# MARYICEF 400 TABLETS (Cefixime tablet 400 mg USP)

## Module 1: Administrative And Product Information

KRUX Pharma Pvt. Ltd

### 1.3 Product Information

### 1.3.1 Summary of product characteristics (SmPC)

**1 Name of the drug product** MARYICEF 400 TABLETS (Cefixime tablet 400 mg USP)

**2. Qualitative and quantitative composition**

Each film coated tablet contains
Cefixime Trihydrate USP equivalent to cefixime ……400 mg
Excipients…… q.s
colour …Titanium dioxide

**Master Formula For 1,00,000 Tablets:**

| Sr. No. | Materials | Item code | Category | Pharmacopoeial Reference | Qty./ Tab (In Mg) | Std. Qty./ Batch (In Kg) |
|---|---|---|---|---|---|---|
| 1. | Cefixime Trihydrate | CKPRMA003 | API | USP | 448.00 | 44.8 |
| 2. | Microcrystalline Cellulose PH 112 | CKPRME040 | Binder | BP | 209.5 | 20.95 |
| 3. | Croscarmellose Sodium | CKPRME001 | Disintegrating Agent | BP | 30.00 | 3.00 |
| 4. | Cross Povidone XL10 | CKPRME002 | Disintegrating Agent | BP | 15.00 | 1.5 |
| 5. | Colloidal Silicon di oxide | CKPRME005 | Glidant | BP | 2.5 | 0.25 |
| 6. | Purified Talcum | CKPRME013 | Glidant | BP | 20 | 2 |
| 7. | Magnesium Stearate | CKPRME007 | Lubricant | BP | 15 | 1.5 |
| | | | | Total | 740.000 | 74.000 |

- Actual quantity of active material will vary depending on assay (as is basis) as follow,

$$\text{Actual Qty. of active material per batch} = \text{Std. Qty. for batch} \times \frac{100}{\%\ \text{Assay on as is basis}}$$

- Microcrystalline cellulose PH 112 Qty. to be compensated to 740.0 mg (core weight tablet) based on active material factor calculation.
- 3 % Extra Qty. of Microcrystalline Cellulose PH 112 shall be dispensed to compensate drying loss.

➢ **Master Formula of Coating Material For 1,00,000 Tablets:**

| Sr. No. | Material | Item code | Category | Pharmacopoeial Reference | Qty./ Tab (In Mg) | Std. Qty./ Batch (In Kg) |
|---|---|---|---|---|---|---|
| 1. | Hydroxy propyl methylcellulose(E-5) | CKPRME009 | Film former polymer | IP/BP | 2.5 | 0.25 |
| 2. | Ethyl cellulose | CKPRME010 | Film former polymer & Thickener | IP/BP | 0.8 | 0.08 |
| 3. | Hydroxy propyl methylcellulose(E-15) | CKPRME008 | Film former polymer | IP/BP | 10.5 | 1.05 |
| 4. | PEG | CKPRME038 | Emulsifier | IP/BP | 0.9 | 0.09 |
| 5. | Titanium dioxide | CKPRME011 | Opacifier | IP/BP | 2.5 | 0.25 |
| 6. | Talcum | CKPRME013 | Lubricant & Bulking Agent | IP/BP | 1.3 | 0.13 |
| 7. | Isopropyl Alcohol | CKPRME014 | Solvent | IP/BP | 120 | 12.00 |
| 8. | Methylene Chloride | CKPRME015 | Solvent | IP/BP | 180 | 18.00 |

3. PHARMACEUTICAL FORM: White to off white, Oval shaped, Biconvex, Film coated tablets, Plain on both sides.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

To reduce the development of drug resistant bacteria and maintain the effectiveness of Cefixime Injection USP and other antibacterial drugs, Cefixime Injection USP should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.

When culture and susceptibility information are available, they should be considered in selecting or modifying antimicrobial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Cefixime Injection USP is indicated in the treatment of the following infections when caused by susceptible strains of the designated microorganisms:

Uncomplicated Urinary Tract Infections caused by Escherichia coli and Proteus mirabilis.

Otitis Media caused by Haemophilus influenzae (beta-lactamase positive and negative strains), Moraxella (Branhamella) catarrhalis, (most of which are beta-lactamase positive) and S. pyogenes*.

Pharyngitis and Tonsillitis, caused by S. pyogenes.

Note: Penicillin is the usual drug of choice in the treatment of S. pyogenes infections, including the prophylaxis of rheumatic fever. Cefixime Injection USP is generally effective in the eradication of S. pyogenes from the nasopharynx; however, data establishing the efficacy of Cefixime Injection USP in the su bsequent prevention of rheumatic fever are not available.

Acute Bronchitis and Acute Exacerbations of Chronic Bronchitis, caused by Streptococcus pneumoniae and Haemophilus influenzae (beta-lactamase positive and negative strains).

Uncomplicated gonorrhea (cervical/urethral), caused by Neisseria gonorrhoeae (penicillinase and non-penicillinase- producing strains).
Appropriate cultures and susceptibility studies should be performed to determine the causative organism and its susceptibility to Cefixime; however, therapy may be started while awaiting the results of these studies. Therapy should be adjusted, if necessary, once these results are known.
*Efficacy for this organism in this organ system was studied in fewer than 10 infections.

**4.2 Posology and method of administration**

Adults: The recommended dose of Cefixime is 400 mg daily. This may be given as a 400 mg tablet daily. For the treatment of uncomplicated cervical/urethral gonococcal infections, a single oral dose of 400 mg is recommended.
Children weighing more than 50 kg or older than 12 years should be treated with the recommended adult dose.
Efficacy and safety in infants aged less than six months have not been established.

In the treatment of infections due to S. pyogenes, a therapeutic dosage of Cefixime Tablets USP should be administered for at least 10 days.
Renal Impairment
Cefixime Tablets USP may be administered in the presence of impaired renal function.
Normal dose and schedule may be employed in patients with creatinine clearances of 60 mL/min or greater.
Patients whose clearance is between 21 and 60 mL/min or patients who are on renal hemodialysis may be given 75% of the standard dosage at the standard dosing interval (i.e., 300 mg daily). Patients whose clearance is < 20 mL/min, or patients who are on continuous ambulatory peritoneal dialysis may be given half the standard dosage at the standard dosing interval (i.e., 200 mg daily). Neither hemodialysis nor peritoneal dialysis remove significant amounts of drug from the body.

**4.3 Contraindications**

Cefixime Tablets USP is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

**4.4 Special warnings and special precautions for use warnings**

before therapy with cefixime tablets usp 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 antibiotics 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 tablets usp occurs, discontinue the drug. Serious acute hypersensitivity reactions may require treatment with epinephrine and other emergency measures, including oxygen, ntravenous fluids, intravenous antihistamines, corticosteroids, pressor amines and airway management, as clinically indicated.

Anaphylactic/anaphylactoid reactions (including shock and fatalities) have been reported with the use of Cefixime.

Antibiotics, including Cefixime Tablets USP, should be administered cautiously to any patient who has demonstrated some form of allergy, particularly to drugs.

Treatment with broad spectrum antibiotics, including Cefixime Tablets USP, 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 severe antibioticassociated diarrhea including pseudomembranous colitis.

Pseudomembranous colitis has been reported with the use of Cefixime Tablets USP and other broad spectrum antibiotics (including macrolides, semisynthetic penicillins, and cephalosporins); therefore, it is important to consider this diagnosis in patients who develop diarrhea in association with the use of antibiotics. Symptoms of pseudomembranous colitis may occur during or after antibiotic treatment and may range in severity from mild to life-threatening. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases,

management should include 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 post marketing experience when Cefixime is administered concomitantly. Drug monitoring may be of assistance in detecting alterations in carbamazepine plasma concentrations.

Warfarin and Anticoagulants: Increased prothrombin time, with or without clinical bleeding, has been reported when Cefixime is administered concomitantly.

**4.6 Pregnancy and lactation**

Pregnancy Category B.

Reproduction studies have been performed in mice and rats at doses up to 400 times the human dose and have revealed no evidence of harm to the fetus due to Cefixime. There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Labor and Delivery

Cefixime has not been studied for use during labor and delivery. Treatment should only be given if clearly needed.

Nursing Mothers

It is not known whether Cefixime is excreted in human milk. Consideration should be given to discontinuing nursing temporarily during treatment with this drug.

**4.7 Effects on ability to drive and use machines**

None

**4.8 Undesirable effects**

Most of adverse reactions observed in clinical trials were of a mild and transient nature. Five percent (5%) of patients in the U.S. trials discontinued therapy because of drugrelated adverse reactions. The most commonly seen adverse reactions in U.S. trials of the tablet formulation were gastrointestinal events, which were reported in 30% of adult patients on either the BID or the QD regimen. Clinically mild gastrointestinal side effects occurred in 20% of all patients, moderate events occurred in 9% of all patients and severe adverse reactions occurred in 2% of all patients. Individual event rates included diarrhea 16%, loose or frequent stools 6%, abdominal pain 3%, nausea 7%, dyspepsia 3%, and flatulence 4%. The incidence of gastrointestinal adverse reactions, including diarrhea and loose stools, in pediatric patients receiving the suspension was comparable to the incidence seen in adult patients receiving tablets.

These symptoms usually responded to symptomatic therapy or ceased when Cefixime was discontinued. Several patients developed severe diarrhea and/or documented pseudomembranous colitis, and a few required hospitalization.

The following adverse reactions have been reported following the use of Cefixime. Incidence rates were less than 1 in 50 (less than 2%), except as noted above for gastrointestinal events.

Gastrointestinal (see above): Diarrhea, loose stools, abdominal pain, dyspepsia, nausea, and vomiting. Several cases of documented pseudomembranous colitis were identified during the studies. 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 Systems: Transient thrombocytopenia, leukopenia,

neutropenia, and eosinophilia. Prolongation in prothrombin time was seen rarely.
Abnormal Laboratory Tests: Hyperbilirubinemia.
Other: Genital pruritus, vaginitis, candidiasis, toxic epidermal necrolysis.
In addition to the adverse reactions listed above which have been observed in patients treated with Cefixime, the following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics:
Adverse reactions: Allergic reactions, superinfection, renal dysfunction, toxic nephropathy, hepatic dysfunction including cholestasis, aplastic anemia, hemolytic anemia, hemorrhage, and colitis.
Several cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced. If seizures associated with drug therapy occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated.
Abnormal Laboratory Tests: Positive direct Coombs test, elevated LDH, pancytopenia, Agranulocytosis.

### 4.9 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

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, 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 pediatric 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 Cmax 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 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

- Microcrystalline Cellulose USP
- Croscarmellose Sodium USP
- Colloidal Anhydrous Silica USP
- Sodium Lauryl Sulphate USP
- Magnesium Stearate USP
- Purified Talc USP
- Color Colorezy IH
- Isopropyl Alcohol USP
- Dichloromethane USP
- Diethyl Phthalate USP

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

24 months

### 6.4 Special precautions for storage

Store in a cool, dry and dark place.

### 6.5 Nature and contents of container

10 tablets are packed in a Alu-Alu blister strip of printed aluminum foil and base foil and such 1 Alu-Alu blister strips packed in a inner carton along with leaflet. Such 10 inner cartons placed in outer carton

### 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 :**

M/s. Krux Pharma Private Limited
Plot no: 10/C & 11/C, Survey no: 256/P1, Balda
Industrial. Park, Village: Balda, Tal: Pardi,
Valsad-396125 india

**Supplier**
**M/s. TIM GREAT PHARMACEUTICALS VENTURES LTD**
**NO 8A, ENUGU ROAD, SABON GARI, KANO**