Efix®
(Cefixime)

Highnoon

COMPOSITION
Efix 400mg Capsule:
Each capsule contains:
Cefixime (as Trihydrate) 400mg

Efix 100mg/5mL Suspension:
After reconstitution each 5mL contains:
Cefixime (as Trihydrate) 100mg

Efix DS 200mg/5mL Suspension:
After reconstitution each 5mL contains:
Cefixime (as Trihydrate) 200mg

DESCRIPTION
Efix (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 nonrenal 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).
- Uncomplicated urinary tract infections (caused by Escherichia coli and Proteus mirabilis).
- 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).
- Is indicated in adults and pediatric patients six months of age or older with pharyngitis and tonsillitis caused by susceptible isolates of streptococcus pyogenes.
- To reduce the development of drug resistant bacteria and maintain the effectiveness of Cefixime and other antibacterial drugs, it should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antimicrobial therapy.

DOSAGE AND ADMINISTRATION
Adults
The recommended dose of cefixime is 400 mg daily. For the treatment of uncomplicated cervical/urethral gonococcal infections, a single oral dose of 400 mg is recommended. The capsule 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 suspension. This may be administered as a single daily dose or may be given in two divided doses, as 4 mg/kg every 12 hours. Suggested dose has been determined for each pediatric weight range as mentioned in the table below.

Suggested doses for pediatric patients

PEDIATRIC DOSAGE CHART
Doses are suggested for each weight range and rounded for ease of administration

		Efix (cefixime) for oral suspension	
		100mg/5mL	200mg/5mL
Patient Weight (Kg)	Dose/Day (mg)	Dose/Day (mL)	Dose/Day (mL)
5 to 7.5*	50	2.5	-
7.6 to 10*	80	4	2
10.1 to 12.5	100	5	2.5
12.6 to 20.5	150	7.5	4
20.6 to 28	200	10	5
28 to 33	250	12.5	6
33.1 to 40	300	15	7.5
40.1 to 45	350	17.5	9
45.1 or greater	400	20	10

*The preferred concentrations of oral suspension to use are 100mg/5mL or 200mg/5mL for pediatric patients in these weight ranges.

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. Dose adjustments for adults with renal impairment is mentioned in the below table.

Doses for adult with renal impairment

Renal dysfunction	Ceficime for oral suspension		Tablet
Creatinine Clearance (mL/min)	100mg/5mL	200mg/5mL	400mg
	Dose/Day(mL)	Dose/Day(mL)	Dose/Day
60 or greater	Normal dose	Normal dose	Normal dose
21 to 59* Or renal hemodialysis	13	6.5	Not appropriate
20 or less, or continuous peritoneal dialysis	8.6	4.4	0.5 tablet

*The preferred concentrations of oral suspension to use are 100mg/5mL or 200mg/5mL for patients with this dysfunction

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.

CONTRAINDICATIONS
- Hypersensitivity to the active substance, any of the excipients, or to other cephalosporin antibiotics.

PRECAUTIONS & 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/or measures should be taken. It should be given with caution to patients who have shown hypersensitivity to other drug.

Hypersensitivity Reactions
Anaphylactic/anaphylactoid reactions (including shock and fatalities) have been reported with the use of Cefixime. Before therapy with Cefixime, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions of cephalosporins, penicillin or other drugs. If this product is to be given to penicillin sensitive patients, should be exercised because cross hypersensitivity among beta-lactam antibacterial drugs has been clearly documented and may occur in patients with a history of penicillin allergy. If an allergic reaction to Cefixime occurs, discontinue the drug.

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 pediatric and adolescent age group in the presence of renal insufficiency. The use of cefixime in these patient-groups is not recommended.

Clostridium Difficile Associated Diarrhea
Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including Cefixime for oral suspension, and may range in severity from mild diarrhea 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.

Risk in patients with Phenylketonuria
Phenylalanine can be harmful to patients with Phenylketouria (PKU). Before prescribing Cefixime in a patient with PKU, consider the combined daily amount of Phenylalanine from all sources.

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

Sucrose
Efix 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.
- 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.

Labor and Delivery
Cefixime has not been studied for use during labor 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 anaemia, 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, hepatitis, jaundice, prolongation in prothrombin time, hyperbilirubinemia, toxic nephropathy, aplastic anemia and hemorrhage.

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.

DIRECTION FOR RECONSTITUTION. (For Suspension)
1. Tap bottle to loosen the powder.
2. Detach the top flat end of provided plastic ampoule of sterile water by twisting and open it.
3. Add approximately half quantity of water into the bottle of powder and shake.
4. Then add remaining water into the bottle of powder.
5. Close the cap tightly and shake well to make suspension.
6. Reconstituted suspension should be used within 7 days at room temperature and within 12 days when stored in refrigerator.

After reconstitution keep tightly closed.
Avoid freezing. Shake well before taking each dose.

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

ایفکس®
(سیفکروائم)

دوا تیار کرنے کا طریقہ: (برائے سسپنشن)
۱۔ بوتل کو اچھی طرح ہلائیں تا کہ اس میں موجود پاؤڈر بوتل کی دیواروں سے علیحدہ ہو جائے۔
۲۔ مہیا کردہ جراثیم سے پاک پانی کے ایمپول کا اوپر کا حصّہ گھما کر علیحدہ کریں اور اسے کھول دیں۔
۳۔ پانی کی تقریباً آدھی مقدار پاؤڈر کی بوتل میں ڈالیں اور بوتل کو ہلائیں۔
۴۔ اس کے بعد پانی کی بقیہ مقدار بوتل میں ڈالیں۔
۵۔ بوتل کا ڈھکن بند کریں اور اچھی طرح ہلا کر سسپنشن تیار کر لیں۔
۶۔ تیار شدہ دوا کمرے کے درجہ حرارت پر ۷ دن اور ریفریجریٹر کے درجہ حرارت پر ۱۲ دن تک استعمال کی جا سکتی ہے۔

سسپنشن بنانے کے بعد ڈھکن کو اچھی طرح بند رکھیں۔
دوا کو منجمد ہونے سے بچائیں۔
استعمال سے پہلے دوا کو اچھی طرح ہلا لیں۔

خوراک و ہدایات:
صرف مستند ڈاکٹر کے نسخہ 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۔

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FOCUS & RULZ
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