1. Name of the finished pharmaceutical product: EXTACEF- 200 DT

(Invented) name of the medicinal product: Cefixime Dispersible Tablets 200 mg

1.1 Strength: Cefixime 200 mg/Tablets

1.2 Pharmaceutical form: Oral Solid (Tablets)

2. Qualitative and quantitative composition

2.1 Qualitative declaration

Each dispersible tablet contains:

Cefixime USP as Trihydrate equivalent

to Anhydrous Cefixime ……..200 mg

Excipients ……q.s.

2.2 Quantitative declaration

Sr. No	Name of API	Grade	Label claim per Tab. in mg	Overages (%)	Input Qty/ Tab. in mg
1.	Cefixime (Trihydrate)	USP	200 mg	--	223.84

223.84 mg Cefixime Trihydrate is equivalent to 200 mg Anhydrous Cefixime.

3. Pharmaceutical form

Off-white, circular flat, beveled uncoated tablets with break line on one side and circle engraved on other side and having strawberry flavor.

Packed in Printed aluminium strip containing 10 tablets, 1 strip packed in a printed carton along with leaflet.

4. Clinical particulars

4.1 Therapeutic indications

EXTACEF 200 DT is indicated in the treatment of following infections when caused by susceptible bacteria:

- Acute otitis media.
- Upper Respiratory Tract Infections (URTIs)
- Lower Respiratory Tract Infections (LRTIs)

- Urinary Tract Infections (UTIs)
- Uncomplicated gonorrhea (cervical/urethral) caused by *Neisseria gonorrhoae* (penicillinase-and non-penicillinase-producing isolates).
- Typhoid fever.

4.2 Posology 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 200 DT 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.

4.3 Method of Administration: By oral route

4.4 Contraindications

EXTACEF 200 DT is contraindicated in patients with known hypersensitivity to Cefixime or to cephalosporin/beta-lactam antibiotics or to any component of the

formulation.

4.5 Special 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 200 DT, 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 200 DT 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.

4.6 Paediatric Population

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.

4.7 Interaction with other medicinal products and other forms of interaction

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.

4.8 Additional information on special population

Elderly population: 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: EXTACEF 200 DT 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 hemodialysis, it is recommended that a dose of 200 mg once daily should not be exceeded.

4.9 Paediatric Population

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.

4.10 Fertility, pregnancy and lactation

Pregnancy

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 200 DT can be administered to pregnant women only if clearly needed and under medical supervision.

Breast-feeding

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

Fertility

There was no evidence of impaired fertility found in animal studies.

4.11 Effects 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.

4.12 Undesirable effects

The most commonly reported adverse reactions were gastrointestinal events like diarrhea, loose or frequent stools, abdominal pain, nausea, dyspepsia, and flatulence.

Other adverse effects that may occur with this formulation include:

Gastrointestinal: Pseudomembranous colitis

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

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: Following adverse reactions have been reported for cephalosporin-class antibiotics: Allergic reactions, superinfection, renal dysfunction, toxic nephropathy, hepatic dysfunction including cholestasis, aplastic anemia, hemolytic anemia, hemorrhage, fixed drug eruption (FDE) and colitis.

4.13 Overdose

Symptoms: 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.

Treatment: 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 Pharmacodynamic properties

Pharmacotherapeutic group: Cephalosporin Antibiotics

ATC Code: J01DD08

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.

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*

5.2 Pharmacokinetic properties

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.

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.

5.3 Preclinical safety data

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.

6. Pharmaceutical particulars

6.1 List of excipients

Microcrystalline Cellulose, Saccharin Sodium, Flavour Strawberry DCS 309 PH, Levomenthol, Magnesium Stearate and Purified Talc.

6.2 Incompatibilities

Not known

6.3 Shelf-life

30 Months

6.4 Special precaution for storage

Store below 30°C in a dry place. Protect from light.

Keep out of reach of children.

6.5 Nature and contents of container

1 x 10's

Printed aluminium strip containing 10 tablets, 1 strip packed in a printed mono carton.

6.6 Special precautions for disposal and other handling

No special requirements.

7. Marketing Authorisation Holder and Manufacturing Site Addresses

Blue Cross Laboratories Pvt Ltd.

A-12, MIDC, Ambad, Nashik – 422010, Maharashtra, India.

8. Marketing authorization number(s)

Rwanda FDA- HMP-MA-1180

9. Date of first authorization/renewal of the authorization

Date of authorization : 06/05/2024

10. Date of Revision of the Text

May 2024.

11. Dosimetry (If Applicable)

Not Applicable.

12. Instructions for Preparation of Radiopharmaceuticals (If Applicable)

Not Applicable.