1.3.1. SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. Name of the medicinal product:
CEFRITE 400 (Cefixime Tablet USP 400mg)

2 Qualitative and quantitative composition:
Each uncoated tablet contains:
Cefixime (as Trihydrate) USP
Eq.to Anhydrous Cefixime ……..400 mg
Excipients…….....……q.s.
Colour: Tartrazine

For the full list of excipients see section 6.1.

3. Pharmaceutical Form
Uncoated Tablets.

Off white to light yellow coloured, oblong shape, biconvex having a break line on one side of uncoated tablets.

4. Clinical particulars

4.1 Therapeutic indications
CEFRITE 400 (cefixime) is indicated in the treatment of the following infections caused by susceptible strains of the designated microorganisms:

Upper Respiratory Tract:
Pharyngitis and tonsillitis caused by S. pyogenes.

Middle Ear:
Otitis media caused by S. pneumoniae, H. influenzae (beta-lactamase positive and negative strains), M. catarrhalis (former B. catarrhalis) (beta-lactamase positive and negative strains) and S. pyogenes.

Paranasal sinuses:
Sinusitis caused by S. pneumoniae, H. influenzae (beta-lactamase positive and negative strains), and M. catarrhalis (former B. catarrhalis) (beta-lactamase positive and negative strains).

Lower Respiratory Tract:
Acute bronchitis caused by S. pneumoniae, M. catarrhalis (former B. catarrhalis) (beta-lactamase positive and negative strains) and H. influenzae (beta-lactamase positive and negative strains).

Urinary Tract:
Acute uncomplicated cystitis and urethritis caused by E. coli, P. mirabilis, and Klebsiella species.

Uncomplicated Gonorrhea:
Uncomplicated gonorrhea (cervical/urethral and rectal) caused by Neisseria gonorrhoeae, including penicillinase (beta-lactamase-positive) and nonpenicillinase (beta-lactamase-negative) producing strains.

Appropriate cultures should be taken for susceptibility testing before initiating treatment with CEFRITE 400. If warranted, therapy may be instituted before susceptibility results are known; however, once these are obtained, therapy may need to be adjusted.

4.2 Posology and method of administration

The recommended dose of CEFRITE 400 (cefixime) is 400 mg once daily. When necessary, a dose of 200 mg (one -half of a 400 mg tablet) given twice daily may be considered except for urinary tract infections where once daily dosing must be used. For treatment of uncomplicated gonococcal infections, a single oral dose of 400 mg is recommended.
The usual course of treatment is 7 days. This may be continued for up to 14 days if required.

Children (≥ 6 months) :

The recommended dose of CEFRITE 400 is 8 mg/kg/day once daily. When necessary, a dose of
4 mg/kg given twice daily may be considered except for urinary tract infe
ctions where once daily
dosing must be used

WEIGHT (Kg)	DOSE/DAY (mg)
6	48
12.5	100
19	152
25	200
35	280

Children weighing more than 50 kg or older than 12 years should be treated with the recommended adult dose. Safety and effectiveness in infants aged less than six months have not been established.
Otitis media should be treated with the suspension. Clinical studies of otitis media were conducted with the suspension only and the suspension results in higher peak blood levels than the tablet when administered at the same dose. Therefore, the tablet should not be substituted for the suspension in the treatment of otitis media..

Duration of Therapy:

Duration of dosage in clinical trials was 10 to 14 days. The duration of treatment should be guided by the patient's clinical and bacteriological response.
In the treatment of infections due to Streptococcus pyogenes, a therapeutic dose of CEFRITE 400 should be administered for at least 10 days.

Renal Impairment:

CEFRITE 400 may be administered in the presence of impaired renal function. Normal dose and schedule may be employed in patients with creatinine clearances of 40 mL/min or greater. Patients whose clearance is between 20 and 40 mL/min should be given 75% of the standard daily dosage. Patients whose creatinine clearance is less than 20 mL/min should be given 50% of the standard daily dosage.

Experience in children with renal impairment is very limited.
NOTE: Neither hemodialysis, nor peritoneal dialysis remove significant amounts of CEFRITE 400 from the body.

Method for administration
For oral administration.

4.3 Contraindications
CEFRITE 400 (cefixime) is contraindicated in patients with known allergies to the cephalosporin or penicillin antibiotics or to any ingredients in the formulation or component of the container.

4.4 Special warnings and precautions for use
WARNINGS:
Hypersensitivity:
In penicillin-sensitive patients, CEFRITE 400 (cefixime) should be administered cautiously. Patients may be sensitive to penicillins and not to cephalosporins such as cefrite-400 or be sensitive to both. Medical literature indicates that patients sensitive to cephalosporins are very likely to be penicillin sensitive.
Antibiotics, including CEFRITE 400, should be administered cautiously to any patient who has demonstrated some form of allergy, particularly to drugs.

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 CEFRITE 400. When severe cutaneous adverse reactions occur, CEFRITE 400 should be discontinued and appropriate therapy and/or measures should be taken.

Clostridium difficile-associated disease (CDAD) has been reported with use of many antibacterial agents, including CEFRITE 400 (see ADVERSE REACTIONS). CDAD may range in severity from mild diarrhea to fatal colitis. It is important to consider this diagnosis in patients who present with diarrhea, or symptoms of colitis, pseudomembranous colitis, toxic megacolon, or perforation of colon subsequent to the administration of any antibacterial agent. CDAD has been reported to occur over 2 months after the administration of antibacterial agents.

Treatment with antibacterial agents may alter the normal flora of the colon and may permit overgrowth of Clostridium difficile. C. difficile produces toxins A and B, which contribute to the development of CDAD. CDAD may cause significant morbidity and mortality. CDAD can be refractory to antimicrobial therapy.

If the diagnosis of CDAD is suspected or confirmed, appropriate therapeutic measures should be initiated. Mild cases of CDAD usually respond to discontinuation of antibacterial agents not directed against Clostridium difficile. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial agent clinically effective against Clostridium difficile. Surgical evaluation should be instituted as clinically indicated, as surgical intervention may be required in certain severe cases

Hemolytic Anemia:
CEFRITE 400 should not be used in patients with a history of cephalosporin-associated hemolytic anemia since the recurrence of hemolysis is much more severe.
An immune mediated hemolytic anemia has been observed in patients receiving cephalosporin class antibacterials, including CEFRITE 400. Severe cases of hemolytic anemia, including fatalities, have been reported with cephalosporins in both adults and children. If a patient develops anemia anytime during, or within 2-3 weeks subsequent to the

administration of CEFRITE 400, the diagnosis of a cephalosporin-associated anemia should be considered and the drug discontinued until the etiology is determined.
Patients may benefit from periodic monitoring for signs and symptoms of hemolytic anemia, including measurement of hematological parameters or drug-induced antibody testing, where appropriate (see ADVERSE REACTIONS).

Acute Renal Failure:
As with other cephalosporins, CEFRITE 400 may cause acute renal failure including tubulointerstitial nephritis. When acute renal failure occurs, CEFRITE 400 should be discontinued and appropriate therapy and/or measures should be taken.

Neurologic:
Several cephalosporins, including cefixime, have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced. If seizures associated with CEFRITE 400 occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated (see DOSAGE AND ADMINISTRATION and OVERDOSAGE).

PRECAUTIONS
General:
If an allergic reaction to CEFRITE 400 (cefixime) occurs, the drug should be discontinued, and, if necessary, the patient should be treated with appropriate agents, e.g., pressor amines, antihistamines, or corticosteroids.
The possibility of the emergence of resistant organisms, which might result in overgrowth, should be kept in mind, particularly during prolonged treatment. In such use, careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.
Broad-spectrum antibiotics such as CEFRITE 400 should be prescribed with caution in individuals with a history of gastrointestinal disease.
Once daily dosing only must be used for urinary tract infections, since twice daily dosing was shown to be not as effective in clinical studies.
Do not use CEFRITE 400 to treat Staphylococcus aureus as this strain of staphylococcus is resistant to cefixime.

Renal Impairment:
CEFRITE 400 should be used with particular care in the presence of severely impaired renal function. Dose modification is recommended for patients with moderate or severe renal impairment (i.e., creatinine clearance of < 40 mL/min).

Bioavailability Differences Between Tablet and Suspension:
The area under the time versus concentration curve is greater by approximately 26.4% and the Cmax is greater by approximately 20.7% with the oral suspension when compared to the tablet after doses of 400 mg. This increased absorption should be taken into consideration if the oral suspension is to be substituted for the tablet. Because of the lack of bioequivalence, tablets should not be substituted for oral suspension particularly in the treatment of otitis media where clinical trial experience with the suspension only is available.

4.5 Interaction with other medicinal products and other forms of interaction
CEFRITE 400 should be administered with caution to patients receiving coumarin-type anticoagulants such as warfarin potassium. Since CEFRITE 400 may enhance effects of the anticoagulants, prolonged prothrombin time with or without bleeding may occur.

4.6 Fertility, pregnancy and lactation

Usage in Pregnancy:

The safety of CEFRITE 400 in the treatment of infection in pregnant women has not been established.

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 fetus due to cefixime. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if the likely benefits of using CEFRITE 400 outweigh the potential risk to the fetus and/or the mother.

Labour and Delivery:

CEFRITE-400 has not been studied for use during labour and delivery.

Nursing Mothers:

It is not known whether CEFRITE 400 is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when CEFRITE 400 is administered to a nursing woman.

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

The following adverse reactions have been observed during clinical trial studies and/or during marketed use.

Blood and lymphatic system disorders:

Thrombocytopenia, thrombocytosis, leucopenia, eosinophilia, neutropenia, agranulocytosis, immune hemolytic anemia (see WARNINGS, Hemolytic Anemia).

Gastrointestinal disorders:

Diarrhea, stool changes, nausea, abdominal pain, dyspepsia, flatulence, vomiting.

General disorders and administration site conditions:

Drug fever, face oedema.

Hepatobiliary disorders:

Jaundice (cholestatic and/or hepatocellular).

Immune system disorders:

Serum sickness-like reaction, anaphylactic reactions (urticaria and angioedema).

Infections and infestations:

Vaginitis, candidiasis, pseudomembranous colitis.

Investigations:

Elevations of alanine aminotransferase (ALT or SGPT), aspartate aminotransferase (AST or SGOT), alkaline phosphatase and bilirubin.

Elevations in Blood Urea Nitrogen (BUN) or creatinine.

Prolongation in prothrombin time.

Nervous system disorders:

Headaches, dizziness, convulsions.

Renal and urinary disorders:

Acute renal failure including tubulointerstitial nephritis.

Reproductive system and breast disorders:

Genital pruritus.

Respiratory, thoracic and mediastinal disorders:

Dyspnea, respiratory distress.

Skin and subcutaneous tissue disorders:
Skin rashes, pruritus, urticaria, toxic epidermal necrolysis (TEN), drug rash with eosinophilia and systemic symptoms (DRESS), bullous skin reactions (erythema multiforme and Stevens-Johnson syndrome).

In addition to the adverse reactions listed above which have been observed in patients treated with CEFRITE 400 the following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics: superinfection, renal dysfunction, toxic nephropathy, hepatic dysfunction including cholestasis, aplastic anemia, hemorrhage, elevated lactate dehydrogenase (LDH) and pancytopenia.

4.9 Overdose
Activated charcoal may be administered to aid in the removal of unabsorbed drug. General supportive measures are recommended.

For management of a suspected drug overdose, contact your regional Poison Control Centre.
No specific antidote exists. General supportive measures are recommended.
CEFRITE 400 (cefixime) is not removed in significant quantities from the circulation by hemodialysis or peritoneal dialysis.

5. Pharmacological properties
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: third generation cephalosporin, 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.

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.

5.2 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 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.

5.3 Preclinical safety data
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.

6. Pharmaceutical particulars
6.1 List of Excipients:
Microcrystalline Cellulose powder BP
Colloidal silicon dioxide BP
Pregelatinized starch BP
Aspartame BP
Colour: Tartrazine supra IH
Dry mix fruit flavour IH
Dry vanilla flavour IH
Talcum BP
Magnesium Stearate BP
Crospovidone BP
Croscarmellose sodium BP

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
36 Months

6.4 Special precautions for storage
Do not store above 25°C

6.5 Nature and contents of container
10 tablets packed in one blister. Such one blister is packed in a printed mono carton with a packing Insert. Such 10 mono cartons are packed in one outer carton.

6.6 Special precautions for disposal and other handling
None stated.

Manufactured by:
HEALTH CARE FORMULATIONS PVT. LTD.
C/8, SARDAR ESTATE, AJWA ROAD,
VADODARA-390 019, GUJARAT, INDIA.

7. Marketing authorisation holder
SAVOCENT PHARMA LTD.
90, Ladipo Road, CleanJohn House,
Matori Industrial Arean, Mushin,
Lagos.

8. Marketing authorisation number(s):
C4-0402

9. Date of first authorisation/renewal of the authorisation:
30-01-2020

10. Date of revision of the text:
13-01-2025