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

TOPCEF DT

1. Generic Name

Cefixime Dispersible Tablets I.P.

2. Qualitative and quantitative composition

TOPCEF-50 DT

Each uncoated dispersible tablet contains:
Cefixime I.P. as Trihydrate equivalent to Anhydrous
Cefixime ..... 50 mg
Colour : Tartrazine
Excipients…q.s.
In a flavoured base

TOPCEF 100 DT

Each uncoated dispersible tablet contains:
Cefixime I.P. as Trihydrate equivalent to Anhydrous
Cefixime ..... 100 mg
Colour : Tartrazine
In a flavoured base

The excipients used are Colloidal silicon dioxide, Colloidal silicon dioxide, Cross povidone, Lake of Tartrazine, Magnesium stearate, Dragoco mango flavour, Microcrystalline cellulose, Saccharin sodium, Sodium starch glycollate, Talc, Tartrazine yellow food grade and Aspartame.

3. Dosage form and strength

Dosage Form: Uncoated Dispersible Tablets
Strength: 50 mg and 100 mg

4. Clinical particulars

4.1 Therapeutic indication

Cefixime is an orally active cephalosporin antibiotic which has marked in vitro bactericidal activity against a wide variety of Gram-positive and Gram-negative organisms.

It is indicated for the treatment of the following acute infections when caused by susceptible micro-organisms:

Upper Respiratory Tract Infections (URTI): e.g. otitis media; and other URTI where the causative organism is known or suspected to be resistant to other commonly used antibiotics, or where treatment failure may carry significant risk.

Lower Respiratory Tract Infection: e.g. bronchitis.

Urinary Tract Infections: e.g. cystitis, cystourethritis, uncomplicated pyelonephritis.
Clinical efficacy has been demonstrated in infections caused by commonly occurring pathogens including Streptococcus pneumoniae, Streptococcus pyogenes, Escherichia coli, Proteus mirabilis, Kliebsiella species, Haemophilus influenzae (beta-lactamase positive and negative), Branhamella catarrhalis (beta-lactamase positive and negative)

and Enterobacter species. Cefixime is highly stable in the presence of beta-lactamase enzymes.

Billiary Tract Infections

Most strains of enterococci (Streptococcus faecalis, group D Streptococci) and Staphylococci (including coagulase positive and negative strains and meticillin-resistant strains) are resistant to Cefixime. In addition, most strains of Pseudomonas, Bacteriodes fragalis, Listeria monocytogenes and Clostridia are resistant to Cefixime

4.2 Posology and method of administration

The usual course of treatment is 7 days. This may be continued for up to 14 days if required.

Posology

Adults and Children over 10 Years or weighing more than 50 kg:

The recommended adult dosage is 200-400 mg daily according to the severity of infection, given either as a single dose or in two divided doses.

Elderly:

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 (See "Dosage in Renal Impairment").

Children under 10 Years:

Topcef DT is not recommended for use in children under 10 years old.

The safety and efficacy of cefixime has not been established in children less than 6 months.

Renal Impairment:

Topcef 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, it is recommended that a dose of 200 mg once daily should not be exceeded. The dose and regimen for patients who are maintained on chronic ambulatory peritoneal dialysis or haemodialysis should follow the same recommendation as that for patients with creatinine clearances of less than 20 ml/min.

Method for administration

For oral administration.

Disperse the tablet in 10ml of boiled and cooled water before administration

Absorption of Topcef DT is not significantly modified by the presence of food.

4.3 Contraindications

Topcef DT is contraindicated in the patients with known hypersensitivity to cephalosporin antibiotics or to any of the excipients.

4.4 Special warnings and precautions for use

Encephalopathy

Beta-lactams, including cefixime, predispose the patient to encephalopathy risk (which may include convulsions, confusion, impairment of consciousness, movement disorders), particularly in case of overdose or renal impairment.

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.

Topcef DT should be given with caution to patients who have shown hypersensitivity to other drugs.

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 Topcef DT, the drug should be discontinued and the patient treated with appropriate agents if necessary.

Haemolytic anaemia
Drug-induced haemolytic anaemia, including severe cases with a fatal outcome, has been described for cephalosporins (as a class). The recurrence of haemolytic anaemia after re-administration of cephalosporins in a patient with a history of cephalosporin (including cefixime) –associated haemolytic anaemia 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.

Renal impairment
Topcef DT should be administered with caution in patients with markedly impaired renal function (See section 4.2).

Paediatric use
Safety of cefixime in premature or newborn infant has not been established.
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.

4.5 Drugs interactions

Anticoagulants

In common with other cephalosporins, increases in prothrombin times have 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 recognised that a positive Coombs test may be due to the drug.

4.6 Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

As per reported data, reproduction studies have been performed in mice and rats at doses up to 400 times the human dose and have revealed no evidence of impaired fertility or harm to the foetus due to cefixime. In the rabbit, at doses up to 4 times the human dose, there was no evidence of a teratogenic effect; there was a high incidence of abortion and maternal death which is an expected consequence of the known sensitivity of rabbits to antibiotic-induced changes in the population of the microflora of the intestine. There are no adequate and well-controlled studies in pregnant women. Topcef DT should therefore not be used in pregnancy or in nursing mothers unless considered essential by the physician.

4.7 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.

4.8 Undesirable effects

Topcef DT is generally well tolerated. The majority of adverse reactions observed in clinical trials were mild and self-limiting in nature.

The following adverse reaction (Preferred term# or equivalent) will be considered listed:

Blood and lymphatic system disorders:	Eosinophilia Hypereosinophilia Agranulocytosis Leucopenia Neutropenia Granulocytopenia Haemolytic anaemia Thrombocytopenia Thrombocytosis
Gastrointestinal disorders:	Abdominal pain

	Diarrhoea* Dyspepsia Nausea Vomiting Flatulance
Hepatobiliary disorders:	Jaundice
Infections and infestations:	Pseudomembranous colitis
Investigations:	Aspartate aminotransferase increased Alanine aminotransferase increased Blood bilirubin increased Blood urea increased Blood creatinine increased
Nervous system disorders:	Dizziness Headache Cases of convulsions have been reported with cephalosporins including cefixime (frequency not known)** Beta-lactams, including cefixime, predispose the patient to encephalopathy risk (which may include convulsions, confusion, impairment of consciousness, movement disorders), particularly in case of overdose or renal impairment (frequency not known)**
Respiratory, thoracic and mediastinal disorders:	Dyspnoea
Renal and urinary disorders:	Renal failure acute including tubulointerstitial nephritis as an underlying pathological condition
Immune system disorders, administrative site conditions, skin and subcutaneous tissue disorders:	Anaphylactic reaction Serum sickness-like reaction Drug rash with eaosinophilia and systemic symptoms (DRESS) Pruritus Rash Drug Fever Arthralgia Erythema multiforme Acute generalized exanthematous pustulosis (AGEP) Stevens-Johnson syndrome Toxic epidermal necrolysis Angio-oedema Urticaria Pyrexia Face oedema Genital pruritus Vaginitis

The above mentioned listed adverse reactions have been observed during clinical studies and/or during marketed use.
Preferred term in MedDRA (v.14.0)
*Diarrhoea has been more commonly associated with higher doses. Some cases of moderate to severe diarrhoea have been reported; this has occasionally warranted cessation of therapy. Topcef DT should be discontinued if marked diarrhoea occurs
** Cannot be estimated from available data

- **Reporting of side effects**

  If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: http://www.torrentpharma.com/Index.php/site/info/adverse_event_reporting.

4.9 Overdose

There is a risk of encephalopathy in cases of administration of beta-lactam antibiotics, including cefixime, particularly in case of overdose or renal impairment.

Adverse reactions seen at dose levels up to 2 g Topcef DT 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

Pharmacotherapeutic group: third generation cephalosporin, ATC code: J01DD08.

The bactericidal action of Topcef DT is due to the inhibition of cell wall synthesis. It binds to one of the penicillin binding proteins (PBPs) which inhibits the final transpeptidation step of the peptidoglycan synthesis in the bacterial cell wall, thus inhibiting biosynthesis and arresting cell wall assembly resulting in bacterial cell death.

5.2 Pharmacodynamic properties

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.

In reported studies, clinical efficacy has been demonstrated in infections caused by commonly occurring pathogens including Streptococcus pneumoniae, Streptococcus pyogenes, Escherichia coli, Proteus mirabilis, Klebsiella species, Haemophilus influenzae (beta-lactamase positive and negative), Branhamella catarrhalis (beta-lactamase positive and negative) and Enterobacter species. It is highly stable in the presence of beta-lactamase enzymes.

Most strains of enterococci (Streptococcus faecalis, group D Streptococci) and Staphylococci (including coagulase positive and negative strains and meticillin-resistant strains) are resistant to cefixime. In addition, most strains of Pseudomonas, Bacteroides fragilis, Listeria monocytogenes and Clostridia are resistant to cefixime.

5.3 Pharmacokinetic properties

The absolute oral bioavailability of cefixime is in the range of 22-54%. Absorption is not significantly modified by the presence of food. Cefixime may therefore be given without regard to meals.

From reported in vitro studies, serum or urine concentrations of 1 mcg/mL or greater were considered to be adequate for most common pathogens against which cefixime is active. Typically, the peak serum levels following the recommended adult or paediatric doses are between 1.5 and 3 mcg/mL. Little or no accumulation of cefixime occurs following multiple dosing.

The pharmacokinetics of cefixime in healthy elderly (age > 64 years) and young volunteers (11-35) compared the administration of 400 mg doses once daily for 5 days. Mean C_{max} and AUC values were slightly greater in the elderly. Elderly patients may be given the same dose as the general population.

Cefixime is predominantly eliminated as unchanged drug in the urine. Glomerular filtration is considered the predominant mechanism. Metabolites of cefixime have not been isolated from human serum or urine.

Serum protein binding is well characterised for human and animal sera; cefixime is almost exclusively bound to the albumin fraction, the mean free fraction being approximately 30%. Protein binding of cefixime is only concentration dependent in human serum at very high concentrations which are not seen following clinical dosing.

Transfer of ^{14}C-labelled cefixime from lactating rats to their nursing offspring through breast milk was quantitatively small (approximately 1.5% of the mothers' body content of cefixime in the pup). No data are available on secretion of cefixime in human breast milk. Placetal transfer of cefixime was small in pregnant rats dosed with labelled cefixime.

6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the Summary of Product Characteristics.

7. Description

TOPCEF 50 DT:
Yellow colored, round, flat, uncoated tablets with breakline on one side, having pleasant flavour and dark yellow spots.

TOPCEF 100 DT:
Yellow colored, round, flat, uncoated tablets with breakline on one side, having pleasant flavour.

TOPCEF-200:
Yellow colored with dark yellow spots, round, flat beveledged, uncoated tablets having deep breakline on one side and plain on other side. The tablets have pleasant taste with mango flavour.

8. Pharmaceutical particulars

8.1 Incompatibilities

None Stated

8.2 Shelf-life

Do not use later than date of expiry

8.3 Packaging information

Available in strip of 10 Tablets

8.4 Storage and handing instructions

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

9. Patient Counselling Information

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

• Keep this leaflet. You may need to read it again.

• If you have any further questions, ask your doctor or pharmacist.

• This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.

• If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 9.4.

What is in this leaflet:

1. What Topcef DT is and what they are used for
2. What you need to know before you use Topcef DT
3. How to use Topcef DT
4. Possible side effects
5. How to store Topcef DT
6. Contents of the pack and other information

9.1 What Topcef DT is and what it is used for.

Topcef DT contains a medicine called cefixime. This belongs to a group of antibiotics called 'cephalosporins'.

Topcef DT is used to treat infections caused by bacteria. These include infections of the:

• Ear
• Nose, sinuses (such as sinusitis)
• Throat (such as tonsillitis, pharyngitis)
• Chest and lungs (such as bronchitis, pneumonia)
• Urinary system (such as cystitis and kidney infections.
• Biliary tract infections

9.2 What you need to know before you use Topcef DT.

Do not use Topcef DT:

- if you are allergic to cefixime, any other cephalosporin antibiotics including penicillin or to any of the other ingredients of this medicine (listed in section 6). Signs of an allergic reaction include: a rash, swallowing or breathing problems, swelling of the lips, face, throat and tongue.

Do not take this medicine if the above applies to you. If you are not sure, talk to your doctor or pharmacist before taking Topcef DT.

Warnings and precautions

Talk to your doctor or pharmacist before taking Topcef DT:

- if you have ever had colitis
- if you have kidney problems

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before taking this medicine.

Other medicines and Topcef DT
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines. This includes medicines you buy without a prescription, including herbal medicines. This is because Topcef DT can affect the way some other medicines work. Also some medicines can affect the way Topcef DT works. In particular, tell your doctor if you are taking the following:

• Medicines to thin the blood such as warfarin

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines
This medicine can cause symptoms including fits (convulsions), feeling confused, feeling less alert or aware of things than usual, unusual muscle movements or stiffness. If you experience any of these effects don't drive or use machinery.

Medical Tests
If you require any tests (such as blood or urine tests) while taking this medicine, please make sure your doctor knows that you are taking Topcef DT

9.3 How to use Topcef DT
Always take Topcef DT exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

• Take this medicine by mouth
• Disperse the tablet in 10ml of boiled and cooled water before administration
• If you feel the effect of the medicine is too weak or too strong, do not change the dose yourself, but ask your doctor.

Carefully read the label from the pharmacist. Ask your pharmacist if you are not sure about the dose to take. The medicine should be taken for the prescribed number of days.

The recommended dose is:

Adults, Elderly and Children over 10 years or weighing more than 50kg
• 1-2 tablets each day given as a single or divided dose

People with kidney problems
• Your doctor may prescribe a lower dose

Children under 10 years old
• Topcef DT should not be given to children under 10 years old

If you take more Topcef DT than you should
If you have too much of this medicine, talk to your doctor straight away.

If you forget to take Topcef DT
If you forget to take a dose, take it as soon as you remember. However, if it is nearly time for the next dose, skip the missed dose. Do not take a double dose to make up for a forgotten dose.

If you stop taking Topcef DT
Do not stop taking this medicine without talking to your doctor. You should not stop taking Topcef DT just because you feel better. This is because the infection may come back or get worse again.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

9.4 Possible Side Effects
Like all medicines, these tablets can cause side effects, although not everybody gets them.

Tell your doctor straight away or go to the nearest hospital casualty department if you notice any of the following serious side effects-you may need urgent medical treatment:

• You have an allergic reaction. The signs may include: a rash, joint pain, swallowing or breathing problems, swelling of your lips, face, throat or tongue

• Blistering or bleeding of the skin around the lips, eyes, mouth, nose and genitals. Also flu-like symptoms and fever. This may be something called 'Stevens-Johnson' syndrome.

• Severe blistering rash where layers of the skin may peel off to leave large areas of raw exposed skin over the body. Also a feeling of being generally unwell, fever, chills and aching muscles. This may be something called 'Toxic epidermal necrolysis'

• You have a skin rash or skin lesions with a pink/red ring and a pale centre which may be itchy, scaly or filled with fluid. The rash may appear especially on the palms or soles of your feet. These could be signs of a serious allergy to the medicine called 'erythema multiforme'

• You get infections more easily than usual. This could be because of a blood disorder. This normally gets better after stopping the medicine

• You bruise or bleed more easily than normal. This could be because of a blood disorder.

This normally gets better after stopping the medicine

• If your child gets nose bleeds, bleeding gums, chills, tiredness, pale skin (often with a yellow tinge), shortness of breath. This may be due to haemolytic anaemia.

• Changes in the way the kidneys are working or blood in your child's urine

• Fits (convulsions) - Frequency not known • A brain condition with symptoms including fits (convulsions), feeling confused, feeling less alert or aware of things than usual, unusual muscle movements or stiffness. This may be something called encephalopathy. This side effect is more likely if you have taken an overdose or you already have a problem with your kidneys.

Stop taking this medicine and contact your doctor without delay if you get:

• Severe watery diarrhoea that will not stop and you are feeling weak and have a fever. This may be something called 'Pseudomembranous colitis'

Tell your doctor or pharmacist if any of the following side effects get serious or lasts longer than a few days:
• Feeling sick (nausea), being sick (vomiting)
• Stomach pains, indigestion or wind

• Headaches
• Feeling dizzy
• Feeling itchy in the genital or vaginal area

Tell your doctor if any of the side effects gets serious or lasts longer than a few days, or if you notice any side effects not listed in this leaflet.

Blood Tests
Topcef DT can cause blood clots or small changes to the way the liver and kidney work. This would be shown up in blood tests. This is not common and goes back to normal after stopping this medicine.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: http://www.torrentpharma.com/Index.php/site/info/adverse_event_reporting.
By reporting side effects, you can help provide more information on the safety of this medicine.

9.5 How to store Topcef DT
Keep out of the sight and reach of children. Do not take this medicine after the expiry date shown on the blister and carton after EXP. The expiry date refers to the last day of that month. Store at a temperature not exceeding 30°c, protected from moisture. Medicines should not be disposed of via household wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help protect the environment

9.6 Contents of the pack and other information

What Topcef DT contains:
The active substance in this product is Cefixime.

The other ingredients are Colloidal silicon dioxide, Colloidal silicon dioxide, Cross povidone, Lake of Tartrazine, Magnesium stearate, Dragoco mango flavour, Microcrystalline cellulose, Saccharin sodium, Sodium starch glycollate, Talc, Tartrazine yellow food grade and Aspartame.

10. Details of manufacturer
Manufactured by:
Torrent Pharmaceuticals Ltd.
Indrad-382 721, Dist.Mehsana, INDIA
At : Village : Sachana, Tal-Viramgam,
Dist. Ahmedabad 382 150

11. Details of permission or licence number with date
Mfg.Lic.no.: G/28A/5366-A dated 16.12.2015

12. Date of revision
Aug 2019

MARKETED BY

TORRENT PHARMACEUTICALS LTD.
IN/TOPCEF DT 50mg, 100mg/Aug-2019/02/PI