SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Cefixime 100 mg/5 ml Powder for Oral Suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, each 5 mL suspension contains Cefixime Trihydrate USP equivalent to Cefixime 100 mg.

Name of Components
Cefixime (as Trihydrate)
Sucrose
Sodium Benzoate
Colloidal Silicon Dioxide
Banana Trusil Flavour
Raspberry Trusil Flavour
Lemon Yellow Colour

3. PHARMACEUTICAL FORM

Powder for oral suspension.

An almost white free flowing powder with a characteristic pleasant odor which forms yellow suspension on reconstitution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Clinical efficacy of **FIX-A** (Cefixime) 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.

FIX-A (Cefixime) is indicated for the treatment of the following acute infections caused by the susceptible microorganisms.

- Upper respiratory tract infections e.g. otitis media and other URT infection 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 infections e.g. bronchitis.
- Urinary tract infections e.g. cystitis, cystourethritis, uncomplicated pyelonephritis.
- Uncomplicated gonorrhea (cervical/urethral).

4.2 Posology and method of administration

Adults: The recommended adult dosage is 10 ml – 20 ml daily according to the severity of infection, given either as a single dose or in two divided doses.

Children: The recommended dosage for children is 8 mg/kg/day administered as a single dose or in two divided doses:

6 months up to 1 year:	3.75 ml daily
1-4 years:	5 ml daily
5-10 years:	10 ml daily

The safety and efficacy of Cefixime has not been established in children less than 6 months.

Dosage in Renal Impairment: FIX-A (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 haemodialysis should follow the same recommendation as that for patients with creatinine clearances of less than 20 ml/min.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

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 cefixime. When severe cutaneous adverse reactions occur, cefixime should be discontinued and appropriate therapy and/or measures should be taken. **FIX-A** (Cefixime) 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 **FIX-A** (Cefixime), 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.

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

FIX-A (Cefixime) should be administered with caution in patients with markedly impaired renal function (See Dosage in Renal Impairment).

Paediatric use

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

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

Carbamazepine: Elevated Carbamazepine levels have been reported in concomitant administration of Cefixime.

Warfarin and Anticoagulants: Increased prothrombin time with or without clinical bleeding has been reported when Cefixime is administered concomitantly. Care should therefore be taken in patients receiving anticoagulation therapy.

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

4.6 Fertility, Pregnancy and Lactation

There are no adequate and well controlled studies in pregnant women. **FIX-A** (Cefixime) 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

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.

4.8 Undesirable effects

FIX-A (Cefixime) is generally well tolerated. The following adverse reactions may happen following the use of Cefixime. Incidence rates were less than 1 in 50 (less than 2%).

Gastrointestinal: The onset of pseudomembranous colitis symptoms may occur during or after therapy.

Hypersensitivity Reactions: Anaphylactic/anaphylactoid reactions (including shock and fatalities), skin rashes, urticaria, drug fever, pruritus, angioedema, and facial edema. Erythema multiforme, Stevens-Johnson syndrome, and serum sickness-like reactions have been reported.

Hepatic: Transient elevations in SGPT, SGOT, alkaline phosphatase, hepatitis, jaundice.

Renal: Transient elevations in BUN or creatinine, acute renal failure.

Central Nervous System: Headaches, dizziness, seizures.

Hemic and Lymphatic System: Transient thrombocytopenia, leukopenia, neutropenia, prolongation in prothrombin time, elevated LDH, pancytopenia, agranulocytosis, and eosinophilia.

Abnormal Laboratory Tests: Hyperbilirubinemia.

Other Adverse Reactions: Genital pruritus, vaginitis, candidiasis, toxic epidermal necrolysis. Adverse Reactions Reported for Cephalosporin-class Drugs Allergic reactions, superinfection, renal dysfunction, toxic nephropathy, hepatic dysfunction including

cholestasis, aplastic anemia, hemolytic anemia, hemorrhage, and colitis. May have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced.

4.9 Overdose

There is no experience with overdoses with Cefixime. Adverse reactions seen at dose levels up to 2 g of Cefixime in normal subjects did not differ from the profile seen in patients treated at the recommended doses. Gastric lavage may be indicated in overdosage. No specific antidote exists. Cefixime is not removed from the circulation in significant quantities by dialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Cefixime is an antibacterial for systemic use, belonging to the class of 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.

5.2 Pharmacokinetics properties

Absorption:

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.

Mean maximum concentration (C_{max}) and area under the curve (**AUC**) values were slightly greater in the elderly.

Distribution:

Serum protein binding is well characterized for human 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. No data are available on secretion of Cefixime in human breast milk.

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.

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 fetus 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, Sodium Benzoate, Colloidal Silicon Dioxide, Banana Trusil Flavor, Raspberry Trusil Flavor, Lemon Yellow Color.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 Months.

After reconstitution: The reconstituted suspension should be used within 14 days of preparation.

6.4 Special precautions for storage

After reconstitution: The reconstituted suspension should be stored in a cool place and used within 14 days of preparation.

6.5 Nature and contents of container

Nature of container: Type III molded, amber coloured, round glass bottle with 75 ml ring mark and with a plastic child resistant cap.

Contents of container:

Bottle of size 75 ml.

Each amber coloured, round glass bottle contains dry powder for the preparation of 75 ml suspension. A 5 ml dropper and a 10 ml measuring cup are given.

7. MARKETING AUTHORISATION HOLDER

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8. NUMBER IN THE NATIONAL REGISTER OF FPP

05048/06761/NMR/2018

9. DATE OF FIRST AUTHORIZATION/ RENEWAL OF THE AUTHORIZATION

Mar 5, 2020

10. DATE OF REVISION OF THE TEXT