Martin Dow

TiXomer™ Dry Suspension/Capsules
(Cefixime)

ٹِکسومر ڈرائی سسپنشن / کیپسولز

COMPOSITION
Tixomer Dry Suspension 100 mg /5ml : Each 5ml contains:
Cefixime Trihydrate USP eqv. to Cefixime 100mg

Tixomer Dry Suspension 200 mg /5ml : Each 5ml contains:
Cefixime Trihydrate USP eqv. to Cefixime 200mg

Tixomer Capsules 400 mg: Each capsule contains:
Cefixime Trihydrate USP eqv. to Cefixime 400mg

DESCRIPTION
Tixomer (Cefixime) is a semisynthetic, third generation cephalosporin antibiotic for oral administration. Chemically, it is (6R,7R)-7-[2-(2-Amino-4-thiazolyl) glyoxylamido]-8-oxo-3-vinyl-5-thia-1-azabicyclo [4.2.0] oct-2-ene-2-carboxylic acid, 72-(Z)- [0- (carboxy methyl) oxime] trihydrate. It has a chemical formula $C_{16}H_{15}N_5O_7S_2.3H_2O$ and a molecular weight of 507.50 as the trihydrate.

THERAPEUTIC INDICATIONS
Tixomer (cefixime) is a cephalosporin antibacterial drug indicated in the treatment of the following infections caused by the following microorganisms susceptible to Cefixime:

Microorganisms
Streptococcus species, Streptococcus pneumoniae, Neisseria gonorrhoeae, Neisseria meningitis, Moraxella catarrhalis, Escherichia coli, Klebsiella pneumoniae, Serratia species, Proteus species, Providencia species, Morganella morganii, Haemophilus influenza, Haemophilus parainfluenza, Salmonella species, Shigella species, Aeromonas hydrophilia, Pasteurella multocida ,Citrobacter freundii, Citrobacter amalonaticus, Citrobacter diversus, Enterobacter species, Acinetobacter lwoffi, Yersinia enterocolitica , Campylobatcer jeujni.

Urinary Tract Infections
Infection of the kidneys and efferent urinary tract, Uncomplicated Urinary Tract Infections caused by susceptible isolates of Escherichia coli and Proteus mirabilis, Complicated and Uncomplicated Urinary Tract Infections except for prostatitis, Pyelonephritis, Cystitis, Gonococcal urethritis, Uncomplicated Gonorrhea (cervical/urethral)

Ear, Nose and Throat Infections
Otitis Media, Pharyngitis, Tonsillitis, Sinusitis, Laryngitis

Respiratory Tract Infection
Infection of Upper and Lower airways, Pulmonary Infections of bacterial etiology, Bronchitis (Acute and Chronic), Pneumonia, Bronchiectasis with infection, Secondary infection in chronic respiratory diseases.

Gastrointestinal Infections
Typhoid

Biliary Tract Infections
Infections of biliary tract, Cholecystitis, Cholangitis

Scarlet Fever

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.

DOSAGE AND ADMINISTRATION
Adult
The recommended dose of cefixime is 400mg daily to be given as 400mg capsule once a day. 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.
The usual course of treatment is 5-14 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.

Note: A suggested dose has been determined for each pediatric weight range. Refer to below table to ensure all orders that specify a dose in milliliters include a concentration, because cefixime for oral suspension is available in two different concentrations (100 mg/5 mL and 200 mg/5 mL).

	Doses are suggested for each weight range and rounded for ease of administration		
		Cefixime for Oral Suspension	
		100 mg/5 mL	200 mg/5 mL
Patient's 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
28.1 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

Children weighing more than 45 kg or older than 12 years should be treated with the recommended adult dose.

In the treatment of infections due to Streptococcus pyogenes, a therapeutic dosage of cefixime should be administered for at least 10 days.

Dosage in Renal Impairment
Cefixime may be administered in the presence of impaired renal function. Normal dose and schedule may be employed in patients with creatinine clearance of 60 ml/min or greater. Neither hemodialysis nor peritoneal dialysis removes significant amounts of drug from the body.

Doses for Adults with Renal Impairment

Renal Dysfunction	Tixomer (Cefixime) for oral suspension	
Creatinine clearance (ml/min)	100mg/5ml	200mg/5ml
	Dose/day (ml)	Dose/day (ml)
60 or greater	Normal dose	Normal dose
21 to 59 * OR renal hemodialysis*	13	6.5
20 or less OR continuous peritoneal dialysis	8.6	4.4

*The preferred concentrations of oral suspension to use are 200 mg/5 ml for patients with this renal dysfunction.

CONTRAINDICATIONS
Cefixime is contraindicated in patients with known allergy to cefixime or other cephalosporins.

WARNING AND PRECAUTIONS
Hypersensitivity Reactions
Anaphylactic/anaphylactoid reactions (including shock and fatalities) may occur with the use of cefixime. Before therapy with Cefixime is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cephalosporins, penicillins or other drugs. If this product is to be given to penicillin-sensitive patients, caution should be exercised because cross hypersensitivity among beta-lactam antibacterial drugs has been clearly documented and may occur in up to 10% of patients with a history of penicillin allergy. If an allergic reaction to cefixime occurs, discontinue the drug.

Clostridium difficile-associated Diarrhea
Clostridium difficile associated diarrhea (CDAD) is known to occur with use of nearly all antibacterial agents, including Cefixime, and may range in severity from mild diarrhea to fatal colitis. CDAD must be considered in all patients who present with diarrhea following antibacterial drug use. If CDAD is suspected or confirmed, ongoing antibacterial drug use not directed against C. difficile may need to be discontinued.

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 patients and increases the risk of the development of drug-resistant bacteria.

DRUG INTERACTION

Carbamazepine
Carbamazepine levels may be elevated when cefixime is administered concomitantly. Drug monitoring may be of assistance in detecting alterations in carbamazepine plasma concentrations.

Warfarin and Anticoagulants
Increased prothrombin time, with or without clinical bleeding, may be 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 Clinitest, Benedict's solution, or Fehling's solution. It is recommended that glucose tests based on enzymatic glucose oxidase reactions (such as Clinistix or TesTape) be used. 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.

CLINICAL PHARMACOLOGY

Mechanism of Action
As with other cephalosporins, bactericidal action of Cefixime results from inhibition of cell-wall synthesis. Cefixime is highly stable in the presence of beta-lactamase enzymes. As a result, many organisms resistant to penicillins and some cephalosporins due to the presence of beta-lactamases may be susceptible to Cefixime.

Pharmacokinetics
Absorption
Cefixime capsule and suspension, given orally, may be about 40% to 50% absorbed whether administered with or without food; however, time to maximal absorption may be increased approximately 0.8 hours when administered with food. The oral suspension produces average peak concentrations approximately 25% to 50% higher than the tablets, when tested in normal adult volunteers. 200 mg and 400 mg doses of oral suspension produce average peak concentrations of 3 mcg/mL (range 1 to 4.5 mcg/mL) and 4.6 mcg/mL (range 1.9 to 7.7 mcg/mL), respectively, when tested in normal adult volunteers. The area under the time versus concentration curve (AUC) is greater by approximately 10% to 25% with the oral suspension than with the tablet after doses of 100 to 400 mg, when tested in normal adult volunteers. This increased absorption should be taken into consideration if the oral suspension is to be substituted for the tablet. Crossover studies of tablet versus suspension have not been performed in children.

The 400 mg capsule is bioequivalent to the 400 mg 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 may occur between 2 and 5 hours following a single administration of 200mg/5ml suspension. Peak serum concentrations may occur between 3 and 8 hours following oral administration of a single 400mg capsule.

Distribution
Serum protein binding is known to be concentration independent with a bound fraction of approximately 65%.

Metabolism and Excretion
There is no evidence of metabolism of cefixime in vivo. Approximately 50% of the absorbed dose may excrete unchanged in the urine in 24 hours.

Special Populations
Geriatrics:
Average AUCs at steady state in elderly patients may be approximately 40% higher than average AUCs in other healthy adults.

Renal Impairment:
The drug may not clear significantly from the blood by hemodialysis or peritoneal dialysis. However, with doses of 400mg, patients undergoing hemodialysis may have similar blood profiles as patients with creatinine clearances of 21 to 60 ml/min.

OVERDOSE

Gastric lavage may be indicated; otherwise, no specific antidote exists. Cefixime may not remove in significant quantities from the circulation by hemodialysis or peritoneal dialysis.

SPECIAL POPULATION

Pregnancy
Pregnancy Category B: There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, 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 may occur in adult patients receiving tablets/capsules.

Geriatric Use
There is no identified difference in responses between the elderly and younger patients.

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.

ADVERSE REACTION

The most common adverse reactions are gastrointestinal events. These include diarrhea, loose or frequent stools, abdominal pain, nausea, dyspepsia, and flatulence.

Gastrointestinal
Pseudomembranous colitis may occur.

Hypersensitivity Reactions
Anaphylactic/anaphylactoid reactions (including shock and fatalities), skin rashes, urticaria, drug fever, pruritus, angioedema, facial edema. Erythema multiforme, Stevens-Johnson syndrome, and serum sickness-like reactions.

Hepatic
Transient elevations in serum glutamic pyruvic transaminase, serum glutamic oxaloacetic transaminase, alkaline phosphatase, hepatitis, jaundice.

Renal
Transient elevations in blood urea nitrogen or creatinine and acute renal failure.

Central Nervous System
Headaches, dizziness, seizures.

Blood Hemic and Lymphatic System
Transient thrombocytopenia, leukopenia, neutropenia, prolongation in prothrombin time, elevated lactate dehydrogenase, pancytopenia, agranulocytosis, and eosinophilia.

Abnormal Laboratory Tests
Hyperbilirubinemia.

Other Adverse Reactions
Genital pruritus, vaginitis, candidiasis, toxic epidermal necrolysis.

PRESENTATION

Tixomer Dry Suspension 100mg/5ml : Pack of 30 ml including distilled water
Tixomer Dry Suspension 200mg/5ml : Pack of 30 ml including distilled water
Tixomer Capsules 400 mg : Pack of 5's

DIRECTION FOR RECONSTITUTION (For 100 & 200 mg Suspension)

Please see reconstitution direction on the outer box.

STORAGE

Suspension:

Shake well before use.

Store below 30 °C.

The reconstituted suspension should be used within 7 days when stored at room temperature (20° to 30 °C) and within 14 days when stored in refrigerator.

Protect from light, heat & moisture.

Keep all medicines out of the reach of children.

سسپنشن :

استعمال سے پہلے بوتل کو اچھی طرح ہلا لیں۔

۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

تیار شدہ دوا کمرے کے درجہ حرارت (۲۰ سے ۳۰ ڈگری سینٹی گریڈ) پر ۷ دن کے بعد اور ریفریجریٹر میں رکھنے پر ۱۴ دن کے بعد استعمال نہ کریں۔

روشنی، گرمی اور نمی سے محفوظ رکھیں۔

تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

Capsules:

Store below 30 °C.

Protect from light, heat and moisture.

Keep all medicines out of the reach of children.

کیپسولز :

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روشنی، گرمی اور نمی سے محفوظ رکھیں۔

تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

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Martin Dow Marker Ltd
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