Summary of Product Characteristic (SmPC)

1. Name of the medicinal product

1.1 (Invented) Name of the medicinal product : Cefixime for oral suspension USP

1.2 Strength

Each 5 ml reconstituted suspension contains

Cefixime USP as Trihydrate eq. to anhydrous Cefixime 100 mg

Excipients Q.S.

1.3 Pharmaceutical Form

Powder for Oral Suspension

2. Qualitative and Quantitative Formula

Sr. No.	Material Name	Specification	Std. Qty/ 5 ml	Overages (%)	Actual Qty./ 5 ml	Qty. for Std. Batch size (5000 bottles)	Unit
DRYING STAGE							
1.	Sucrose refine	USP	1842.167 mg	-	1842.167 mg	184.216	Kg
MIXING STAGE							
2.	Cefixime Trihydrate eq.to Cefixime 100 mg	USP	120.000	-	120.00	12.000	Kg
3.	Sodium Benzoate	USP	5.000	-	5.000	0.500	Kg
4.	Colour Ponceau 4R supra	IH	0.500		0.500	0.050	Kg
5.	Xanthan Gum	USP	9.667	-	9.667	0.967	Kg
6.	Colloidal Anhydrous Silica	USP	8.667	-	8.667	0.867	Kg
7.	Essence Dry vanilla	IH	14.00	-	14.00	1.400	Kg
TOTAL WEIGHT			**2000.00 mg**		**2000.00 mg**	**200.000**	**Kg**

Note: * Quantity mentioned is an per molecular weight correction. Quantity includes to compensate and water content. 120 mg of the Cefixime Trihydrate is eq. to 100 mg of Cefixime.

3. Pharmaceutical form

Powder for oral suspension

4. Clinical particulars

4.1 Therapeutic Indication:

Cefixime is indicated for the treatment of the following infections when caused by susceptible organisms.

- Acute exacerbations of chronic bronchitis
- Community-acquired Pneumonia
- Lower urinary tract infections
- Pyelonephritis

In the treatment of:

Otitis media

Sinusitis

Pharyngitis

The use of Cefixime should be reserved for infections where the causative organism is known or suspected to be resistant to other commonly used antibiotics, or where treatment failure may carry significant risk. Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Contraindications

Patients with known hypersensitivity to cefixime, other cephalosporin antibiotics or to any of the excipients.

Cefixime is also contraindicated in patients with previous, immediate and/or severe hypersensitivity to penicillin or any beta-lactam antibiotics and preterm and term newborn infants (0-27 days).

4.3 Special warnings and precautions for use:

Cefixime should be given with caution to patients who have shown hypersensitivity to other drugs. Cephalsporins should be given with caution to penicillin-sensitive patients, as there is some evidence of partial cross-allerginicity between penicillin and cephalsporins.

Patients have had severe reactions (including anaphylaxis) to both classes of drugs. Special care is indicated in patients who have experienced any allergic reaction to penicillins or any beta-lactam antibiotics as cross-reactions may occur.

If severe hypersensitivity reactions or anaphylactic reactions occur after administration of Cefixime, the medicine should be discontinued immediately and appropriate emergency measures should be initiated. Prolonged use of cefixime may result in the overgrowth of non-susceptible organisms.

Treatment with a broad spectrum of antibiotics alters the normal flora of the colon and may permit the overgrowth of *Clostridia*. Studies indicate that a toxin produced by *Clostridium difficile* is a primary cause for antibiotic-associated diarrhoea. Pseudomembranous colitis is associated with the use of broad-spectrum antibiotics (including macrolides, semi-synthetic penicillins, lincosamides and cephalsporins). It is therefore important to consider its diagnosis in patients who develop diarrhoea in association with the use of antibiotics.

In patients who develop severe diarrhoea during or after use of cefixime, the risk of life threatening pseudo-membranous colitis should be taken into. The use of cefixime should be discontinued and appropriate treatment measures should be established. Management of pseudomembranous colitis should include sigmoidoscopy, appropriate bacteriologic studies, fluids, electrolyte 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 antibioticassociated pseudomembreanous colitis produced by *C. Difficile*. Other causes of colitis should be excluded. The use of medicinal products inhibiting the intestinal peristalsis is contra-indicated.

Cefixime contains sucrose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Use of Nifedipine, a calcium channel blocker, may increase bioavailability of Cefixime upto 70%.

Renal insufficiency

Cefixime should be administered with caution in adult patients with creatinine clearance <20ml/min. There are insufficient data regarding use of cefixime in the pediatric and adolescent age group in the presence of renal insufficiency: the use of cefixime in these patient-groups is not recommended.

4.4 Interaction with other medicinal products and other forms of interaction

The administration of cephalsporins may interfere with the results of some laboratory tests.

A false positive reaction for glucose in the urine may occur with the 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.

In common with other cephalsporins, increases in prothrombin times have been noted in a few patients. Care should therefore be taken in patients receiving anticoagulation therapy.

In use with Nifedipine, a calcium channel blocker, may increase bioavailability of Cefixime upto 70%.

4.5 Adverse Drug Reactions

Cefixime, like other cephalsporin antibiotics, may be associated with adverse events.

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

The following undesirable effects have been divided in the following categories:

Very common: >1/10

Common: >1/100 to <1/10

Uncommon: >1/1,000 to <1/100

Rare: >1/10,000 to <1/1,000

Very rare: <1/10,000

Not known: cannot be estimated from the available data

MedDRA System Organ Class	Adverse Reaction	Frequency
Infections and infestations	Superinfection bacterial, superinfection fungal	Rare
	Antibiotic-associated colitis	Very rare
Blood and lymphatic system disorders	Eosinophilia	Rare
	Leucopenia, agranulocytosis, pancytopenia, thrombocytopenia, haemolytic anaemia	Very rare
Immune system disorders	Hypersensitivity	Rare
	Anaphylactic shock, serum sickness	Very rare
Metabolism and nutrition disorders	Anorexia	Rare
Nervous system disorders	Headache	Uncommon
	Vertigo, dizziness	Rare
	Psychomotor hyperactivity	Very rare
Gastrointestinal disorders	Diarrhoea	Common
	Abdominal pain, nausea, vomiting	Uncommon
	Flatulence	Rare
	Cases of pseudomembraneous colitis	Very rare
Hepatobiliary disorders	Hepatitis, cholestatic jaundice	Very rare
Renal and urinary disorders	Interstitial nephritis	Very rare
General disorders and administration site conditions	Mucosal inflammation, pyrexia	Rare

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antibacterial for systemic use, belonging to the class of cephalsporins, ATC code: J01DD08.

Mode of action

Cefixime is an antibiotic belonging to the third generation cephalosporin group. Like other cephalsporins, cefixime exerts antibacterial activity by binding to and inhibiting the action of penicillin-binding 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.

5.2 Pharmacokinetic properties

Absorption

The absolute 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 for meals.

Distribution

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.

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.

Metabolism and elimination

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.

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 labelled cefixime.

Special age groups

The pharmacokinetics of cefixime in healthy elderly (aged > 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.

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 vitro* studies 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

Sucrose USP

Sodium Benzoate USP

Colour Ponceau 4R INH

Colloidal Silicon Dioxide USP

Essence Dry Vanilla INH

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

Unopened: 24 months

6.4 Special precautions for storage

Powder for Oral Suspension: Please Do not store above 30°C. Keep the container tightly closed. Store in the original container.

Oral Suspension: Store at 2°C - 8°C. Do not freeze. Keep the container tightly closed.

6.5 Nature and contents of container

100 ml ring white HDPE bottle with 25 mm white cap with induction seal and measuring cup in a carton along with pack insert.

6.6 Special precautions for disposal

No special requirements. Any unused product or waste material should be disposed of in accordance with local requirements.

7. MANUFACTURER

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8. DATE OF REVISION OF THE TEXT:

Not Applicable

9. NAME AND ADDRESS OF MANUFACTURER

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