1.6 Product information:

1.6.1 Prescribing Information (Summary of Product Characteristics)

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

Cefixime for Oral Suspension USP 50 mg/5ml

1.1 Strength

50mg/5mL

1.2 Pharmaceutical form

Powder for oral suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

2.1 Qualitative declaration

Each 5 mL of reconstitution suspension contains:
Cefixime USP as Trihydrate
Eq. to anhydrous Cefixime 50 mg
Excipients q.s.
Colour: Approved colour used.

2.2 Quantitative declaration

S. No.	Ingredients	Specification	Qty. Req. per batch in Kg	Overages	Actual Qty per batch	Actual Qty per Bottle (mg)	Function
Active Pharmaceutical Ingredient							
1.	Cefixime Trihydrate*	USP	3.360	Nil	3.360	672.0	Cephalosporin antibiotic
Excipients							
2.	Xanthan Gum	BP	0.800	Nil	0.800	160.0	Suspending Agent

3.	Sodium benzoate	BP	0.600	Nil	0.600	120.0	Preservative
4.	Hydrophobic Colloidal Anhydrous Silica	BP	1.000	Nil	1.000	200.0	viscosity-increasing agent
5.	Colour Sunset yellow FCF	IH	0.003	Nil	0.003	0.6	Colour
6.	Flavour Vanilla	IH	1.000	Nil	1.000	200.0	Flavour
7.	Sugar (Pharma Grade)	BP	143.237	Nil	143.237	28647.4 - Additional quantity of Cefixime Trihydrate dispensed then the theoretical quantity	Sweetener
8.	Additional Sugar**	BP	7.163	Nil	7.163	1432.6	Sweetener

***Material has been calculated on 100% Assay**

**** Additional quantity to be added to compensate the loss during drying.**

2.3 Salts and hydrates

Cefixime as Trihydrate.

2.4 Esters and pro-drugs

Not Applicable

2.5 Oral powders for solution or suspension

Each 5 mL of reconstitution suspension contains:

Cefixime USP as Trihydrate	
Eq. to anhydrous Cefixime	50 mg
Excipients	q.s.
Colour: Approved colour used.	

2.6 Parenterals excluding powders for reconstitution

Not Applicable

2.7 Powders for reconstitution prior to Parenteral administration

Not Applicable

2.8 Concentrates

Not Applicable

2.9 Transdermal patches

Not Applicable

2.10 Multidose solid or semi-solid products

Not Applicable

2.11 Biological medicinal products

Not Applicable

3. PHARMACEUTICAL FORM

Powder for oral suspension.

White to light yellow granular powder filled in white HDPE bottle. Light yellow to orange colour suspension after reconstitution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Uncomplicated Urinary Tract Infections: Cefixime is indicated in the treatment of adults and pediatric patients six months of age or older with uncomplicated urinary tract infections caused by susceptible isolates of Escherichia coli and Proteus mirabilis.

Otitis Media

Cefixime is indicated in the treatment of adults and pediatric patients six months of age or older with otitis media caused by susceptible isolates of Haemophilus influenzae, Moraxella catarrhalis, and Streptococcus pyogenes. (Efficacy for Streptococcus pyogenes in this organ system was studied in fewer than 10 infections.)

Pharyngitis and Tonsillitis

Cefixime is indicated in the treatment of adults and pediatric patients six months of age or older with pharyngitis and tonsillitis caused by susceptible isolates of Streptococcus pyogenes. (Note: Penicillin is the usual drug of choice in the treatment of Streptococcus pyogenes infections. Cefixime is generally effective in the eradication of Streptococcus pyogenes from the nasopharynx; however, data establishing the efficacy of Cefixime in the subsequent prevention of rheumatic fever is not available.)

Acute Exacerbations of Chronic Bronchitis

Cefixime is indicated in the treatment of adults and pediatric patients six months of age or older with acute exacerbations of chronic bronchitis caused by susceptible isolates of Streptococcus pneumoniae and Haemophilus influenzae.

Uncomplicated Gonorrhea (cervical/urethral)

Cefixime is indicated in the treatment of adults and pediatric patients six months of age or older with uncomplicated gonorrhea (cervical/urethral) caused by susceptible isolates of Neisseria gonorrhoeae (penicillinase-and non-penicillinase-producing isolates).

4.2 Posology and method of administration

Posology

Adults and children of 12 years and over (or more than 50kg body weight): The usual daily dose is 200-400mg in single or twice daily dosage regimen.
In uncomplicated upper respiratory tract infections or urinary tract infections a daily dose of 200 mg may be sufficient.
Children aged 9 to 12 years: The usual total daily dose is 300mg (15ml of oral suspension) in single or twice daily regimen.
Children aged 5 to 8 years: The usual total daily dose is 200 mg (10ml of oral suspension) in single or twice daily dosage regimen.
Children aged 2 to 4 years: The usual total daily dose is 100 mg (5ml of oral suspension) in single or twice daily dosage regimen.
Children aged 6 months to 2 years: The usual total daily dose is 8 mg/kg in single or twice daily regimen. The safety and efficacy of use in infants less than 6 months of age has not been established.
Elderly: The usual dosage is as for adults with appropriate modifications on the basis of renal impairment.
Patients with Renal Impairment: Dosage does not require modification in patients with a creatinine clearance of 20 ml/minute or greater.
In patients with a creatinine clearance less than 20 ml/minute a dose of 200 mg once daily should not be exceeded. The same dosage regimen is applied to those patients maintained on chronic ambulatory peritoneal dialysis or haemodialysis

4.3 Method of administration

Route of Administration: Oral

4.4 Contraindications

Cefixime is contraindicated in patients with known hypersensitivity to the cephalosporin group of antibiotics or any of the other components of the product.

4.5 Special warnings and precautions for use

Hypersensitivity Reactions: Anaphylactic/anaphylactoid reactions (including shock and fatalities) have been reported with the use of cefixime.

Before therapy with Cefixime is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cephalosporins, penicillins, or other drugs. If this product is to be given to penicillin-sensitive patients, caution should be exercised because cross hypersensitivity among beta-lactam antibacterial drugs has been clearly documented and may occur in up to 10% of patients with a history of penicillin allergy. If an allergic reaction to Cefixime occurs, discontinue the drug.

Clostridium difficile-Associated Diarrhea: Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including Cefixime, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C. difficile.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing isolates of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibacterial drug use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibacterial drug use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibacterial drug treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated.

Dose Adjustment in Renal Impairment: The dose of Cefixime should be adjusted in patients with renal impairment as well as those undergoing continuous ambulatory peritoneal dialysis (CAPD) and hemodialysis (HD). Patients on dialysis should be monitored carefully.

Coagulation Effects: Cephalosporins, including Cefixime, may be associated with a fall in prothrombin activity. Those at risk include patients with renal or hepatic impairment, or poor nutritional state, as well as patients receiving a protracted course of antimicrobial therapy, and patients previously stabilized on anticoagulant therapy. Prothrombin time should be monitored in patients at risk and exogenous vitamin K administered as indicated.

Development of Drug-Resistant Bacteria: Prescribing Cefixime in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

The product also causes neurological problems like dizziness and Headache..

4.6 Paediatric population

Following a single oral dose of 1.5, 3.0 and 6.0 mg/kg of cefixime in Japanese paediatric patients, maximum serum concentrations at around 3 to 4 hours were 1.14, 2.01 and 3.97 mg/L, respectively.

4.7 Interaction with other medicinal products and other forms of Interaction

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.
A false positive direct Coomb's test may occur with cefixime.
The administration of cefixime may result in false-positive results for glucose in the urine using Benedict's solution, Fehling's solution, or Clinitest. It is recommended that glucose tests based on enzymatic glucose oxidase reactions (e.g. Tes-Tape) be used.

4.8 Additional information on special populations

Not Applicable.

4.9 Paediatric population

Following a single oral dose of 1.5, 3.0 and 6.0 mg/kg of cefixime in Japanese paediatric patients, maximum serum concentrations at around 3 to 4 hours were 1.14, 2.01 and 3.97 mg/L, respectively.

4.10 Fertility, pregnancy and lactation

Pregnancy: Safety of Cefixime in pregnant women has not been established.
Lactation: It is not known whether cefixime is excreted in human milk.

4.11 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, which may influence the ability to drive and use machines.

4.12 Undesirable effects

The following adverse reactions will be considered listed:
Blood and lymphatic system class: Eosinophilia, Granulocytopenia, Haemolytic anaemia, Thromocytopenia, Prolonged PT/Coagulation
Gastrointestinal disorders: Abdominal pain, Diarrhoea, Dyspepsia, Nausea, Vomiting, Anorexia, Flatulence
General disorders and administration site conditions: Pyrexia, Face oedema
Hepatobiliary disorders: Jaundice, Hepatitis
Infections and infestations: Pseudomembranous colitis, Vaginitis
Immune System Disorders: Anaphlactic reaction, Serum sickness-like reaction
Investigations: Aspartate aminotransferase increased, Alanine aminotransferase increased, Blood alkaline phosphatase increased, Blood bilirubin increased, Blood urea increased, Blood creatinine increased
Nervous System Disorders: Dizziness, Headache
Respiratory, thoracic and mediastinal disorders: Dyspnoea
Renal and urinary disorders: Renal failure acute including tubulointerstitial nephritis as an underlying pathological condition

Skin and subcutaneous tissue disorders: Drug Rash with eosinophilia and systemic symptoms (DRESS), Erythema multiforme, Pruritus, Rash, Stevens-Johnson syndrome, Toxic epidermal necrolysis, Urticaria, Genital pruritus..

4.13 Overdose

Gastric lavage may be indicated; otherwise, no specific antidote exists. Cefixime is not removed in significant quantities from the circulation by hemodialysis or peritoneal dialysis. Adverse reactions in small numbers of healthy adult volunteers receiving single doses up to 2 g of cefixime did not differ from the profile seen in patients treated at the recommended doses.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Broad-spectrum cephalosporin antibiotic; ATC code: J01DD08
Cefixime inhibits the cell wall synthesis of various bacteria. Cefixime has high affinity for penicillin binding proteins (PBP) 1 (1a, 1b and 1c) and 3 and prevents cross-linking

reaction. Cefixime has broad spectrum activity against Gram-positive and Gram-negative bacteria. Sensitivity will vary according to area, and local prescribing guidelines should always be consulted. Where possible microbiological sensitivity tests should guide treatment as resistance can emerge. Its mechanism of action is bactericidal.

5.2 Pharmacokinetic properties

Absorption: Following oral administration of cefixime to healthy volunteers, peak serum concentrations are generally attained in 3 to 4 hours. After a single oral dose of 50, 100 and 200mg mean peak serum concentrations were 1.02, 1.46 and 2.63 mg/L respectively in 12 healthy volunteers of Western origin and 0.69, 1.13 and 1.95 mg/L respectively in 12 healthy Japanese volunteers.
Paediatric Populations: Following a single oral dose of 1.5, 3.0 and 6.0 mg/kg of cefixime in Japanese paediatric patients, maximum serum concentrations at around 3 to 4 hours were 1.14, 2.01 and 3.97 mg/L, respectively.
Distribution: In human plasma, cefixime is approximately 70% protein bound, a value not concentration dependent in the range 0.5 to 30mg/L. Cefixime is distributed to target organs/tissues such as tonsils, maxillary sinus mucosal tissue, lung tissue and gallbladder tissue.
Metabolism & Excretion: No biologically active metabolites of cefixime were identified in plasma or urine following oral administration to healthy volunteers. Around 20% of a 200mg dose of cefixime is recovered unchanged over 24 hours in the urine of healthy volunteers. The elimination half-life is 2-4 hours.

5.3 Preclinical safety data

There are no findings from chronic toxicity investigations suggesting that any side effects unknown to date could occur in humans. Furthermore, in vivo and in vitrostudies did not yield any indication of a potential to cause mutagenicity. Long-term studies on carcinogenicity have not been conducted. Reproduction studies have been performed in mice and rats at does 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 hypersensitivity of rabbits to antibiotic-induced changes in the population of the microflora of the intestine.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Xanthan Gum	BP
Sodium benzoate	BP
Hydrophobic Colloidal Anhydrous Silica	BP
Colour Sunset yellow FCF	IH
Flavour Vanilla	IH
Sugar (Pharma Grade)/Sucrose	BP
Additional Sugar	BP

6.2 Incompatibilities

None

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Sore protected from light at a temperature not exceeding 30°C.

6.5 Nature and contents of container

60 mL white HDPE bottle packed in a unit carton along with leaflet.

6.6 Special precautions for disposal and other handling

None

7 Marketing Authorisation Holder And Manufacturing Site Addresses

Scott-Edil Advance Research Laboratories & Education Limited.
Hill Top Ind. Area, Bhatoli Kalan,
Baddi-173205, Himachal Pradesh, INDIA

MANUFACTURING SITE ADDRESS

Scott-Edil Advance Research Laboratories & Education Limited.
Hill Top Ind. Area, Bhatoli Kalan,
Baddi-173205, Himachal Pradesh, INDIA

8 MARKETING AUTHORISATION NUMBER

Not Applicable

9 DATE OF FIRST REGISTRATION/RENEWAL OF THE REGISTRATION

Not Applicable.

10 DATE OF REVISION OF THE TEXT

Not Applicable

11 DOSIMETRY

Not Applicable