Xineen™
(Cefixime)

زینین
(سیفیکزائم)
۴۰۰ ملی گرام کیپسولز
۱۰۰ ملی گرام/۵ ملی لیٹر سسپنشن یو۔ایس۔پی
۲۰۰ ملی گرام/۵ ملی لیٹر سسپنشن یو۔ایس۔پی ڈی ایس

Capsules 400mg
Dry Powder for Oral Suspension U.S.P. 100mg/5mL
Dry Powder for Oral Suspension U.S.P. 200mg/5mL DS

QUALITATIVE AND QUANTITATIVE COMPOSITION

Xineen™ Capsules 400mg
Each capsule contains:
Cefixime (as trihydrate) U.S.P.....400mg
Manufacturer's Specifications
Xineen™ Dry Powder for Oral Suspension U.S.P. 100mg/5mL
Each 5mL contains:
Cefixime (as trihydrate) U.S.P. 100mg
Xineen™ Dry Powder for Oral Suspension U.S.P. 200mg/5mL DS
Each 5mL contains:
Cefixime (as trihydrate) U.S.P. 200mg

DESCRIPTION

Cefixime is a semisynthetic, cephalosporin antibacterial for oral administration. It has marked in vitro bactericidal activity against a wide variety of Gram-positive and Gram-negative organisms.

CLINICAL PHARMACOLOGY

Mechanism of Action: Cefixime is a semisynthetic cephalosporin antibacterial drug. **Pharmacokinetics: Absorption:** Cefixime tablets and suspension, given orally, are about 40% to 50% absorbed whether administered with or without food; however, time to maximal absorption is increased approximately 0.8 hours when administered with food. The oral suspension produces average peak concentrations approximately 25% to 50% higher than the tablets. The 400mg capsule is bioequivalent to the 400mg tablet under fasting conditions. However, food reduces the absorption following administration of the capsule by approximately 15% based on AUC and 25% based on Cmax. Peak serum concentrations occur between 2 and 6 hours following oral administration of a single 200 mg tablet, a single 400 mg tablet or 400 mg of cefixime suspension. Peak serum concentrations occur between 2 and 5 hours following a single administration of 200 mg of suspension. Peak serum concentrations occur between 3 and 8 hours following oral administration of a single 400 mg capsule. **Distribution:** Serum protein binding is concentration independent with a bound fraction of approximately 65%. In a multiple dose study conducted with a research formulation which is less bioavailable than the tablet or suspension, there was little accumulation of drug in serum or urine after dosing for 14 days. Adequate data on CSF levels of cefixime are not available. **Metabolism and Excretion:** There is no evidence of metabolism of cefixime in vivo. Approximately 50% of the absorbed dose is excreted unchanged in the urine in 24 hours. In animal studies, it was noted that cefixime is also excreted in the bile in excess of 10% of the administered dose. The serum half-life of cefixime in healthy subjects is independent of dosage form and averages 3 to 4 hours but may range up to 9 hours in some normal volunteers.
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 and Proteus mirabilis.*

INDICATIONS AND USAGE

Cefixime is a cephalosporin antibacterial drug indicated in the treatment of adults and pediatric patients six months and older with the following infections:
•Uncomplicated Urinary Tract Infections
•Otitis Media
•Pharyngitis and Tonsillitis
•Acute Exacerbations of Chronic Bronchitis
•Uncomplicated Gonorrhea (cervical/urethral)
To reduce the development of drug-resistant bacteria and maintain the effectiveness of Cefixime and other antibacterial drugs, Cefixime should be used only to treat infections that are proven or strongly suspected to be caused by bacteria.

CONTRAINDICATIONS

Cefixime is contraindicated in patients with known allergy to cefixime or other cephalosporins & children less than six months old as safety and efficacy of cefixime in these patients have not been established. Cefixime 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).

INTERACTIONS

Carbamazepine: Elevated carbamazepine levels have been reported in postmarketing experience when cefixime is administered concomitantly. **Warfarin and Anticoagulants:** Increased prothrombin time, with or without clinical bleeding, has been reported when cefixime is administered concomitantly. **Drug/Laboratory Test Interactions:** A false-positive reaction for ketones in the urine may occur with tests using nitroprusside but not with those using nitroferricyanide. The administration of cefixime may result in a false-positive reaction for glucose in the urine using reagent tablet (copper reduction) & sodium hydroxide, Benedict's solution, or Fehling's solution. A false-positive direct Coombs test has been reported during treatment with other cephalosporins; therefore, it should be recognized that a positive Coombs test may be due to the drug. In use with Nifedipine, a calcium channel blocker, may increase bioavailability of Cefixime up to 70%.

USE IN SPECIFIC POPULATION

Pregnancy: Category B: This drug should be used during pregnancy only if clearly needed. **Labor and Delivery:** Cefixime has not been studied for use during labor and delivery. Treatment should only be given if clearly needed. **Nursing Mothers:** It is not known whether cefixime is excreted in human milk. Consideration should be given to discontinuing nursing temporarily during treatment with this drug. **Pediatric Use:** Safety and effectiveness of cefixime in children aged less than six months old have not been established. The incidence of gastrointestinal adverse reactions, including diarrhea and loose stools, in the pediatric patients receiving the suspension, was comparable to the incidence seen in adult patients receiving tablets. **Geriatric Use:** Clinical studies did not include sufficient numbers of subjects aged 65 and older to determine whether they respond differently than younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. A pharmacokinetic study in the elderly detected differences in pharmacokinetic parameters. These differences were small and do not indicate a need for dosage adjustment of the drug in the elderly. **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. In adults Reduce dose if eGFR less than 20 mL/minute/1.73 m^2 (max. 200mg once daily). In children Reduce dose if estimated glomerular filtration rate less than 20 mL/minute/1.73 m^2.

PRECAUTIONS

Hypersensitivity Reactions: Anaphylactic/anaphylactoid reactions (including shock and fatalities) have been reported with the use of cefixime. **Clostridium difficile-Associated Diarrhea:** Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including Cefixime, and may range in severity from mild diarrhea to fatal colitis. **Dose Adjustment in 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.

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. **Risk in Patients with Phenylketonuria:** Phenylalanine can be harmful to patients with phenylketonuria (PKU). Cefixime chewable tablets contain aspartame, a source of phenylalanine. Each 100 mg, 150 mg and 200 mg strength contains 3.3 mg, 5 mg and 6.7 mg of phenylalanine, respectively. Before prescribing Cefixime chewable tablets in a patient with PKU, consider the combined daily amount of phenylalanine from all sources, including Cefixime chewable tablets.

ADVERSE REACTIONS

Gastrointestinal: Several cases of documented *pseudomembranous colitis* were identified in clinical trials. The onset of pseudomembranous colitis symptoms may occur during or after therapy. **Hypersensitivity Reactions:** Anaphylactic/anaphylactoid reactions (including shock and fatalities), skin rashes, urticaria, drug fever, pruritus, angioedema, and facial edema. Erythema multiforme, Stevens-Johnson syndrome, and serum sickness-like reactions have been reported. **Hepatic:** Transient elevations in SGPT, SGOT, alkaline phosphatase, hepatitis, jaundice. **Renal:** Transient elevations in BUN or creatinine, acute renal failure. **Central Nervous System:** Headaches, dizziness, seizures. **Hemic and Lymphatic System:** Transient thrombocytopenia, leukopenia, neutropenia, prolongation in prothrombin time, elevated LDH, pancytopenia, agranulocytosis, and eosinophilia. **Abnormal Laboratory Tests:** Hyperbilirubinemia. **Other Adverse Reactions:** Genital pruritus, vaginitis, candidiasis, toxic epidermal necrolysis. **Adverse Reactions Reported for Cephalosporin-class Drugs:** Allergic reactions, superinfection, renal dysfunction, toxic nephropathy, hepatic dysfunction including cholestasis, aplastic anemia, hemolytic anemia, hemorrhage, and colitis. Several cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced. If seizures associated with drug therapy occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated. **Side effects:** Most common adverse reactions are gastrointestinal such as diarrhea, nausea, loose stools, abdominal pain, dyspepsia and vomiting.

DOSAGE AND ADMINISTRATION

Cefixime capsules can be taken with or without food. **Adults and children over 10 years:** The recommended adult dose of Cefixime is 200 - 400mg daily according to the severity of infection, given either as a single dose or in two divided doses. For the treatment of uncomplicated cervical/urethral gonococcal infections, a single oral dose of 400mg is recommended. The capsule and tablet may be administered without regard to food. In the treatment of infections due to *Streptococcus pyogenes*, a therapeutic dosage of cefixime should be administered for at least 10 days. **Pediatric Patients (6 months or older):** The recommended dose is 8 mg/kg/day of the suspension. This may be administered as a single daily dose or may be given in two divided doses, as 4mg/kg every 12 hours. As a general guide for prescribing in children the following daily doses in terms of volume of Pediatric Oral Suspension 100mg/5mL are suggested: **Acute infections due to sensitive Gram-positive and Gram - negative bacteria**

Child 6–11 months: 75 mg daily. **Child 1–4 years:** 100 mg daily.

Child 5–9 years: 200 mg daily.

Adult: 200–400 mg daily in 1–2 divided doses.

Uncomplicated gonorrhoea

Adult: 400 mg for 1 dose, For Pediatric Oral Suspension 200mg/5mL, the dose is followed as suggested by the physician. 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 infection). The safety and efficacy of cefixime has not been established in children less than 6 months. In the treatment of infections due to *Streptococcus pyogenes*, a therapeutic dosage of cefixime should be administered for at least 10 days.

Duration of therapy: The usual course of treatment is 7 days. In severe cases, this can be extended to 14 days. **Renal Impairment:** Cefixime may be administered in the presence of impaired renal function. Normal dose and schedule may be employed in patients with creatinine clearances of 60 mL/min or greater. Neither hemodialysis nor peritoneal dialysis removes significant amounts of drug from the body. **Overdosage:** Gastric lavage may be indicated; otherwise, no specific antidote exists. Cefixime is not removed in significant quantities from the circulation by hemodialysis or peritoneal dialysis. Adverse reactions in small numbers of healthy adult volunteers receiving single doses up to 2 g of cefixime did not differ from the profile seen in patients treated at the recommended doses.

INSTRUCTIONS:

Dosage as directed by the physician. Store at 20°C-25°C, excursions permitted to 15°C-30°C. Protect from light and moisture. **Direction for reconstitution:** Tap the bottle before reconstitution. To make 30mL suspension add some water invert bottle and shake well until all granules are dispersed. Then slowly add more water up to the mark on the bottle and shake well. Use only cool boiled water. **After reconstitution:** The reconstituted suspension can be used for up to 7 days, when stored at room temperature and up to 14 days when refrigerated. **SHAKE WELL BEFORE USE.** Keep the bottle tightly closed. Keep all medicines out of the reach of children. To be sold on the prescription of a registered medical practitioner only. Do not use suspension if seal is damaged or opened.

PRESENTATION

Xineen™ (Cefixime) Capsules 400mg are available in Alu-Alu blister pack of 1x5's capsules with leaflet.

Xineen™ (Cefixime) Dry Powder for Oral Suspension U.S.P. 100mg/5mL is available in 30mL pack (HDPE bottle) with leaflet.

Xineen™ (Cefixime) Dry Powder for Oral Suspension U.S.P. 200mg/5mL DS is available in 30mL pack (HDPE bottle) with leaflet.

زینین

(سیفیکزائم)

ہدایات: خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔ ۲۰ سے ۲۵ ڈگری سینٹی گریڈ پر رکھیں، محفوظ رکھنے کی حد ۱۵ سے ۳۰ ڈگری سینٹی گریڈ ہے۔ روشنی اور نمی سے محفوظ رکھیں۔

سسپنشن تیار کرنے کیلئے: سسپنشن تیار کرنے سے پہلے بوتل کو اچھی طرح ہلالیں۔ اُبلا ہوا ٹھنڈا پانی بوتل میں شامل کریں اور بوتل کو اچھی طرح ہلائیں تا کہ تمام دوا اچھی طرح حل ہو جائے۔ پھر مزید پانی بوتل پر دیئے ہوئے نشان تک شامل کر دیں اور بوتل کو دوبارہ اچھی طرح ہلالیں۔

سسپنشن تیار کرنے کے بعد: تیار شدہ سسپنشن کو کمرے کے درجہ حرارت پر ۷ دن تک استعمال کیا جا سکتا ہے جبکہ ۱۴ دن تک ریفریجریٹر میں محفوظ رکھا جا سکتا ہے۔ استعمال سے پہلے بوتل کو اچھی طرح ہلالیں۔

ڈھکن مضبوطی سے بند کر کے رکھیں۔ تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

صرف رجسٹرڈ ڈاکٹر کے نسخہ پر فروخت کریں۔

سسپنشن کی سیل خراب یا کھلی ہونے کی صورت میں استعمال نہ کریں۔

For detailed information please contact.

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