

Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

FIX 200

Cefixime Tablets USP 200mg

2. Qualitative and quantitative composition

Each film coated tablet contains:

Cefixime USP (as Trihydrate)

equivalent to anhydrous Cefixime 200 mg

Excipientsq.s

Colour – Titanium Dioxide BP, Sunset yellow

3. Pharmaceutical form

An orange coloured, round shaped, film coated tablet having both sides plain.

4. Clinical particulars

4.1 Therapeutic indications

Cefixime Tablets USP 200mg 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*, *Klebsiella* species, *Haemophilus influenzae* (beta-lactamase positive and negative), *Branhamella catarrhalis* (beta-lactamase positive

and negative) and *Enterobacter* species. Cefixime Tablets USP 200mg 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 methicillin-resistant strains) are resistant to Cefixime Tablets USP 200mg. In addition, most strains of *Pseudomonas*, *Bacteriodes fragalis*, *Listeria monocytogenes* and *Clostridia* are resistant to Cefixime Tablets USP 200mg.

4.2 Posology and method of administration

Posology - As directed by physician.

Method of administration:

Oral.

4.3 Contraindications

Hypersensitivity to cephalosporin antibiotics or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

1.1 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 Tablets USP 200mg 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 Tablets USP 200mg, the drug should be discontinued and the patient treated with appropriate agents if necessary.

Haemolytic anaemia

Drug-induced haemolytic anaemia, including severe cases with a fatal outcome, has been described for cephalosporins (as a class). The recurrence of haemolytic anaemia after re-administration of cephalosporins in a patient with a history of cephalosporin (including cefixime) – associated haemolytic anaemia has also been reported.

Acute renal failure

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 Tablets USP 200mg should be administered with caution in patients with markedly impaired renal function (see section 4.2).

Paediatric use

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

4.5 Interaction with other medicinal products and other forms of interaction

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 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.

4.6 Pregnancy and Lactation

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 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 sensitivity of rabbits to antibiotic-induced changes in the population of the microflora of the intestine. There are no adequate and well-controlled studies in pregnant women. Cefixime Tablets USP 200mg should therefore not be used in pregnancy or in nursing mothers unless considered essential by the physician.

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

Cefixime Tablets USP 200mg 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 Hypereosinophil ia Agranulocytosis Leucopenia Neutropenia
	Granulocytopen ia Haemolytic anaemia Thrombocytope nia Thrombocytosis
Gastrointestinal disorders:	Abdominal pain Diarrhoea* Dyspepsia Nausea Vomiting Flatulence
Hepatobiliary disorders:	Jaundice

Infections and infestations:	Pseudomembra nous colitis Vaginitis
Investigations:	Aspartate aminotransferas e increased Alanine aminotransferas e increased Blood bilirubin increased Blood urea increased Blood creatinine increased
Nervous system disorders:	Dizziness Headache Cases of convulsions have been reported with cephalosporins including cefixime (frequency not known)** 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 (frequency not known)**
Respiratory, thoracic and mediastinal disorders:	Dyspnoea
Renal and urinary disorders:	Acute renal failure with tubulointerstitia l nephritis
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)
General disorders and administrative site conditions:	Drug Fever Arthralgia Pyrexia Face oedema Genital pruritus

The above mentioned listed adverse reactions have been observed during clinical studies and/or during marketed use.

Preferred term in MedDRA (v.14.0)

*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 Tablets USP 200mg should be discontinued if marked diarrhoea occurs.

**Cannot be estimated from available data

Reporting of suspected adverse reactions: Healthcare professionals are requested to report any suspected adverse reactions to the National Regulatory Agents.

4.9 Overdose

There is a risk of encephalopathy associated with beta-lactam antibiotics such as cefixime, particularly in case of overdose or renal impairment.

Adverse reactions seen at dose levels up to 2 g Fix 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

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 methicillin-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 – 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 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.

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

Sr. No.	Ingredients	Specifications
Dry mixing		
1.	Microcrystalline cellulose (PH 112)	BP
Lubrication		
2.	Pregelatinized starch	BP
3.	Colloidal Silicon Dioxide	USP
4.	Magnesium Stearate	BP
5.	Sodium Starch Glycolate	BP
6.	Propyl gallate	BP
7.	Calcium Hydrogen Phosphate Dihydrate	BP
8.	Kyron T-314	IH
Film coating		
9.	Film coat sunset yellow	IH
10.	Film coat white	IH
11.	IPA	BP
12.	MDC	IH

6.2 Incompatibilities

Not applicable

6.3 Shelf-Life

36 months

6.4 Special Precautions for storage

Store below 30°C and protect from light.

6.5 Nature and Content of container

Ten tablets packed in one blister. One such blister packed in monocarton with package insert.

6.6 Special precautions for disposal and other handling

No special requirements.

7. Marketing Authorization Holder

Lexine Technochem Pvt. Ltd, Opp Ramakaka, Deri, Chhani,
Vadodara-391740, Gujarat, India.

8. Marketing Authorization Number

NA

9. Date of first authorization/renewal of the authorization

NA

10. Date of revision of the text

30TH.06.2030