Omixim
(Cefixime)

Capsule:400mg
Tablet: 200mg
Suspension: 100mg/5ml & 200mg/5ml

COMPOSITION

Omixim 400 mg Capsule
Each film coated Capsule contains:
Cefixime (as trihydrate) ..... 400mg (Manufacture Specification)

Omixim 200 mg Tablet
Each film coated Tablet contains:
Cefixime (as trihydrate) ..... 200mg (Manufacture Specification)

Omixim 100mg/5ml & 200mg/5ml Suspension
Each 5ml Suspension contains:
Cefixime (as trihydrate) respectively…….. 100mg/5ml & 200mg/5ml (Manufacture Specification)

PROPRIETARY NAME AND DOSAGE FORM

Therapeutic indications

Cefixime is an orally active cephalosporin antibiotic, indicated in the treatment of adults and pediatric patients six months of age or older with the following infections when caused by susceptible isolates of the designated bacteria.

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 occuring pathogens including *Streptococcus pneumoniae, Streptococcus pyogenes, Escherichia coli, Proteus mirabilis, Kliebsiella* species, *Haemophilus influenzae* (beta-lactamase positive and negative), *Branhamella catarrhalis* (beta- lactamase positive and negative) and *Enterobacter* species. Cefixime is highly stable in the presence of beta-lactamase enzymes.

Posology and method of administration

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

Adult Dosage

The recommended adult dosage is 200-400 mg daily according to the severity of infection, given either as a single dose or in two divided doses. For the treatment of uncomplicated cervical/urethral gonococcal infections, a single oral dose of 400 mg is recommended. The capsule and tablet may be administered without regard to food.

In the treatment of infections due to *Streptococcus pyogenes*, a therapeutic dosage of cefixime should be administered for at least 10 days.

Pediatric Dosage

The recommended dose is 8 mg/kg/day of the suspension. This may be administered as a single daily dose or may be given in two divided doses, as 4 mg/kg every 12 hours.

TABLE 1: PEDIATRIC DOSAGE CHART

Patient Weight (kg)	**Dose/Day (mg)**	**Dose/Day (mL) 100 mg/5 mL**	**Dose/Day (mL) 200 mg/5 mL**
5 to 6.2	50	2.5	1.25
6.3 to 12.5	100	5	2.5
12.6 to 18.8	150	7.5	3.75
18.9 to 25	200	10	5
25.1 to 31.3	250	12.5	6.25
31.4 to 37.5	300	15	7.5
37.6 to 43.8	350	17.5	8.75
43.9 to 50	400	20	10

Note: A suggested dose has been determined for each pediatric weight range. Refer to Table 1.

Children weighing more than 50 kg or older than 12 years should be treated with the recommended adult dose.

In the treatment of infections due to *Streptococcus pyogenes*, a therapeutic dosage of cefixime should be administered for at least 10 days

***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. 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 hemodialysis should follow the same recommendation as that for patients with creatinine clearances of less than 20 ml/min.

Method for administration

For oral administration.

Absorption of Cefixime is not significantly modified by the presence of food.

Contraindications

Hypersensitivity to cephalosporin antibiotics or to any of the excipients

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 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.

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.

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.

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 recognized that a positive Coombs test may be due to the drug.

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.

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.

Undesirable effects

Cefixime is generally well tolerated. The majority of adverse reactions observed in clinical trials were mild and self-limiting in nature. The below mentioned listed adverse reactions have been observed during clinical studies and/or during marketed use.

Blood and lymphatic system disorders: Leucopenia, Neutropenia, Granulocytopenia, Haemolytic anaemia, Thrombocytopenia, Thrombocytosis, Eosinophilia, Hypereosinophilia, Agranulocytosis.

Gastrointestinal disorders: Abdominal pain, Diarrhoea (more commonly associated with higher doses), Dyspepsia, Nausea, Vomiting, Flatulance

Hepatobiliary disorders: Jaundice

Infections and infestations: Pseudomembranous colitis

Investigations: Aspartate aminotransferase increased, Alanine aminotransferase 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: Renal failure acute including tubulointerstitial nephritis as an underlying pathological condition

Immune system disorders, administrative site conditions, skin and subcutaneous tissue disorders: Anaphylactic reaction, Serum sickness-like reaction, Drug rash with eosinophilia and systemic symptoms (DRESS), Pruritus, Rash, Drug Fever, Arthralgia, Erythema multiforme, Stevens-Johnson syndrome, Toxic epidermal necrolysis, Angio-oedema, Urticaria, Pyrexia, Face oedema, Genital pruritus & Vaginitis

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at pv@searlecompany.com

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 Cefixime 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.

Pharmacological properties

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.

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 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. Placental transfer of cefixime was small in pregnant rats dosed with labelled cefixime.

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

PRESENTATION

Omixim Capsule 400mg: Box containing 1 strip of 5 capsules.
Omixim Tablets 200mg: Box containing 1 strip of 10 tablets.
Omixim Suspension 100mg/5mI: Bottle containing powder for the preparation of 30ml suspension.
Omixim Suspension 200mg/5mI: Bottle containing powder for the preparation of 30ml suspension

INSTRUCTIONS

-To be sold on the prescription of a registered medical practitioner only. -Protect from sunlight, moisture and heat.
- Store below 30°C
- Keep all medicines out of sight & reach of children.
- Product contains lactose

REGISTRATION NUMBER

OMIXIM 400 mg Capsules (Product Specs: NovaMed): 062441
OMIXIM 200 mg Tablets: 064844
OMIXIM Suspension 100mg/5ml (Product Specs: U.S.P.): 062443
OMIXIM Suspension 200mg/5ml (Product Specs: U.S.P.): 062444
Diluent Registration Number: 007909

CERTIFICATE OF REGISTRATION – 000590

DILUENT MANUFACTURING LICENCE NUMBER: 000090

MANUFACTURED BY:
NovaMed Pharmaceuticals (Pvt.) Ltd. 28-Km Ferozepur Road, Lahore, Pakistan.
The Searle Company Limited. 32-Km, Multan Road, Lahore – Pakistan.

FOR DILUENT MANUFACTURED BY:
Geofman Pharmaceuticals 20/23 Korangi Industrial Area, Karachi – Pakistan

DATE OF PUBLICATION

July 2021

SPL/SPC-OMIX.T/721-000(001)