Published on: 22 Sep 2014

Omnix Tablets / DT / Dry Syrup (Cefixime)

Composition

OMNIX-50 DT
Each uncoated dispersible tablet contains:
Cefixime, IP, as a trihydrate equivalent to
Anhydrous Cefixime ..... 50 mg
In a flavoured base
Colour:Lake Quinoline Yellow WS
OMNIX-100 DT
Each uncoated dispersible tablet contains:
Cefixime, IP, as a trihydrate equivalent to
Anhydrous Cefixime ..... 100 mg
In a flavoured base
Colour:Lake Quinoline Yellow WS
OMNIX-200 DT
Each uncoated dispersible tablet contains:
Cefixime, IP, as a trihydrate equivalent to
Anhydrous Cefixime ..... 200 mg
In a flavoured base
Colour:Lake Quinoline Yellow WS
OMNIX-50 Dry Syrup
Each 5 ml (after reconstitution) contains:
Cefixime, IP, as a trihydrate equivalent to
Anhydrous Cefixime ..... 50 mg
OMNIX-100 Dry Syrup
Each 5 ml (after reconstitution) contains:
Cefixime IP as trihydrate equivalent to
Anhydrous Cefixime ..... 100 mg

Dosage Form/s

Dispersible tablet and dry powder for oral suspension.

Pharmacology

▶ Pharmacodynamics

Cefixime is a semi-synthetic, oral third-generation cephalosporin, which has marked *in vitro* bactericidal activity against a wide variety of gram-positive and gram-negative organisms. Bactericidal action of cefixime results from inhibition of cell-wall synthesis.
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.
Cefixime has been shown to be active against most isolates of the following bacteria both *in vitro* and in clinical infections:

Gram-positive Bacteria

Streptococcus pneumoniae
Streptococcus pyogenes

Gram-negative Bacteria

Haemophilus influenzae(beta-lactamase-positive and -negative)
Moraxella catarrhalis
Escherichia coli
Proteus mirabilis
Neisseria gonorrhoeae

Also, clinical efficacy has been demonstrated in infections caused by commonly occurring pathogens, including *Branhamella catarrhalis* (beta-lactamase-positive and -negative) and *Enterobacter* species.
The following *in vitro* data are available, but their clinical significance is unknown. Cefixime exhibits *in vitro* MICs of 1 mcg/mL or less against most (≥90%) isolates of the following bacteria; however, the safety and effectiveness of cefixime in treating clinical infections due to these bacteria have not been established in adequate and well-controlled clinical trials.

Gram-positive Bacteria

Streptococcus agalactiae

Gram-negative Bacteria

Haemophilus parainfluenzae
Proteus vulgaris
Klebsiella pneumoniae
Klebsiella oxytoca
Pasteurella multocida
Providencia species
Salmonella species
Shigella species
Citrobactera malonaticus
Citrobacter diversus
Serratia marcescens

▶ Pharmacokinetics

The absolute oral bioavailability of cefixime is in the range of 22 to 54%. Cefixime tablets and suspension, given orally, are about 40 to 50% absorbed whether administered with or without food; however, time to maximal absorption is increased approximately 0.8 hours when administered with food. Typically, the peak serum levels following the recommended adult or paediatric doses are between 1.5 and 3 mcg/ml. A single 200 mg tablet of cefixime produces an

average peak serum concentration of approximately 2 mcg/mL (range: 1 to 4 mcg/mL). The oral suspension produces average peak concentrations approximately 25 to 50% higher than the tablets, when tested in normal adult volunteers. Oral suspension 200 mg doses produce average peak concentrations of 3 mcg/mL (range: 1 to 4.5 mcg/mL), when tested in normal adult volunteers. The area under the time versus concentration curve (AUC) is greater by approximately 10 to 25% with the oral suspension than with the tablet after doses of 100 to 400 mg, when tested in normal adult volunteers. This increased absorption should be taken into consideration if the oral suspension isto be substituted for the tablet. Because of the lack of bioequivalence, tablets should not be substituted for oral suspension in the treatment of otitis media. Crossover studies of tablet versus suspension have not been performed in children. Average AUCs at the steady state in elderly patients are approximately 40% higher than average AUCs in other healthy adults. Elderly patients may be given the same dose as the general population.

Absorption is not significantly modified by the presence of food. Cefixime may, therefore, be given without regard to meals.

Peak serum concentrations occur between 2 and 6 hours following oral administration of a single 200 mg tablet, a single 400 mg tablet, or 400 mg of cefixime suspension. Peak serum concentrations occur between 2 and 5 hours following a single administration of 200 mg of suspension.

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.

Cefixime is almost exclusively bound to the albumin fraction. Serum protein binding is concentration independent, with a bound fraction of approximately 65%. Protein binding of cefixime is only concentration-dependent in human serum at very high concentrations, which are not seen following clinical dosing. In a multiple-dose study conducted with a research formulation, which is less bioavailable than the tablet or suspension, there was little accumulation of drug in serum or urine after dosing for 14 days. Adequate data on cerebrospinal fluid (CSF) levels of cefixime are not available.

There is no evidence of metabolism of cefixime *in vivo*. Approximately 50% of the absorbed dose is excreted unchanged in the urine in 24 hours. Glomerular filtration is considered the predominant mechanism. Metabolites of cefixime have not been isolated from human serum or urine. In animal studies, it was noted that cefixime is also excreted in the bile in excess of 10% of the administered dose. The serum half-life of cefixime in healthy subjects is independent of dosage form and averages 3 to 4 hours, but may range up to 9 hours in some normal volunteers.

In subjects with moderate impairment of renal function (20 to 40 mL/min creatinine clearance), the average serum half-life of cefixime is prolonged to 6.4 hours. In severe renal impairment (5 to 20 mL/min creatinine clearance), the half-life increased to an average of 11.5 hours. The drug is not cleared significantly from the blood by haemodialysis or peritoneal dialysis. However, a study indicated that with doses of 400 mg, patients undergoing haemodialysis have similar blood profiles as subjects with creatinine clearances of 21 to 60 mL/min.

Indications

To reduce the development of drug-resistant bacteria and maintain the effectiveness of cefixime and other antibacterial drugs, cefixime should be used only to treat 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.

OMNIX DT/Dry Syrup is indicated in the treatment of adults and paediatric patients, 6 months of age or older, with the following infections when caused by susceptible isolates of the designated bacteria:

Uncomplicated Urinary Tract Infections (e.g. cystitis, cystourethritis, uncomplicated pyelonephritis) caused by

Escherichia coli and Proteus mirabilis.

Upper Respiratory Tract Infections (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.

Otitis Media caused by *Haemophilus influenzae, Moraxella catarrhalis,* and *Streptococcus pyogenes.*

Note: For patients with otitis media caused by *Streptococcus pneumoniae,* overall response was approximately 10% lower for cefixime than for the comparator.

Pharyngitis and Tonsillitis caused by *Streptococcus pyogenes.*

Note: Penicillin is the usual drug of choice in the treatment of *Streptococcus pyogenes* infections. Cefixime is generally effective in the eradication of *Streptococcus pyogenes* from the nasopharynx; however, data establishing the efficacy of cefixime in the subsequent prevention of rheumatic fever is not available.

Acute Exacerbations of Chronic Bronchitis caused by *Streptococcus pneumoniae* and *Haemophilus influenzae*.

Uncomplicated Gonorrhoea (cervical/urethral) caused by *Neisseria gonorrhoeae* (penicillinase- and non-penicillinas--producing isolates).

Dosage And Administration

Adults

The recommended adult dosage is 200 to 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. In the treatment of infections due to *Streptococcus pyogenes,* a therapeutic dosage of cefixime should be administered for at least 10 days.

Paediatric Patients (Aged 6 Months or Older)

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.

A suggested dose has been determined for each paediatric weight range in Table 1.

Table 1: Suggested doses for paediatric patients

PAEDIATRIC DOSAGE CHART
Doses are suggested for each weight range and rounded for ease of administration

		OMNIX Dry Syrup	
		50 mg/5 mL	**100 mg/5 mL**
Patient Weight (kg)	***Dose/Day (mg)***	***Dose/Day (mL)***	***Dose/Day (mL)***
5 to 7.5	50	5	2.5
7.6 to 10	80	8	4

10.1 to 12.5	100	10	5
12.6 to 20.5	150	15	7.5
20.6 to 28	200	20	10
28.1 to 33	250	--	12.5
33.1 to 40	300	--	15
40.1to 45	350	--	17.5
45.1 or greater	400	--	20

OMNIX-50 Dry Syrup may be substituted with **OMNIX-50 DT**.

Children weighing more than 45 kg or older than 12 years should be treated with the recommended adult dose, 200 to 400 mg daily depending on the severity of infection).

Otitis media should be treated with suspension.

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

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.

▶ Renal Impairment

Normal dose and schedule may be employed in patients with creatinine clearances of 60 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. Patients whose clearance is between 21 and 60 mL/min or patients who are on renal haemodialysis may be given 75% of the standard dosage at the standard dosing interval (i.e. 300 mg daily).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. Neither haemodialysis nor peritoneal dialysis removes significant amounts of drug from the body.

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

Administration

Absorption of **OMNIX DT/Dry Syrup** is not significantly modified by the presence of food.

OMNIX DT

Disperse the tablet in a teaspoonful (5 ml) of boiled and cooled water before administration.

OMNIX Dry Syrup

Direction for Preparing the Suspension

At the time of dispensing, the dry powder should be reconstituted to form an oral suspension. First, shake the bottle to loosen the powder. Twist and open the vial of sterile water given with the pack. Slowly add half quantity of the sterile water into the bottle. Recap the bottle, and shake it vigorously. Adjust the suspension volume up to the red arrow mark by adding more sterile water, if necessary, and shake again. Store the reconstituted suspension in cool place.
After reconstitution, the contents should be consumed within 7 days. Keep tightly closed. Shake well before each use. Discard the unused portion after 7 days.

Contraindications

Cefixime is contraindicated in patients with a known allergy to cefixime or other cephalosporins or any of the other components of the product.

Warnings And Precautions

Anaphylactic/anaphylactoid reactions (including shock and fatalities) have been reported with the use of cefixime. There is some evidence of partial cross-allergenicity between the penicillins and cephalosporins. Before therapy with cefixime 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 occurs, discontinue the drug.
Clostridium difficile-associated diarrhoea (CDAD) has been reported with the use of nearly all antibacterial agents, including cefixime, and may range in severity from mild diarrhoea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon, leading to overgrowth of *C. difficile*.
If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated.
Studies indicate that a toxin produced by *C. 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.
The dose of cefixime should be adjusted in patients with renal impairment as well as those undergoing continuous ambulatory peritoneal dialysis (CAPD) and haemodialysis (HD). Patients on dialysis should be monitored carefully.
Cephalosporins, including cefixime, may be associated with a fall in prothrombin activity. Those at risk include patients with renal or hepatic impairment, or poor nutritional state, as well as patients receiving a protracted course of antimicrobial therapy, and patients previously stabilized on anticoagulant therapy. Prothrombin time should be monitored in patients at risk and exogenous vitamin K administered as indicated.
Prescribing cefixime in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to

the patient and increases the risk of the development of drug-resistant bacteria.

▶ Drug Interactions

Carbamazepine

Elevated carbamazepine levels have been reported in postmarketing experience when cefixime is administered concomitantly. Drug monitoring may be of assistance in detecting alterations in carbamazepine plasma concentrations.

Warfarin and Anticoagulants

In common with other cephalosporins, increases in prothrombin times with or without clinical bleeding have been noted in a few patients. Care should, therefore, be taken in patients receiving anticoagulation therapy.

Effects on Laboratory Tests

A false-positive reaction for ketones in the urine may occur with tests using nitroprusside, but not with those using nitroferricyanide.

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 Coomb's test has been reported during treatment with other cephalosporins; therefore, it should be recognized that a positive Coomb's test may be due to the drug.

▶ Renal Impairment

The dose of cefixime should be adjusted in patients with renal impairment as well as those undergoing continuous ambulatory peritoneal dialysis (CAPD) and haemodialysis (HD). Patients on dialysis should be monitored carefully. Please refer to **DOSAGE AND ADMINISTRATION.**

▶ Hepatic Impairment

No data on dosing is available for patients with impaired hepatic function.

▶ Pregnancy

Pregnancy Category B

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.

▶ Lactation

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

▶ Paediatric Use

Safety and effectiveness of cefixime in children aged less than 6 months old have not been established. **Please refer to DOSAGE AND ADMINISTRATION**. The incidence of gastrointestinal adverse reactions, including diarrhoea and loose stools, in the paediatric patients receiving the suspension, was comparable to the incidence seen in adult patients receiving tablets. No data are available in case of paediatric patients with impaired renal or hepatic function.

▶ Geriatric Use

Clinical experience has not identified differences in responses between the elderly and younger patients. The differences pharmacokinetic parameters were small and do not indicate a need for dosage adjustment of the drug in the elderly.

Undesirable Effects

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical

trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Cefixime is generally well tolerated. The majority of adverse reactions observed in clinical trials were mild and self-limiting in nature.

Gastrointestinal Disturbances

The most commonly seen adverse reactions were gastrointestinal events, which were reported in 30% of adult patients on either the twice-daily or the once-daily regimen. Therapy was discontinued by 5% of patients because of drug-related adverse reactions.

Individual adverse reactions included diarrhoea (16%), loose or frequent stools (6%), abdominal pain (3%), nausea (7%), dyspepsia (3%), and flatulence (4%).

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 should be discontinued if marked diarrhoea occurs.

Other gastrointestinal side effects seen less frequently are vomiting and flatulence. Pseudomembranous colitis has been reported.

The incidence of gastrointestinal adverse reactions, including diarrhoea and loose stools, in paediatric patients receiving the suspension was comparable with the incidence seen in adult patients receiving tablets.

Central Nervous System

Headache and dizziness.

Hypersensitivity Reactions

Allergies in the form of rash, pruritus, drug fever and arthralgia have been observed, including rare cases of urticaria or angio-oedema. These reactions usually subsided upon discontinuation of therapy. Rarely, erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported.

Haematological and Clinical Chemistry

Thrombocytosis, thrombocytopenia, leucopenia, hypereosinophilia, neutropenia and agranulocytosis have been reported. These reactions were infrequent and reversible. Mild transient changes in liver and renal function tests have been observed.

Hepatic Disorders

Transient rises in liver transaminases, alkaline phosphatase and jaundice can also occur.

Miscellaneous

Other possible reactions include genital pruritus and vaginitis.

Postmarketing Experience

The following adverse reactions have been reported following the use of cefixime. Incidence rates were less than 1 in 50 (less than 2%).

Gastrointestinal

Several cases of documented pseudomembranous colitis were identified in clinical trials. 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, angio-oedema, and facial oedema. Erythema multiforme, Stevens-Johnson syndrome, and serum sickness-like reactions have been reported.

Hepatic

Transient elevations in SGPT, SGOT, alkaline phosphatase, hepatitis, and jaundice.

Renal

Transient elevations in BUN or creatinine, acute renal failure.

Central Nervous System

Headaches, dizziness, seizures.

Haemic and Lymphatic System

Transient thrombocytopenia, leucopenia, neutropenia, prolongation in prothrombin time, elevated LDH, pancytopenia, agranulocytosis, and eosinophilia.

Abnormal Laboratory Tests

Hyperbilirubinaemia.

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 anaemia, haemolytic anaemia, haemorrhage, 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.

Overdosage

There is no experience with overdoses with cefixime. Gastric lavage may be indicated; otherwise, no specific antidote exists. Cefixime is not removed in significant quantities from the circulation by haemodialysis or peritoneal dialysis. Adverse reactionsin 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.

Storage And Handling Instructions

OMNIX DT

Store in a cool, dry place. Protect from light.

OMNIX Dry Syrup

Before Opening

Store below 25°C. Protect from light.

After Reconstitution

The contents should be consumed within 7 days. Keep the bottle tightly closed. Shake well before each use. Discard the unused portion after 7 days.

Packaging Information

OMNIX-50 DT: Strip pack of 10 dispersible tablets

OMNIX-100 DT: Strip pack of 10 dispersible tablets

OMNIX-200 DT: Strip pack of 10 dispersible tablets

OMNIX-50 DT: Bottle of 30 ml dry syrup

OMNIX-100 DT: Bottle of 30 ml dry syrup

Last updated: November 2013

Last reviewed: November 2013

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