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

SEFDIN

1. Generic Name

Cefdinir Capsules I.P. 300 mg

2. Qualitative and quantitative composition

Each capsule contains:

Cefdinir I.P. ……300 mg

Excipients…….q.s.

Approved colours used in capsule shell.

The excipients used are Carboxymethylcellulose Calcium, Croscarmellose Sodium, Sodium Lauryl Sulphate, Sodium Starch Glycolate, Magnesium Stearate and Talc.

3. Dosage form and strength

Dosage form: Capsules

Strength: 300mg

4. Clinical particulars

4.1 Therapeutic indication

It is indicated for treatment of community acquired pneumonia, acute exacerbation of chronic bronchitis, uncomplicated skin & skin structure infection, pharyngitis/tonsillitis, acute maxillary sinusitis & acute bacterial otitis media-additional.

4.2 Posology and method of administration

Posology

Capsules

The recommended dosage and duration of treatment for infections in adults and Adolescents are described in the following chart; the total daily dose for all infections is 600 mg. Once-daily dosing for 10 days is as effective as BID dosing. Once-daily dosing Has not been studied in pneumonia or skin infections; therefore, Cefdinir Capsules Should be administered twice daily in these infections. Cefdinir Capsules may be taken without regard to meals.

Adults and Adolescents (Age 13 years and Older)

Type of Infection Dosage Duration	**Dosage**	**Duration**
Community-Acquired Pneumonia	300 mg q12h	10 days
Acute exacerbation of chronic bronchitis	300 mg q12h or 600 mg q24h	5 to 10 days 10 days

Type of Infection Dosage Duration	Dosage	Duration
Acute Maxillary Sinusitis	300 mg q12h or 600 mg q24h	10 days 10 days
Pharyngitis/Tonsillitis	300 mg q12h or 600 mg q24h	5 to 10 days 10 days
Uncomplicated Skin and Skin Structure Infections	300 mg q12h	10 days

4.3 Contraindications

Cefdinir is contraindicated in patients with known allergy to the cephalosporin class of antibiotics.

4.4 Special warnings and precautions for use

WARNINGS

Before therapy with Cefdinir is instituted, Careful inquiry should be made to determine whether the Patient has had previous hypersensitivity reactions to Cefdinir, other cephalosporins, penicillins, or other drugs. If Cefdinir is to be given to penicillin-sensitive patients, Caution should be exercised because cross-hypersensitivity

Among b -lactam antibiotics has been clearly documented and may occur in up to 10% of patients with a history of Penicillin allergy. If an allergic reaction to Cefdinir Occurs, the drug should be discontinued.

Serious acute Hypersensitivity reactions may require treatment with Epinephrine and other emergency measures, including Oxygen, intravenous fluids, intravenous antihistamines, Corticosteroids, pressor amines, and airway management, as clinically indicated.

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including Cefdinir, and may range in severity from mild- to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of antibacterial agents.

Treatment with antibacterial agents 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 colitis".

After the diagnosis of pseudomembranous colitis has been established, appropriate therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against Clostridium difficile.

As with other broad-spectrum antibiotics, prolonged treatment may result in the possible emergence and overgrowth of resistant organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate alternative therapy should be administered.

Cefdinir, as with other broad-spectrum antimicrobials (antibiotics), should be prescribed with caution in individuals with a history of colitis.

In patients with transient or persistent renal insufficiency (creatinine clearance <30 mL/min), the total daily dose of Cefdinir should be reduced because high and prolonged plasma concentrations of Cefdinir can result following recommended doses

4.5 Drugs interactions

Antacids: (aluminium- or magnesium-containing): Concomitant administration of 300-mg Cefdinir capsules with 30 mL Maalox® TC suspension reduces the rate (Cmax) and extent (AUC) of absorption by approximately 40%. Time to reach Cmax is also prolonged by 1 hour. There are no significant effects on Cefdinir pharmacokinetics if the antacid is administered 2 hours before or 2 hours after Cefdinir. If antacids are required during CEFDINIR therapy, CEFDINIR should be taken at least 2 hours before or after the antacid.

Probenecid: As with other b-lactam antibiotics, probenecid inhibits the renal excretion of Cefdinir, resulting in an approximate doubling in AUC, a 54% increase in peak Cefdinir plasma levels, and a 50% prolongation in the apparent elimination half-life.

Iron Supplements and Foods Fortified with Iron: Concomitant administration of Cefdinir with a therapeutic iron supplement containing 60 mg of elemental iron (as FeSO4) or vitamins supplemented with 10 mg of elemental iron reduced extent of absorption by 80% and 31%, respectively. If iron supplements are required during.

CEFDINIR therapy, CEFDINIR should be taken at least 2 hours before or after the supplement. The effect of foods highly fortified with elemental iron (primarily iron-fortified breakfast cereals) on Cefdinir absorption has not been studied. Concomitantly administered iron-fortified infant formula (2.2 mg elemental iron/6 oz.) has no significant effect on Cefdinir pharmacokinetics. Therefore, CEFDINIR for Oral Suspension can be administered with iron-fortified infant formula. There have been rare reports of reddish stools in patients who have received Cefdinir in Japan. The reddish colour is due to the formation of a non-absorbable complex between Cefdinir or its breakdown products and iron in the gastrointestinal tract.

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

Pregnancy - Teratogenic Effects

Pregnancy Category B: Cefdinir was not teratogenic in rats at oral doses up to 1000 mg/kg/day (70 times the human dose based on mg/kg/day, 11 times based on mg/m2 /day) or in rabbits at oral doses up to 10 mg/kg/day (0.7 times the human dose based on mg/kg/day, 0.23 times based on mg/m2 /day). Maternal toxicity (decreased body weight gain) was observed in rabbits at the maximum tolerated dose of 10 mg/kg/day without adverse effects on offspring. Decreased body weight occurred in rat foetuses at ^{3}100 mg/kg/day, and in rat offspring at ^{3}32 mg/kg/day. No effects were observed on maternal reproductive parameters or offspring survival, development, behaviour, or reproductive function.

There are, however, 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.

Labour and Delivery

Cefdinir has not been studied for use during labour and delivery.

Nursing Mothers

Following administration of single 600-mg doses, Cefdinir was not detected in human Breast milk.

Paediatric Use

Safety and efficacy in neonates and infants less than 6 months of age have not been Established. Use of Cefdinir for the treatment of acute maxillary sinusitis in paediatric Patients (age 6 months through 12 years) is supported by evidence from adequate and Well-controlled studies in adults and adolescents, the similar pathophysiology of acute Sinusitis in adult and paediatric patients, and comparative pharmacokinetic data in the paediatric population.

4.7 Effects on ability to drive and use machines

Not applicable

4.8 Undesirable effects

Clinical Trials - CEFDINIR Capsules (Adult and Adolescent Patients): In clinical trials, 5093 adult and adolescent patients (3841 US and 1252 non-US) were treated with the recommended dose of Cefdinir capsules (600 mg/day). Most adverse events were mild and self-limiting. No deaths or permanent disabilities were attributed to Cefdinir. One hundred forty-seven of 5093 (3%) patients discontinued medication due to adverse events thought by the investigators to be possibly, probably, or definitely associated with Cefdinir therapy. The discontinuations were primarily for gastrointestinal, disturbances, usually diarrhea or nausea. Nineteen of 5093 (0.4%) patients were discontinued due to rash thought related to Cefdinir administration.

In the US, the following adverse events were thought by investigators to be possibly, probably, or definitely related to Cefdinir capsules in multiple-dose clinical trials (N = 3841 Cefdinir-treated patients):

Adverse Events Associated with Cefdinir Capsules Trials in Adult And Adolescent Patients (N = 3841)

Incidence ³1%

- Vaginal moniliasis 4% of women
- Nausea 3%
- Headache 2%
- Abdominal pain 1%
- Vaginitis 1% of women
- Incidence <1% but >0.1%
- Rash 0.9%
- Dyspepsia 0.7%
- Flatulence 0.7%
- Vomiting 0.7%
- Abnormal stools 0.3%
- Anorexia 0.3%

- Constipation 0.3%
- Dizziness 0.3%
- Dry mouth 0.3%
- Asthenia 0.2%
- Insomnia 0.2%
- Leucorrhoea 0.2% of women
- Moniliasis 0.2%
- Pruritus 0.2%
- Somnolence 0.2%
- Diarrhea 15%

Laboratory Value Changes Observed with Cefdinir Capsules Trials In Adult And ADOLESCENT PATIENTS (N = 3841)

Incidence ≥1%

- Increased Urine leukocytes 2%
- Increased Urine protein 2%
- Increased Gamma-glutamyltransferase1%
- Decreased Lymphocytes, - Lymphocytes 1%, 0.2%
- Increased Microhematuria 1%

Incidence <1% but >0.1%

- Increased Glucosea0.9%
- Increased Urine glucose 0.9%
- Increased White blood cells, ¯ White blood cells 0.9%, 0.7%
- Increased Alanine aminotransferase (ALT) 0.7%
- Increased Eosinophils 0.7%
- Increased Urine specific gravity, ¯ Urine specific gravity 0.6%, 0.2%
- Decreased Bicarbonatea 0.6%
- Increased Phosphorus, ¯ Phosphorus a 0.6%, 0.3%
- Increased Aspartate aminotransferase (AST) 0.4%
- Increased Alkaline phosphatase 0.3%
- Increased Blood urea nitrogen (BUN) 0.3%
- Increased Hemoglobin 0.3%
- Increased Polymorphonuclear neutrophils (PMNs), ¯ PMNs 0.3%, 0.2%
- Increased Bilirubin 0.2%
- Increased Lactate dehydrogenasea 0.2%
- Increased Platelets 0.2%

- Increased Potassiuma 0.2%
- Increased Urine pH 0.2%

Cephalosporin Class Adverse Events

The following adverse events and altered laboratory tests have been reported for cephalosporin-class antibiotics in general:

Allergic reactions, anaphylaxis, Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis, renal dysfunction, toxic nephropathy, hepatic dysfunction including cholestasis, aplastic anemia, hemolytic anemia, hemorrhage, false-positive test for urinary glucose, neutropenia, pancytopenia, and agranulocytosis. Pseudomembranous colitis symptoms may begin during or after antibiotic treatment.

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.

Reporting of adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Report suspected adverse reactions via any point of contact available at www.torrentpharma.com.

4.9 Overdose

Information on Cefdinir overdosage in humans is not available. In acute rodent toxicity studies, a single oral 5600-mg/kg dose produced no adverse effects. Toxic signs and symptoms following overdosage with other b-lactam antibiotics have included nausea, vomiting, epigastric distress, diarrhea, and convulsions. Hemodialysis removes Cefdinir from the body. This may be useful in the event of a serious toxic reaction from overdosage, particularly if renal function is compromised.

5. Pharmacological properties

5.1 Mechanism of Action

As with other cephalosporins, bactericidal activity of Cefdinir results from inhibition of cell wall synthesis by acting on penicillin binding proteins (PBPs).

5.2 Pharmacodynamics

Cefdinir is a third generation cephalosporin with a broad spectrum of activity against enteric gram-negative rods. Cefdinir is stable in the presence of some, but not all, b-lactamase enzymes. As a result, many organisms resistant to penicillins and some cephalosporins are susceptible to Cefdinir. Cephalosporins work the same way as penicillins: they interfere with the peptidoglycan synthesis of the bacterial wall by inhibiting the final transpeptidation needed for the cross-links. This effect is bactericidal.

5.3 Pharmacokinetic properties

Absorption: Oral Bioavailability: Maximal plasma cefdinir concentrations occur 2 to 4 hours post dose following capsule or suspension administration. Plasma cefdinir concentrations increase with dose, but the increases are less than dose-proportional from 300 mg (7 mg/kg) to 600 mg (14 mg/kg). Following administration of suspension to healthy adults, cefdinir bioavailability is 120% relative to capsules. Estimated bioavailability of

cefdinir capsules is 21% following administration of a 300 mg capsule dose, and 16% following administration of a 600 mg capsule dose. Estimated absolute bioavailability of cefdinir suspension is 25%. Effect of Food: Although the rate (Cmax) and extent (AUC) of cefdinir absorption from the capsules are reduced by 16% and 10%, respectively, when given with a high-fat meal, the magnitude of these reductions is not likely to be clinically significant. Therefore, cefdinir may be taken without regard to food. Cefdinir Capsules: Cefdinir plasma concentrations and pharmacokinetic parameter values following administration of single 300- and 600-mg oral doses of cefdinir to adult subjects are presented in the following table:

Mean (±SD) Plasma Cefdinir Pharmacokinetic Parameter Values Following Administration of Capsules to Adult Subjects

Dose	**Cmax (µg/mL)**	**tmax (hr)**	**AUC (µg×hr/mL)**
300 mg	1.60(0.55)	2.9 (0.89)	7.05 (2.17)
600 mg	2.87(1.01)	3.0 (0.66)	11.1(3.87)

Multiple Dosing: Cefdinir does not accumulate in plasma following once- or twice-daily administration to subjects with normal renal function.

Distribution The mean volume of distribution (Vdarea) of cefdinir in adult subjects is 0.35 L/kg (±0.29); in pediatric subjects (age 6 months-12 years), cefdinir Vdarea is 0.67 L/kg (±0.38). Cefdinir is 60% to 70% bound to plasma proteins in both adult and pediatric subjects; binding is independent of concentration.

Skin Blister:

In adult subjects, median (range) maximal blister fluid cefdinir concentrations of 0.65 (0.33-1.1) and 1.1 (0.49-1.9) µg/mL were observed 4 to 5 hours following administration of 300- and 600-mg doses, respectively. Mean (±SD) blister Cmax and AUC (0-¥) values were 48% (±13) and 91% (±18) of corresponding plasma values.

Tonsil Tissue:

In adult patients undergoing elective tonsillectomy, respective median tonsil tissue cefdinir concentrations 4 hours after administration of single 300- and 600-mg doses were 0.25 (0.22-0.46) and 0.36 (0.22-0.80) µg/g. Mean tonsil tissue concentrations were 24% (±8) of corresponding plasma concentrations.

Sinus Tissue:

In adult patients undergoing elective maxillary and ethmoid sinus surgery, respective median sinus tissue cefdinir concentrations 4 hours after administration of single 300- and 600-mg doses were

Lung Tissue: In adult patients undergoing diagnostic bronchoscopy, respective median bronchial mucosa cefdinir concentrations 4 hours after administration of single 300- and 600-mg doses were

Metabolism and Excretion

Cefdinir is not appreciably metabolized. Activity is primarily due to parent drug. Cefdinir is eliminated principally via renal excretion with a mean plasma elimination half-life (t1/2) of 1.7 (– 0.6) hours. In healthy subjects with normal renal function, renal clearance is 2.0 (– 1.0) ml/min/kg, and apparent oral clearance is 11.6 (– 6.0) and 15.5 (– 5.4) ml/min/kg

following doses of 300 mg and 600 mg, respectively. Mean percent of dose recovered unchanged in the urine following 300 and 600 mg doses are 18.4% (– 6.4) and 11.6% (– 4.6), respectively. Cefdinir clearance is reduced in patients with renal dysfunction.

Special Populations: Patients with Renal Insufficiency: Cefdinir pharmacokinetics were investigated in 21 adult subjects with varying degrees of renal function. Decreases in cefdinir elimination rate, apparent oral clearance (CL/F), and renal clearance were approximately proportional to the reduction in creatinine clearance (CLcr). As a result, plasma cefdinir concentrations were higher and persisted longer in subjects with renal impairment than in those without renal impairment. In subjects with CLcr between 30 and 60 mL/min, Cmax and t½ increased by approximately 2-fold and AUC by approximately 3-fold. In subjects with CLcr

Hemodialysis: Cefdinir pharmacokinetics were studied in 8 adult subjects undergoing hemodialysis. Dialysis (4 hours' duration) removed 63% of cefdinir from the body and reduced apparent elimination t½ from 16 (±3.5) to 3.2 (±1.2) hours. Dosage adjustment is recommended in this patient population.

Hepatic Disease: Because cefdinir is predominantly renally eliminated and not appreciably metabolized, studies in patients with hepatic impairment were not conducted. It is not expected that dosage adjustment will be required in this population

Geriatric Patients: The effect of age on cefdinir pharmacokinetics after a single 300-mg dose was evaluated in 32 subjects 19 to 91 years of age. Systemic exposure to cefdinir was substantially increased in older subjects (N = 16), Cmax by 44% and AUC by 86%. This increase was due to a reduction in cefdinir clearance. The apparent volume of distribution was also reduced, thus no appreciable alterations in apparent elimination half-life were observed (elderly: 2.2 ± 0.6 hours vs young: 1.8 ± 0.4 hours). Since cefdinir clearance has been shown to be primarily related to changes in renal function rather than age, elderly patients do not require dosage adjustment unless they have markedly compromised renal function (creatinine clearance <30 ml/mim).

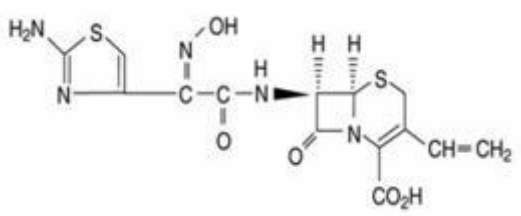
6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

Carcinogenesis, Mutagenesis, Impairment of Fertility The carcinogenic potential of cefdinir has not been evaluated. No mutagenic effects were seen in the bacterial reverse mutation assay (Ames) or point mutation assay at the hypoxanthine-guanine phosphoribosyl transferase locus (HGPRT) in V79 Chinese hamster lung cells. No clastogenic effects were observed in vitro in the structural chromosome aberration assay in V79 Chinese hamster lung cells or in vivo in the micronucleus assay in mouse bone marrow. In rats, fertility and reproductive performance were not affected by cefdinir at oral doses up to 1000 mg/kg/day (70 times the human dose based on mg/kg/day, 11 times based on mg/m2 /day).

7. Description

Cefdinir is 5-thia 1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid having molecular formula of $C_{14}H_{13}N_5O_5S_2$ and molecular weight of 395.4 with structural formula as:



Cefdinir is a white to light yellow crystalline powder which is sparingly soluble in 0.1M phosphate buffer pH 7 solution; practically insoluble in water, in ethanol, and in diethyl ether.

Cefdinir Capsules are red/yellow size '1', hard gelatin capusles containing white to off-white granular powder. The excipients used are Carboxymethylcellulose Calcium, Croscarmellose Sodium, Sodium Lauryl Sulphate, Sodium Starch Glycolate, Magnesium Stearate and Talc.

8. Pharmaceutical particulars

8.1 Incompatibilities

Not Available

8.2 Shelf-life

Do not use later than the date of expiry

8.3 Packaging information

SEFDIN is available in strip of 10 capsules.

8.4 Storage and handing instructions.

Store in dry place at temperature not exceeding 25°C. Protect from light

9. Patient Counselling Information

Ask the patients to inform the treating physicians in case of any of the below:

- Have any allergies
- Have kidney or liver problems
- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed
- Have any serious illness
- Are taking any medicines (prescription, over-the-counter, vitamins, or herbal products)

10. Details of manufacturer

Manufactured in India by:

Maxim Pharmaceuticals Pvt. Ltd.

Plot No. 11 & 12, GAT No. 1251-1261, Alandi Markal Road,

Markal – Khed – Pune 412105.

11. Details of permission or licence number with date

Mfg Lic No. PD-72 issued on 10.10.2019

12. Date of revision

FEB-2026

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/SEFDIN 300 mg/Feb-26/02/PI