Summary of Product Characteristics

1. Name of the medicinal product

a) Trade name : TAXIM-O 400 mg

b) Generic name : Cefixime Capsules 400 mg

c) Pharmaceutical form : Capsules

d) Composition : Each capsule contains:

Each capsule contains:
Cefixime (as trihydrate) USP
Equivalent to anhydrous Cefixime ……400 mg.
Excipients…… q.s.
Approved colour used in capsule shells

2. Qualitative and Quantitative composition

Qualitative Composition

Each capsule contains:
Cefixime (as trihydrate) USP
Equivalent to anhydrous Cefixime ……400 mg.
Excipients…… q.s.
Approved colour used in capsule shells

For full list of Excipients, see section 6.1

3. Pharmaceutical form

Capsules.

Description: Hard gelatin capsules size '0' having Green colour caps & Green colour body containing almost white powder.

4. Clinical Particulars

4.1 Therapeutic Indications

TAXIM-O 400 mg is indicated in the treatment of the following infections:

- Urinary tract infections (cystitis and kidney infections)
- Upper respiratory tract infections (sinusitis, tonsillitis, pharyngitis and otitis media)
- Lower respiratory tract infections (bronchitis and pneumonia)

4.2 Posology and method of administration

The usual course of treatment is 7 days. This may be continued for up to 14 days if required.

Posology

Dosage regime for adults and children over 10 years or weighing more than 50 kg and warning statement for children under 10 years:

TAXIM-O 400 mg are not recommended for use in children under 10 years old. The safety and efficacy of cefixime has not been established in children less than 6 months.

Elderly:

Elderly patients may be given the same dose as recommended for adults. Renal function should be assessed and dosage should be adjusted in severe renal impairment (See “Dosage in Renal Impairment”).

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.

Method of administration
Oral.

4.3 Contraindications
TAXIM-O 400 mg is contraindicated in Patients with known hypersensitivity to cephalosporin antibiotics or any of the other components of the product.

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 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, 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 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 difficult 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 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 Fertility, 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 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 Capsules 400 mg 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, and Thrombocytosis, Haemolytic anaemia, Neutropenia.

Gastrointestinal: Abdominal pain, Diarrhoea, Nausea, Vomiting.

Hepatobiliary disorders: Jaundice

Infections and infestations: Pseudomembranous colitis

Investigations: Aspartate amino-transferase increased.

Nervous system disorders: Dizziness, Headache.

Immune system disorders, administrative site conditions, skin and subcutaneous tissue disorders: Anaphylactic reaction, Rash, Stevens-Johnson syndrome, Pyrexia, Face oedema, Vaginitis.

4.9 Overdose

There is a risk of encephalopathy in cases of administration of beta-lactam antibiotics, including cefixime, particularly in case of overdose or renal impairment.

Adverse reactions seen at dose levels up to 2 g cefexime 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: Antibacterial for systemic use, belonging to the class of Cephalosporins, **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 meticillin-resistant strains) are resistant to Cefixime. In addition, most strains of *Pseudomonas, Bacteroidesfragilis, 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 and 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 characterized 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 ^{14}C-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. Placetal transfer of Cefixime was small in pregnant rats dosed with labelled Cefixime.

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 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.

6. Pharmaceutical particulars

6.1 List of Excipients

Excipients	Ref.	Each/Cap. (mg)	Function
Sodium Starch Glycolate	USP	32.500	Super Disintegrant
Magnesium Stearate	USP	2.500	Lubricant
Talc	USP	2.500	Glidant

Colloidal Silicon Dioxide	USP	2.500	Glidant
Capsule Shell‘0’colour GR/ GR	USP	1 NO.	Drug Vehicle
Cap		Avg. weight (%)	
Gelatin	BP	q.s for 100%	To Fill medicament
Sodium Lauryl Sulphate	BP	0.20%	surfactant
Sodium methyl paraben	BP	0.40%	Preservative
Titanium dioxide	BP	0.500%	pigment
Brilliant Blue	IH	0.121%	Colorant
Tartrazine	IH	0.158%	Colorant
Body			
Gelatin	BP	q.s for 100%	To Fill medicament
Sodium Lauryl Sulphate	BP	0.20%	surfactant
Sodium methyl paraben	BP	0.40%	Preservative
Titanium dioxide	BP	0.500%	pigment
Brilliant Blue	IH	0.121%	Colorant
Tartrazine	IH	0.158%	Colorant

6.2 Incompatibilities
Not applicable.

6.3 Shelf Life
24 months from the date of manufacturing.

6.4 Special Precautions for Storage
Store below 30°C. Protect from light and moisture.
Keep all the medicine out of the reach and sight of Children.

6.5 Nature and Contents of container
5 Capsules packed in Alu/Alu blister and such one blister packed in a printed mono carton along with package insert.

6.6 Special precautions for disposal
Any unused product or waste material should be disposed of in accordance with local requirements

Prescription Only Medicine

7. Marketing Authorization Holder
Alkem Laboratories Limited
Devashish Building, Alkem House, Senapati Bapat Road, Lower Parel,
Mumbai-400 013, (Maharashtra), India.

Manufactured in India by:
East African (India) Overseas
Plot No. 1, Pharmacity,
Selaqui, Dehradun, Uttarakhand (India).

8. Marketing Authorization Number
TAN 22 HM 0217

9. Date of First Authorization/Renewal of Authorization
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10. Date of Revision of the Text