Caution should be exercised when prescribing to pregnant women. Cefixime should not be used in pregnant mothers unless considered essential by the physician.

Breast-feeding
It is not known whether cefixime is excreted in human milk. Consideration should be given to discontinuing nursing temporarily during treatment with this drug.

Labour and Delivery
Cefixime has not been studied for use during labour and delivery. Treatment should only be given if clearly needed.

Paediatric Use
Safety and effectiveness of cefixime in children aged less than six months old have not been established.

Renal Impairment
The dose of cefixime should be adjusted in patients with renal impairment as well as those undergoing continuous ambulatory peritoneal dialysis (CAPD) and hemodialysis (HD). Patients on dialysis should be monitored carefully.

SIDE EFFECTS
The reported adverse events of cefixime are; diarrhoea, loose stool, superinfection bacterial, superinfection fungal, eosinophilia, hypersensitivity, anorexia, vertigo, dizziness, flatulence, angioneurotic edema, pruritus, mucosal inflammation, pyrexia, blood urea increased, headache, abdominal pain, nausea, vomiting, rash, hepatic enzyme increased (transaminase, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase), pseudomembranous colitis, leucopenia, agranulocytosis, pancytopenia, thrombocytopenia, hemolytic anemia, anaphylactic shock, serum sickness - like reaction, psychomotor hyperactivity, Stevens-Johnson Syndrome, toxic epidermal necrolysis, (Lyell syndrome), candidiasis, renal failure acute including tubulointerstitial nephritis as an underlying pathological condition, blood creatinine increased, vaginitis, granulocytopenia, hypereosinophilia, neutropenia, thrombocytosis, dyspepsia, drug rash with eosinophilia and systemic symptoms (DRESS), drug fever, erythema multiforme, urticaria, face edema, arthralgia, dyspnea, genital pruritus, blood bilirubin increased, seizures and hemorrhage.

DIRECTIONS FOR RECONSTITUTION:
Cefia 100mg/5mL and Cefia DS Suspension (30mL)
Shake the bottle to dislodge powder from inner surface. Add approximately half quantity of given water (10mL) into the bottle and shake. Then add remaining water (10mL) into the bottle. Close the bottle with cap tightly and shake well to make suspension. Shake well before each use and close the bottle with cap tightly after use. Reconstituted suspension should be used within 7 days at room temperature and within 12 days when stored in refrigerator.

Cefia 100mg/5mL Suspension (60mL)
Shake the bottle to dislodge powder from inner surface. Add freshly boiled & cooled water (20mL) into the bottle and shake. Then add freshly boiled & cooled water (20mL) up to the mark on bottle label. Close the bottle with cap tightly and shake well to make suspension. Shake well before each use and close the bottle with cap tightly after use. Reconstituted suspension should be used within 7 days at room temperature and within 12 days when stored in refrigerator.

Cefia 100mg/5mL and Cefia DS Suspension (Physician's sample 15mL)
Shake the bottle to dislodge powder from inner surface. Add approximately half quantity of given water (5mL) into the bottle and shake. Then add remaining water (5mL) into the bottle. Close the bottle with cap tightly and shake well to make suspension. Shake well before each use and close the bottle with cap tightly after use. Reconstituted suspension should be used within 7 days at room temperature and within 12 days when stored in refrigerator.

OVERDOSAGE
There is no experience with overdoses with cefixime. Adverse reactions seen at dose levels up to 2 g of cefixime in normal subjects did not differ from the profile seen in patients treated at the recommended doses cefixime is not removed from the circulation in significant quantities by dialysis. No specific antidote exists. General supportive measures are recommended.

DOSAGE AND INSTRUCTIONS
To be sold and used on the prescription of a registered medical practitioner only. Keep out of reach of children. Do not store above 30°C. Keep in a dry place. Protect from light.

PRESENTATIONS
Cefia 200mg Capsules: Alu. Alu. Blister Pack of 2 x 5's.
Cefia 400mg Capsules: Alu. Alu. Blister Pack of 1 x 5's.
Cefia 100mg/5mL Suspension:
Glass Amber Bottle of 30mL and 60mL.
Cefia DS 200mg/5mL Suspension:
Glass Amber Bottle of 30mL.

سیفیا®
(سیفکزائم)

خوراک و ہدایات:
صرف مستند ڈاکٹر کے نسخے کے مطابق ہی دوا فروخت اور استعمال کی جائے۔
بچوں کی پہنچ سے دور رکھیں۔ 30°C سے زیادہ درجہ حرارت پر نہ رکھیں۔
خشک جگہ پر رکھیں۔ روشنی سے بچائیں۔

Manufactured by
CUREXA HEALTH (PVT) LTD
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