Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

CACHMAX DS 100mg/5ml

2. Qualitative and quantitative composition

Each 5 ml of reconstituted suspension contains 100 mg of cefixime trihydrate.

Excipient(s) with known effects

Each 5 ml of reconstituted suspension contains 2310.0 mg of sucrose.

This medicine contains less than 1mmol (23 mg) sodium in each 5 ml, that is to say essentially sodium free.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Powder for oral suspension.
An off white free flowing granular powder. Upon reconstitution with water, gives lemon flavor off-white homogenous suspension

4. Clinical particulars

4.1 Therapeutic indications

Cefixime Suspension 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 Suspension 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 Suspension. In addition, most strains of Pseudomonas, Bacteriodes fragalis, Listeria monocytogenes and Clostridia are resistant to Cefixime Suspension.

4.2 Posology and method of administration

Route of Administration: Oral
Absorption of Cefixime is not significantly modified by the presence of food. The usual course of treatment is 7 days. This may be continued for up to 14 days if required.

Posology

Adults

Adults and children over 10 years or weighing more than 50kg:
The usual daily dose is 200-400 mg in single or twice daily dosage regimen. The recommended dose of cefixime is 400 mg daily. For the treatment of uncomplicated cervical/urethral gonococcal infections, a single oral dose of 400 mg is recommended. The capsule may be administered without regard to food.
In the treatment of infections due to Streptococcus pyogenes, a therapeutic dosage of cefixime should be administered for at least 10 days.

Pediatric Patients (6 months or older)

The recommended dose is 8 mg/kg/day of the suspension. This may be administered as a single daily dose or may be given in two divided doses, as 4 mg/kg every 12 hours

PEDIATRIC DOSAGE CHART		
	100 mg/5 mL	200 mg/5 mL

Patient Weight (kg)	Dose/Day (mg)	Dose/Day (mL)	Dose/Day (mL)
5 to 6.2	50	2.5	1.25
6.3 to 12.5	100	5	2.5
6.3 to 12.5	150	7.5	3.75
18.9 to 25	200	10	5
25.1 to 31.3	250	12.5	6.25
31.4 to 37.5	300	15	7.5
37.6 to 43.8	350	17.5	8.75
43.9 to 50	400	20	10

Otitis media should be treated with the chewable tablets or suspension. Clinical trials of otitis media were conducted with the chewable tablets or suspension, and the chewable tablets or suspension results in higher peak blood levels than the chewable tablet when administered at the same dose.

Therefore, the tablet or capsule should not be substituted for the chewable tablets or suspension in the treatment of otitis media.

In the treatment of infections due to Streptococcus pyogenes, a therapeutic dosage of cefixime should be administered for at least 10 days

Dosage in Renal Impairment:
Cefixime 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 hemodialysis should follow the same recommendation as that for patients with creatinine clearances of less than 20 ml/min.

Strength	Bottle size	Reconstitution Directions

100 mg/5 mL and 200 mg/5 mL	100 mL	To reconstitute, suspend with **68 mL water**. Method: Tap the bottle several times to loosen powder contents prior to reconstitution. Add approximately half the total amount of water for reconstitution and shake well. Add the remainder of water and shake well.
100 mg/5 mL and 200 mg/5 mL	75 mL	To reconstitute, suspend with **51 mL water**. Method: Tap the bottle several times to loosen powder contents prior to reconstitution. Add approximately half the total amount of water for reconstitution and shake well. Add the remainder of water and shake well.
100 mg/5 mL and 200 mg/5 mL	50 mL	To reconstitute, suspend with **34 mL water**. Method: Tap the bottle several times to loosen powder contents prior to reconstitution. Add approximately half the total amount of water for reconstitution and shake well. Add the remainder of water and shake well.
200 mg/5 mL	37.5 mL	To reconstitute, suspend with **26 mL water**. Method: Tap the bottle several times to loosen powder contents prior to reconstitution. Add approximately half the total amount of water for reconstitution and shake well. Add the remainder of water and shake well.

200 mg/5 mL	25ml	To reconstitute, suspend with **17 mL water**. Method: Tap the bottle several times to loosen powder contents prior to reconstitution. Add approximately half the total amount of water for reconstitution and shake well. Add the remainder of water and shake well.
500 mg/5 mL	20mL	To reconstitute, suspend with **14 mL water**. Method: Tap the bottle several times to loosen powder contents prior to reconstitution. Add approximately half the total amount of water for reconstitution and shake well. Add the remainder of water and shake well.

500 mg/5 mL	10mL	To reconstitute, suspend with **8 mL water**. Method: Tap the bottle several times to loosen powder contents prior to reconstitution. Add approximately half the total amount of water for reconstitution and shake well. Add the remainder of water and shake well.

After reconstitution, the suspension may be kept for 14 days either at room temperature, or under refrigeration, without significant loss of potency. Keep tightly closed. Shake well before using. Discard unused portion after 14 days

4.3 Contraindications

Cefixime is contraindicated in patients with known allergies to the cephalosporin or any other cephalosporin antibiotic
or a known immediate and severe hypersensitivity reaction to penicillin or any beta-lactam antibiotic or to any ingredients in the formulation or component.

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 (SCARS) including toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS) drug rash with

eosinophilia and systemic symptoms (DRESS), and acute generalised exanthematous pustulosis (AGEP) have been reported in association with cefixime. Patients should be informed about the signs and symptoms of serious skin manifestations and monitored closely. Treatment should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of skin hypersensitivity. Cefixime dry syrup 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 Cefixime dry syrup the drug should be discontinued and the patient treated with appropriate agents if necessary.

Renal failure acute

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

Cefixime should be administered with caution in patients with markedly impaired renal function. **Paediatric use**

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

Antibiotic-associated colitis

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 Interaction with other medicinal products and other forms of interaction

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, 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.

Concomitant intake with potentially nephrotoxic substances (such as aminoglycoside antibiotics, colistin, polymyxin and viomycin) and strong- acting diuretics (e.g. ethacrynic acid or furosemide) induce an increased risk of impairment of renal function.

Nifedipine, a calcium channel blocker, may increase bioavailability of cefixime up to70%.

4.6 Pregnancy and Lactation Pregnancy Category B

There are no adequate data from the use of Cefixime in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/ foetal development, parturition or postnatal development (see section 5.3).

Cefixime should not be used in pregnant mothers unless considered essential by the physician. The risk/benefit of administration of Cefixime should be highly critically considered, in particular during the first 3 months of pregnancy.

Lactation

It is unknown whether cefixime is excreted in human breast milk. Animal studies have shown excretion of cefixime in breast milk. A decision on whether to continue/discontinue breast- feeding or to continue/discontinue therapy with cefixime should

be made taking into account the benefit of breast-feeding to the child and the benefit of cefixime therapy to the woman.
However, until further clinical experience is available, cefixime should not be prescribed to breast-feeding mothers or they should use a breast pump for the duration of therapy and dispose of the milk.

Fertility
Reproduction studies performed in mice and rats have revealed no evidence of impaired fertility.

4.7 Effects on ability to drive and use machines

Cefixime has no known influence on the ability to drive and use machines. However, side effects may occur such as vertigo which may influence the ability to drive and use machines.

4.8 Undesirable effects

Cefixime Suspension 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 Flatulence
Hepatobiliary disorders:	Jaundice
Infections and infestations:	Pseudomembranous colitis Vaginitis
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 nefexim (frequency not known)** Beta-lactams, including nefexim, 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:	Acute renal failure with tubulointerstitial nephritis (see section 4.4).
Immune system disorders:	Anaphylactic reaction Angio-oedema Serum sickness-like reaction

Skin and subcutaneous tissue disorders:	Drug rash with eosinophilia and systemic symptoms (DRESS) Erythema multiforme Stevens-Johnson syndrome Toxic epidermal necrolysis Urticaria Rash Pruritus Acute generalised exanthematous pustulosis(AGEP) (see section 4.4)
General disorders and administrative site conditions:	Drug Fever Arthralgia Pyrexia Face oedema Genital pruritus

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.

Cefixime should be discontinued if marked diarrhoea occurs. Severe acute hypersensitivity reactions may manifest as:

- Facial oedema, swollen tongue, swelling of the inner larynx with restriction of airway, racing heart, shortness of breath (respiratory distress), decrease of blood pressure leading to life- threatening shock. Any of these occurrences requires immediate medical treatment.
- As with other cephalosporins, a raised tendency to convulsive attacks cannot be ruled out.

Lyell syndrome and Stevens-Johnson syndrome may result in life-threatening conditions

Reporting of suspected 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.Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons

board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

4.9 Overdose

There is no experience with overdoses 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 Pharmacodynamic properties

Pharmacotherapeutic group:
third generation cephalosporin**,** ATC code: J01DD08 Mode of Action Cefixime is an antibacterial agent of the cephalosporin class. Like other cephalosporins, cefixime exerts antibacterial activity by binding to and inhibiting the action of penicillinbindin proteins involved in the synthesis of bacterial cell walls. This leads to bacterial cell lysis and cell death.

PK/PD relationship
The time that the plasma concentration of cefixime exceeds the MIC of the infecting organism has been shown to best correlate with efficacy in PK/PD studies.
Mechanisms of resistance
Bacterial resistance to cefixime may be due to one or more of the following mechanisms:

Hydrolysis by extended-spectrum beta-lactamases and / or by chromosomally- encoded (AmpC) enzymes that may be induced or de- repressed in certain aerobic gramnegative bacterial species Reduced affinity of penicillin-binding proteins
Reduced permeability of the outer membrane of certain gram- negative organisms restricting access to penicillin-binding proteins Drug efflux pumpsBreakpoints
Clinical minimum inhibitory concentration (MIC) breakpoints established by EUCAST(May 2009) for cefixime are:
H. influenzae: sensitive ≤0.12 mg/L, resistant > 0.12 mg/L

M. catarrhalis: sensitive ≤0.5 mg/L, resistant > 1.0 mg/L Neisseria gonorrhoeae: sensitive ≤0.12 mg/L, resistant > 0.12 mg/L Enterobacteriaceae: sensitive ≤1.0 mg/L, resistant > 1.0 mg/L (for uncomplicated urinary tract infections only). The breakpoints for Enterobacteriaceae will detect reduced susceptibility mediated by most clinically

important beta-lactamases in Enterobacteriaceae

Occasional ESBL-producing strains will be reported susceptible. For purposes of infection control, epidemiology and surveillance, laboratories may wish to use specifictests to screen for and confirm ESBL-production.

Non-species related breakpoints: insufficient data.

Susceptibility

The prevalence of resistance may vary geographically and over time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

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 and Streptococcus pyogenes

- Gram-negative bacteria; Haemophilus influenzae, Moraxella catarrhalis Escherichia coli,Proteus mirabilis, Neisseria gonorrhoeae
- Cefixime has poor activity against staphylococci (regardless of susceptibility to methicillin)

- Natural intermediate susceptibility.

% Extended spectrum beta-lactamase (ESBL) producing strains are always resistant. & Resistance rate <10% in isolates of female patients with uncomplicated cystitis, otherwise ≥10%.

5.2 Pharmacokinetic

properties Absorption

The absolute oral bioavailability of cefixime is in the range of 40-50%. whether administered with or without food; however, time to maximal absorption is increased approximately 0.8 hours when administered with food.

A single 200 mg tablet of cefixime produces an average peak serum concentration of approximately 2 mcg/mL (range 1 to 4 mcg/mL); a

single 400 mg tablet produces an average peak concentration of approximately 3.7 mcg/mL (range 1.3 to 7.7 mcg/mL). The oral suspension produces average peak concentrations approximately 25% to 50% higher than the tablets, when tested in normal *adult* volunteers. Two hundred and 400 mg doses of oral suspension produce average peak concentrations of 3 mcg/mL (range 1 to 4.5 mcg/mL) and 4.6 mcg/mL (range 1.9 to 7.7 mcg/mL), respectively, when tested in normal *adult* volunteers. The area under the time versus concentration curve (AUC) is greater by approximately 10% to 25% with the oral suspension than with the tablet after doses of 100 to 400 mg, when tested in normal *adult* volunteers. 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 in the treatment of otitis media *[see Dosage and Administration (2)]*.
Cross-over studies of tablet versus suspension have not been performed in children.

The 400 mg capsule is bioequivalent to the 400 mg tablet under fasting conditions. However, food reduces the absorption following administration of the capsule by approximately 15% based on AUC and 25% based on Cmax.
Peak serum concentrations occur between 2 and 6 hours following oral administration of a single 200 mg tablet, a single 400 mg tablet or 400 mg of cefixime suspension. Peak serum concentrations occur between 2 and 5 hours following a single administration of 200 mg of suspension. Peak serum concentrations occur between 3 and 8 hours following oral administration of a single 400 mg capsule.

Distribution
Serum protein binding is well characterised for human and animal sera; cefixime is almost exclusively bound to the albumin fraction, with a bound fraction of approximately 65% and 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. From in vitro studies, serum or urine concentrations of 1 mg/L 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 mg/L. Little or no accumulation of cefixime occurs following multiple dosing.

Adequate data on CSF levels of cefixime are not available.

Metabolism and Elimination

There is no evidence of metabolism of cefixime *in vivo.* 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 Cmax and AUC values were slightly greater in the elderly. Elderly patients may be given the same dose as the general population.

Approximately 50% of Cefixime is 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. In animal studies, it was noted that cefixime is also excreted in the bile in excess of 10% of the administered dose.

Transfer of 14C-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. Placental transfer of cefixime was small in pregnant rats dosed with labeled cefixime.

5.3 Preclinical safety data

Carcinogenesis, Mutagenesis, Impairment of Fertility

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.

Sucrose
Xanthan gum
Colloidal Silicon Dioxide
Sodium benzoate
Trusil Pineapple flavor

6.2 Preclinical safety data

Not applicable

6.3 Shelf life

Unopened: 24 months

After reconstitution: The reconstituted suspension may be stored for 7 days in refrigerator or below 30°C.

6.4 Special precautions for storage:

Store below 30 °C, protected from moisture and light. Keep out of the reach and sight of children.

Proposed shelf life (after reconstitution or dilution): After reconstitution when stored at 20°c-25°c, use within 7 days and when stored in a refrigerator use within 14 days.

6.5 Nature and contents of container

CACHMAX-DS DRY SYRUP is an-off white free flowing granular powder filled in 60 ml amber round glass bottle. Upon reconstitution with water, it is a lemon flavour off-white homogeneous suspension. Packed in a mono carton along with measuring cap and printed insert.

6.6 Special precautions for disposal and other handling:

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORIZATION HOLDER.

Cachet Pharmaceuticals Pvt. Ltd
415, Shah Nahar, Worli, Mumbai 400 018. India.
Phone No. Office +91-22-40829991
www.cachetindia.com

8. MARKETING AUTHORISATION NUMBER(S)

CTD9204

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

28/04/2023

10. DATE OF REVISION OF THE TEXT

08 MAY 2025.