For the use of only a Registered Medical Practitioner or a Hospital or a Laboratory

Not to be sold by retail without the prescription of a Registered Medical Practitioner

Prescribing Information

1. Generic Name

Cefixime Dispersible Tablets IP 50 mg / 100 mg / 200 mg

(Brand Name: EXTACEF® 50 DT / 100 DT / 200 DT)

2. Qualitative and Quantitative Composition

Each dispersible uncoated tablet contains:

Cefixime IP as Trihydrate equivalent to Anhydrous Cefixime ….. 50 mg/ 100 mg/ 200 mg.

Excipients …….q.s.

3. Dosage Form and Strength

Dosage Form: Dispersible Tablets.

Dosage Strength: Cefixime 50 mg, 100 mg, 200 mg per tablet.

4. Clinical Particulars

4.1 Therapeutic Indication

EXTACEF is indicated in the treatment of following infections when caused by susceptible bacteria:

- Acute otitis media.
- Upper Respiratory Tract Infections (URTIs): E.g., Pharyngitis and tonsillitis.
- Lower Respiratory Tract Infections (LRTIs): E.g., Bronchitis, pneumonia.
- Urinary Tract Infections (UTIs): E.g., Cystitis, cystourethritis, uncomplicated pyelonephritis.
- Uncomplicated gonorrhea (cervical/urethral) caused by *Neisseria gonorrhoae* (penicillinase-and non-penicillinase-producing isolates).
- Typhoid fever.

4.2Posology and Method of Administration

For oral administration.

Adults and Children over 10 Years:

Usual Recommended Dose: Cefixime 200 to 400 mg daily according to the severity of infection, and given either as a single dose or in two divided doses.

Uncomplicated Gonorrhea: Cefixime 400 mg as single dose.

Or, as prescribed by the physician.

Children above 6 Months:

Usual Recommended Dose: Cefixime 8 mg/kg/day administered as a single dose or in two divided doses.
Typhoid Fever: Cefixime up to 20 mg/kg/day as a single dose or in 2 divided doses.
Or, as prescribed by the physician.

Children weighing more than 50 kg or older than 10 years should be treated with the recommended adult dose. The safety and efficacy of cefixime has not been established in children less than 6 months.

Absorption of cefixime is not significantly modified by the presence of food. Thus, EXTACEF may be taken regardless of food. The usual duration of treatment is 7 days. This may be continued for up to 14 days if required (such as in case of typhoid fever and other complicated and severe infections).

Directions for Reconstitution of the Dispersible Tablets
Dispersible Tablets should be reconstituted by the addition of an adequate amount of clean potable water (5 to 10 ml) immediately before use. Stir well until the tablet gets properly dispersed in the water and then swallow.

4.3Contraindications
EXTACEF Tablets are contraindicated in patients with known hypersensitivity to cefixime or to cephalosporin/beta-lactam antibiotics or to any component of the formulation.

4.4Special Warnings and Precautions for Use
Hypersensitivity to penicillins: As with other cephalosporins, cefixime should be given with caution to patients with a history of hypersensitivity to penicillin, as there is some evidence of partial cross-allergenicity between the penicillins and cephalosporins. Patients have had severe reactions (including anaphylaxis) to both classes of drugs. If an allergic effect occurs with EXTACEF, the drug should be discontinued and the patient treated with appropriate agents if necessary.
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. EXTACEF should be given with caution to patients who have shown hypersensitivity to other drugs.
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.
Acute renal failure: 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.

Antibiotic-associated diarrhoea: Treatment with broad spectrum antibiotics alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is a primary cause of antibiotic-associated diarrhoea. Pseudomembranous colitis is associated with the use of broad-spectrum antibiotics (including macrolides, semi-synthetic penicillins, lincosamides and cephalosporins); it is therefore important to consider its diagnosis in patients who develop diarrhoea in association with the use of antibiotics.

Symptoms of pseudomembranous colitis may occur during or after antibiotic treatment. Management of pseudomembranous colitis should include sigmoidoscopy, appropriate bacteriologic studies, fluids, electrolytes and protein supplementation. If the colitis does not improve after the drug has been discontinued, or if the symptoms are severe, oral vancomycin is the drug of choice for antibiotic-associated pseudomembranous colitis produced by *C. difficile*. Other causes of colitis should be excluded.

4.5Drug Interactions

Anticoagulants: As with other cephalosporins, increase in prothrombin time has been noted in a few patients. 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.

Other forms of interaction: A false positive reaction for glucose in the urine may occur with 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.

4.6Use in Special Populations

Pregnant Women

Pregnancy Category B. Reproduction studies have been performed in mice and rats at doses up to 400 times the human dose and has revealed no evidence of impaired fertility or harm to the fetus due to cefixime. In rabbits, at doses up to 4 times the human dose, there was no evidence of a teratogenic effect. There are no adequate and well-controlled studies in pregnant women. Thus, EXTACEF can be administered to pregnant women only if clearly needed and under medical supervision.

Lactating Women

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

Paediatric Patients

Safety of cefixime in premature or newborn infants has not been established. Use of cefixime under 6 months of age is not recommended. For dosage, please refer 'Posology and Method of Administration' section.

Geriatric 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 renal impairment.

Renal Impairment Patients

EXTACEF may be administered in the presence of impaired renal function. Normal dose and schedule may be given in patients with creatinine clearances of 20 ml/min or greater. In patients whose creatinine clearance is less than 20 ml/min or patients on peritoneal dialysis or haemodialysis, it is recommended that a dose of 200 mg once daily should not be exceeded.

4.7Effect on Ability to Drive and Use Machines

In the case of side effects such as encephalopathy (which may include convulsion, confusion, impairment of consciousness, movement disorders), the patient should not operate machines or drive a vehicle.

4.8Undesirable Effects

Clinical Trials Experience

The most commonly reported adverse reactions were gastrointestinal events. Individual adverse reactions included diarrhea (16%), loose or frequent stools (6%), abdominal pain (3%), nausea (7%), dyspepsia (3%), and flatulence (4%).

Post-Marketing Experience

Acute Generalized Exanthematous Pustulosis (AGEP) as an adverse drug reaction reported with the use of cefixime.

The following adverse reactions have been reported following the use of cefixime. Incidence rates were less than 1 in 50 (< 2%).

Gastrointestinal: Several cases of documented pseudomembranous colitis were identified in clinical trials. The onset of 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.

Hematologic System: Transient thrombocytopenia, leukopenia, neutropenia, prolongation in prothrombin time, elevated LDH, pancytopenia, agranulocytosis, and eosinophilia.

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

Abnormal Laboratory Tests: Hyperbilirubinemia.
Adverse Reactions Reported for Cephalosporin-Class Drugs: Allergic reactions, superinfection, renal dysfunction, toxic nephropathy, hepatic dysfunction including cholestasis, aplastic anemia, hemolytic anemia, hemorrhage, fixed drug eruption (FDE) 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.

4.9Overdose

There is no experience regarding overdose with cefixime. Adverse reactions seen at dose levels up to 2 g 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.

5. Pharmacological Properties

5.1 Mechanism of Action

Cefixime is an oral third generation cephalosporin which has marked *in vitro* bactericidal activity against a wide variety of Gram-positive and Gram-negative organisms.
Cefixime inhibits bacterial cell wall synthesis during cell multiplication and produces bactericidal action.

5.2Pharmacodynamic Properties

Cefixime has been shown to be active against most isolates of the following bacteria both *in vitro* and in clinical infections:

Gram-positive bacteria

- *Streptococcus pneumoniae*
- *Streptococcus pyogenes*

Gram-negative bacteria

- *Haemophilus influenzae*
- *Moraxella catarrhalis*
- *Escherichia coli*
- *Proteus mirabilis*
- *Neisseria gonorrhoeae*

The following *in vitro* data are available, but their clinical significance is unknown. Cefixime exhibits *in vitro* MICs of 1 mcg/ml or less against most (≥ 90%) isolates of the following bacteria; however, the safety and effectiveness of cefixime in treating clinical infections due to these bacteria have not been established in adequate and well-controlled clinical trials.

Gram-positive bacteria

- *Streptococcus agalactiae*

Gram-negative bacteria

- *Haemophilus parainfluenzae*
- *Proteus vulgaris*
- *Klebsiella pneumoniae*
- *Klebsiella oxytoca*
- *Pasteurella multocida*
- *Providencia species*
- *Salmonella species*
- *Shigella species*
- *Citrobacter amalonaticus*
- *Citrobacter diversus*
- *Serratia marcescens*

5.3Pharmacokinetic Properties

Absorption and Distribution: The absolute oral bioavailability of cefixime is in the range of 22 to 54%. Absorption is not significantly modified by the presence of food. Cefixime may therefore be given without regard to meals. Typically, the peak serum levels following the recommended adult or pediatric doses are between 1.5 and 3 mcg/ml. Little or no accumulation of cefixime occurs following multiple dosing. Serum protein binding is concentration-independent with a bound fraction of approximately 65%. Cefixime is almost exclusively bound to the albumin fraction. Protein binding of cefixime is only concentration-dependent in human serum at very high concentrations which are not seen following clinical dosing.

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 volunteers.

6. Nonclinical Properties

6.1 Animal Toxicology

Lifetime studies in animals to evaluate carcinogenic potential have not been conducted. Cefixime did not cause point mutations in bacteria or mammalian cells, DNA damage, or chromosome damage in vitro and did not exhibit clastogenic potential in vivo in the mouse micronucleus test. In rats, fertility and reproductive performance were not affected by cefixime at doses up to 25 times the adult therapeutic dose.

7. Description

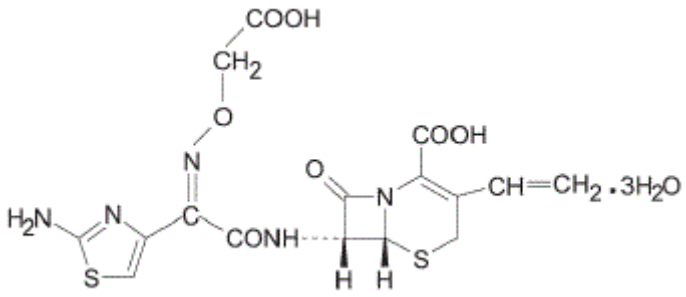
EXTACEF 50 DT are off-white coloured, flat round, beveled edged uncoated tablets with break line on one side and circle engraved on other side and having strawberry flavour.

EXTACEF 100 DT are off-white coloured, flat beveled, circular, uncoated tablets with break line on one side and circle engraved on other side and having strawberry flavour.

EXTACEF 200 DT are off-white, circular, flat beveled uncoated tablets with break line on one side and circle engraved on other side and having strawberry flavour.

EXTACEF 50 Tablets contain 50 mg of cefixime; EXTACEF 100 Tablets contain 100 mg of cefixime; EXTACEF 200 Tablets contain 200 mg of cefixime. These preparations are administered orally in adults and children.

Cefixime is a broad-spectrum, third-generation cephalosporin class of beta-lactam antibiotic.
Molecular Weight: 507.5 g/mol.
Molecular Formula: C16H21N5O10S2.
Chemical Name: (6R,7R)-7-[[(2Z)-2-(2-amino-1,3-thiazol-4-yl)-2-(carboxymethoxyimino)acetyl]amino]-3-ethenyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid; trihydrate.
Structural Formula:



Inactive ingredients (excipients) of EXTACEF 50 DT, EXTACEF 100 DT & EXTACEF 200 DT are Microcrystalline Cellulose, Saccharin Sodium, Flavour Capsaroma Strawberry , Menthol, Magnesium Stearate & Talc.

8. Pharmaceutical Particulars

8.1 Incompatibilities

None known.

8.2Shelf-life

24 Months

8.3Packaging Information

Strip of 10 tablets.

8.4Storage and Handling Instructions

Store protected from light and moisture at a temperature not exceeding 30°C.

Keep out of reach of children.

9. Patient Counseling Information

Administration Instructions

- Patients should be counseled that antibacterial drugs should only be used to treat bacterial infections. Not to use this medicine to treat infections caused by viruses.
- Patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may decrease the effectiveness of the treatment and increase the likelihood that bacteria will develop resistance to antibiotic.
- Advise patients that diarrhea is a common problem caused by antibacterial drugs which usually ends when the antibacterial drug is discontinued.
- Sometimes after starting treatment with antibacterial drugs, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months after having taken the last dose of the antibacterial drug. If this occurs, patients should contact their physician as soon as possible.

10.Details of Manufacturer

Blue Cross Laboratories Pvt Ltd.
A-12, MIDC, Ambad, Nashik - 422 010.

11.Details of Permission or License Number with Date

EXTACEF 50 DT : Mfg. Lic. No. : BD/28. Date of FDA Product Permission - 16/01/2002
EXTACEF 100 DT : Mfg. Lic. No. : BD/28.Date of FDA Product Permission - 30/11/2000
EXTACEF 200 DT : Mfg. Lic. No. : BD/28.Date of FDA Product Permission - 30/11/2000

12. Date of Revision

September 2022.