CEFIXIME
TERGECEF®

100 mg & 200 mg Capsule
100 mg/5 mL Granules for Suspension
20 mg/mL Granules for Suspension (Oral Drops)
ANTIBACTERIAL

FORMULATIONS
Each capsule contains:
Cefixime ..... 100 mg or 200 mg
Each 5 mL suspension contains:
Cefixime ..... 100 mg
Each mL suspension (oral drops) contains:
Cefixime ..... 20 mg

PRODUCT DESCRIPTIONS
Cefixime is a third generation cephalosporin which has antibacterial activity similar to penicillins, carbacephems and cephamycins. It has a vinyl group at the 3 position and a carboxymethoxylimino group at the 7 position of 7-aminocephalosporanic acid.

Descriptions of Cefixime (Tergecef®) capsules, granules for oral drops and granules for suspension are shown below.

Product	Capsule Size	Weight	Capsule Color
Cefixime (Tergecef®) Capsule 100 mg	No. 4	Approx. 0.16 g	Buff, opaque
Cefixime (Tergecef®) Capsule 200 mg	No. 2	Approx. 0.30 g	Maroon Opaque cap and rich yellow opaque body

Product	Color	Odor	Taste
Cefixime (Tergecef®) Granules for Suspension	Off white to cream colored	Strawberry	Pleasant
Cefixime (Tergecef®) Granules for Suspension (Oral Drops)	Off white to cream colored	Strawberry	Pleasant

PHARMACODYNAMICS
Cefixime exerts its bactericidal activity by interfering with the synthesis of the bacterial cell wall. It binds to specific penicillin-binding proteins responsible for the synthesis of peptidoglycan, a heteropolymeric structure that gives the cell wall its mechanical stability. The final stage of peptidoglycan synthesis involves completion of the cross-linking of the terminal glycine residue of the pentaglycine bridge to the fourth residue of the pentapeptide. The transpeptidase that catalyzes this step is inhibited by cephalosporins. Thus, inhibition of the transpeptidase interrupts peptidoglycan synthesis, causing formation of defective cell walls and osmotically unstable spheroplasts and lysis of the bacteria.

ANTIMICROBIAL SPECTRUM OF ACTIVITY
Cefixime is active against the following organisms, both *in vitro* and in clinical infections:

Gram-positive organisms	Gram-negative organisms
Streptococcus pneumoniae *Streptococcus pyogenes*	*Haemophilus influenzae* (β-lactamase positive and negative strains) *Moraxella catarrhalis* (most of which are β-lactamase positive) *Escherichia coli* *Proteus mirabilis* *Neisseria gonorrhoeae* (including penicillinase - and nonpenicillinase - producing strains) *Salmonella* spp. including *S. typhi* *Shigella* spp.

Cefixime has been shown to be active *in vitro* against most strains of Gram-positive organisms such as *Streptococcus agalactiae* and most strains of Gram-negative organisms such as *Haemophilus parainfluenzae* (β-lactamase positive and negative strains), *Proteus vulgaris, Klebsiella pneumoniae, Klebsiella oxytoca, Pasteurella multocida, Providencia* spp., *Citrobacter amalonaticus, Citrobacter diversus,* and *Serratia marcescens;* however, clinical efficacy has not been established.

PHARMACOKINETICS
Cefixime is about 30% to 50% absorbed after oral administration; food has no effect on its absorption. Peak serum concentrations (C_{max}) after a single, oral 200 or 400 mg dose of cefixime as capsule, tablet or oral suspension are attained between 2 to 6 hours. Although there are differences in pharmacokinetic parameters between the formulations, results of controlled, cross-over studies in healthy adults indicate that the capsules are essentially bioequivalent to tablets. However, oral suspension is more completely absorbed than tablets, thus, tablets theoretically should not be substituted for oral suspension.

Peak serum concentrations of cefixime are approximately 15-50% higher when the drug is administered as an oral suspension rather than as tablets. When 200 and 400 mg doses of cefixime are administered as an oral suspension, peak serum concentrations average 3-3.4 mcg/mL and 4.6 mcg/mL, respectively. Areas under the concentration-time curves (AUCs) of 100-400 mg cefixime oral suspension are approximately 10-25% higher than cefixime tablets. This lack of bioequivalence between dosage forms should be considered if the oral suspension is to be substituted for tablets.

Cefixime is not extensively bound to protein; the free drug is about 31% and is concentration-dependent. The absolute bioavailability based on comparisons of the concentration-time curve values after 200 mg intravenous, 200 mg oral solution, and 200 and 400 mg capsule doses ranged from 40-52%, showing a comparable bioavailability for cefixime at single 200 and 400 mg oral doses. In a four-way cross-over study, the serum concentration time curve values of cefixime was 52.3%, 47.9%, and 40.2% after the 200 mg oral solution, 200 mg capsule and 400 mg capsule doses, respectively. Respective ratios based on 24-hour urinary recovery data were 44.7%, 41.7%, and 40.5% for the 200 mg oral solution, 200 mg capsule and 400 mg capsule doses.

The serum elimination half-life of cefixime in adults with normal renal function ranges from 2.4-4 hours. Cefixime is eliminated by renal and nonrenal mechanisms. Urinary concentrations of cefixime generally range from 2.2-103 mcg/mL during the first 2 hours and from 15.07-305 mcg/mL 6-8 hours after a single 200 or 400 mg oral dose of the drug. Fecal concentrations of cefixime in healthy adults may range from 0.237-1.55 g/kg following usual oral doses of the drug as capsules or tablets.

Studies in children using cefixime doses of 4 to 8 mg/kg body weight indicate that serum concentrations of cefixime are not directly dose proportional. In a dose proportionality study in healthy adults using an oral dose range of 200 to 2000 mg cefixime, C_{max} and AUC increased linearly but were not also directly proportional with dose. Upon multiple dosing for 2 weeks with a 400 mg capsule daily or 200 mg twice daily regimen, serum concentrations and urinary recovery of unchanged drug were similar for each group showing that there was no drug accumulation.

INDICATIONS
For the treatment of the following infections due to susceptible microorganisms:
- Acute bronchitis, acute exacerbations of chronic bronchitis, bronchiectasis with infection, secondary infections in chronic respiratory tract diseases, pneumonia
- Urinary tract infections including pyelonephritis and cystitis
- Gonococcal urethritis
- Cholecystitis, cholangitis
- Scarlet fever
- Sinusitis, tonsillitis, pharyngitis, otitis media
- Typhoid fever (enteric fever) including multi-drug resistant typhoid fever

DOSAGE AND ADMINISTRATION
A. Cefixime (Tergecef®) 100 mg and 200 mg capsule

Age Group	General Recommended Oral Cefixime Dose
Adults and children older than 12 years (or weighing more than 50 kg)	400 mg once daily **or** 200 mg every 12 hours.
Children 7 to 12 years old who can swallow capsule whole	200 to 300 mg once daily **or** 100 mg every 12 hours
Or, as prescribed by a physician. Usual treatment duration: 7 to 14 days	

B. Oral Cefixime Dose for Specific Infections in Adults

Uncomplicated Cervical / Urethral Gonococcal Infections	Single 400 mg dose
Uncomplicated Urinary Tract Infection	100 mg twice daily **or** 200 mg once daily for 7 to 14 days
Uncomplicated Cystitis	200 mg twice daily **or** 400 mg once daily for 3 days
Uncomplicated Acute Pyelonephritis	200 mg twice daily **or** 400 mg once daily for 14 days
Typhoid Fever	200 mg twice daily **or** 400 mg once daily for 7 to 14 days

C. Cefixime (Tergecef®) 100 mg/5 mL suspension and Cefixime (Tergecef®) 20 mg/mL suspension (oral drops)
Dose in children: Usual recommended total daily dose is 8 mg/kg body weight given as a single dose or in two divided doses every 12 hours.

Typhoid Fever in children:
15 - 20 mg/kg body weight once daily or divided into two equal doses every 12 hours for 7 to 14 days.
Maximum dose is 400 mg/day.

AGE GROUP	CEFIXIME 20 mg/mL suspension (oral drops)		CEFIXIME 100 mg / 5mL suspension	
	Dose in mL		Dose in mL (Dose in teaspoonful)	
	Given once a day	Given every 12 hours	Given once a day	Given every 12 hours
6 to 11 months	2.5 to 5 mL	1.25 to 2.5 mL	(-)	(-)
1 to 2 years	2.5 to 5 mL	1.25 to 2.5 mL	2.5 to 5 mL (½ to 1 teaspoonful)	1.25 to 2.5 mL (¼ to ½ teaspoonful)
3 to 6 years	(-)	(-)	5 to 10 mL (1 to 2 teaspoonsful)	2.5 to 5 mL (½ to 1 teaspoonful)
7 to 12 years	(-)	(-)	10 to 15 mL (2 to 3 teaspoonsful)	5 mL to 7.5 mL (1 to 1 ½ teaspoonsful)
Children over 12 years old and Adults	(-)	(-)	20 mL (4 teaspoonsful)	10 mL (2 teaspoonsful)
Or, as prescribed by a physician. Usual treatment duration: 7 to 14 days.				

DIRECTIONS FOR RECONSTITUTION

Cefixime (Tergecef®) dosage format	Volume of Distilled Water to be added	Directions
Cefixime 20 mg/mL oral drops (10 mL)	6.8 mL	Tap the bottle several times to loosen the granules before reconstitution. Add the required amount of distilled water and shake vigorously until all contents are evenly suspended. Keep bottle tightly closed. Shake well before use.
Cefixime 100 mg/5mL suspension (30 mL)	19.8 mL	
Cefixime 100 mg/5mL suspension (60 mL)	39.6 mL	
Protect from light. Store for not more than 7 days at 25°C – 30°C (Room) or not more than 14 days at 4°C – 8°C (Refrigerator). Discard unused portion after 7 or 14 days depending on how the reconstituted product is stored.		

CONTRAINDICATIONS
- History of allergy to any ingredient in this product or other cephalosporins
- History of hypersensitivity to penicillins

WARNINGS AND PRECAUTIONS
A thorough inquiry about the patient's previous hypersensitivity history should be made. Cefixime, like other cephalosporins, penicillins and other drugs, may cause serious hypersensitivity reactions and should be used with caution in any patient who has demonstrated some allergy to any drug. Although it has not been established, allergic reactions to antibiotics may occur more frequently in atopic individuals.

Serious acute hypersensitivity reactions may require treatment with epinephrine and other emergency measures including oxygen, intravenous fluids and intravenous antihistamines, corticosteroids, pressor amines, and airway management as clinically indicated.

Clostridium difficile-associated diarrhea (CDAD) and colitis have been observed with the use of nearly all antibacterial agents, including cefixime, and may range in severity from mild to life threatening. It is important to consider this diagnosis in patients who present with diarrhea following administration of antibacterial agents.

A false-positive Coombs test has been reported during treatment with other cephalosporin antibiotics; therefore, it should be recognized that a positive Coombs test may be due to the drug, e.g., Coombs testing of newborns whose mothers have received cephalosporin antibiotics before parturition or in hematologic studies or in transfusion cross-matching procedures when antiglobulin tests are performed.

General

As with other broad-spectrum antibiotics, cefixime should be given with caution in individuals with a history of colitis. The safety and efficacy of cefixime have not been established in patients with gastrointestinal malabsorption.

Cephalosporins may be associated with a fall in prothrombin activity. Patients who are at risk are those with kidney or liver 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.

Prescribing cefixime in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of antibiotic resistance.

As with other antibacterial drugs, long term or repeated use may result in overgrowth of non-susceptible organisms, including fungi.

Carcinogenesis, Mutagenesis, Impairment of Fertility:

Studies have not been performed to date to evaluate the carcinogenic potential of cefixime.

INTERACTIONS WITH OTHER MEDICAMENTS
- **Carbamazepine:** Elevated carbamazepine levels have been reported when administered concomitantly with cefixime. Drug monitoring when these drugs are given together is advised.
- **Warfarin and other anticoagulants:** Increased prothrombin time, with or without clinical bleeding, has been reported when cefixime is given concomitantly
- **Probenecid:** Concomitant administration of probenecid reportedly increases peak serum concentration and AUC of cefixime and decreases renal clearance and volume of distribution of the drug.
- **Salicylates:** Concomitant administration of 650 mg oral dose of aspirin and a 400 mg oral dose of cefixime in healthy adult men may result in a 20-25% decrease in peak serum concentration of cefixime and AUC of the drug but did not affect protein binding, serum half-life or renal clearance. This effect may not be clinically important since serum concentrations of cefixime remained higher than the MIC values reported for most susceptible organisms. However, some clinicians state that this effect may be clinically important in certain infections.

Interference with Laboratory Tests:
- **Nitroprusside test:** A false-positive reaction for ketones in the urine may occur with tests using nitroprusside but not with those using nitroferricyanide.
- **Coombs test:** A false-positive direct Coombs test has been reported during treatment with other cephalosporin antibiotics; therefore it should be recognized that a positive Coombs test may be due to the drug.
- **Clinitest®, Benedict's solution, Fehling's solution:** A false-positive reaction for glucose in the urine using Clinitest®, Benedict's solution, or Fehling's solution may result when done during therapy with cefixime. It is recommended that other tests based on enzymatic glucose oxidase reactions be used instead.

STATEMENT ON USAGE FOR HIGH RISK GROUPS
- ***Use in Pediatric Patients :*** Safety and efficacy of cefixime in children less than six (6) months old have not been established.
- ***Renal Insufficiency:*** Administer cefixime with caution in the presence of markedly impaired renal function. Modification of usual dosage is not necessary in patients with moderate or severe renal impairment. However, because clinical experience with cefixime under such condition is limited, close clinical observation and appropriate laboratory studies should be made.

Pregnancy and Lactation
- ***Pregnancy:*** (Pregnancy category B) There are no adequate and well-controlled studies in pregnant women. Potential benefit should justify the potential risk when cefixime is used during pregnancy.
- ***Labor and Delivery:*** The effect of cefixime in labor and delivery is unknown.
- ***Lactation:*** It is not known whether cefixime is excreted in human milk. Consideration should be given to discontinuing breastfeeding temporarily during treatment with cefixime.

UNDESIRABLE EFFECTS
Most adverse effects reported with cefixime were similar to those reported with other oral cephalosporins and were usually mild and transient in nature.
- ***Hypersensitivity Reactions:*** Anaphylactic/anaphylactoid reactions (including shock and fatalities), skin rashes, urticaria, fever, pruritus, arthralgia, angioedema, facial edema; erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, serum sickness-like reactions
- ***Gastrointestinal Effects:*** Diarrhea, loose or frequent stools, abdominal pain, anorexia, flatulence, dry mouth, dyspepsia, nausea, and vomiting. Several cases of documented pseudomembranous colitis were identified during the clinical studies on cefixime. The onset of pseudomembranous colitis symptoms may occur during or after therapy.
- ***Hepatic Effects:*** Transient elevation of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase, hepatitis, and jaundice
- ***Renal Effects:*** Transient elevations in blood urea nitrogen (BUN) or creatinine levels, and rarely, acute renal failure
- ***Central Nervous System Effects:*** Headache, dizziness, nervousness, insomnia, somnolence, malaise, fatigue, seizures
- ***Hematologic Effects:*** Transient thrombocytopenia, leukopenia, neutropenia, and eosinophilia; prolongation of prothrombin time was seen rarely.
- ***Abnormal Laboratory Test:*** Hyperbilirubinemia
- ***Other Adverse Events:*** Rarely, genital pruritus, vaginitis, and candidiasis

The following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics:
- Allergic reactions, superinfection, renal dysfunction, toxic nephropathy, hepatic dysfunction including cholestasis, aplastic anemia, hemolytic anemia, hemorrhage, and colitis.
- **Abnormal Laboratory Tests:** Positive Coombs test, elevated lactate dehydrogenase (LDH), pancytopenia, agranulocytosis

OVERDOSE AND TREATMENT
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.

STORAGE
Keep the product out of sight and reach of children.
Store at temperatures not exceeding 30°C.

CAUTION: Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

Trusted Quality Healthcare

AVAILABILITY
- Cefixime (Tergecef®) 100 mg Capsule - in box of 50 capsules (in flex foil)
- Cefixime (Tergecef®) 200 mg Capsule - in box of 30 capsules (in flex foil)
- Cefixime (Tergecef®) 20 mg/mL Granules for Suspension (Oral Drops) in bottle of 10 mL
- Cefixime (Tergecef®) 100 mg/5mL Granules for Suspension in bottles of 30 and 60 mL

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