ZIPRAX Dispersible Tablets / Dry Syrup (Cefixime)

Qualitative and Quantitative Composition

ZIPRAX-50 DT

Each uncoated dispersible tablet contains:

Cefixime, IP, as a trihydrate equivalent to

Anhydrous Cefixime ..... 50 mg

In a flavoured base

ZIPRAX-100 DT

Each uncoated dispersible tablet contains:

Cefixime, IP, as a trihydrate equivalent to

Anhydrous Cefixime ..... 100 mg

In a flavoured base

ZIPRAX-200 DT

Each uncoated dispersible tablet contains:

Cefixime, IP, as a trihydrate equivalent to

Anhydrous Cefixime ..... 200 mg

In a flavoured base

ZIPRAX-50 Dry Syrup

Each 5 ml (after reconstitution) contains:

Cefixime, IP, as a trihydrate equivalent to

Anhydrous Cefixime ..... 50 mg

ZIPRAX-100 Dry Syrup

Each 5 ml (after reconstitution) contains:

Cefixime, IP, as a trihydrate equivalent to

Anhydrous Cefixime ..... 100 mg

Dosage Form/S and Strengths

Dispersible tablet and dry powder for oral suspension.

Clinical Particulars

Therapeutic 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.

ZIPRAX 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 susceptible isolates of *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 susceptible isolates of *Haemophilus influenzae*, *Moraxella catarrhalis*, and *Streptococcus pyogenes.*

(Efficacy for *Streptococcus pyogenes* in this organ system was studied in fewer than 10 infections).

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-penicillinase-producing isolates).

Posology and Method of Administration

Dosage

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

Adults

The recommended 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			
Patient Weight (kg)	***Dose/Day (mg)***	**ZIPRAX Dry Syrup**	
		50 mg/5 mL	**100 mg/5 mL**
		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
ZIPRAX-50 Dry Syrup may be substituted with **ZIPRAX-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 the suspension. Clinical trials of otitis media were conducted with the suspension, and the suspension results in higher peak blood levels than the tablet when administered at the same dose. Therefore, the tablet should not be substituted for the suspension in the treatment of otitis media.

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

Cefixime may be administered in the presence of impaired renal function. Doses for patients with renal impairment are shown in Table 2.

Table 2: Doses for Patient with Renal Impairment

Renal Dysfunction	**Cefixime for Oral Suspension**		
Creatinine Clearance (mL/min)	500 mg/5 mL	100 mg/5 mL	200 mg/5 mL
	Dose/Day (mL)	Dose/Day (mL)	Dose/Day (mL)
60 or greater	Normal dose	Normal dose	Normal dose
21 to 59* OR renal haemodialysis*	2.6	13	6.5
20 or less OR continuous peritoneal dialysis	1.8	8.6	4.4

*The preferred concentrations of oral suspension to use are 200 mg/5 mL or 500 mg/5mLfor patients with this renal dysfunction.

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 (CAPD) or haemodialysis should follow the same recommendation as that for patients with creatinine clearance of less than 20 ml/min. Neither haemodialysis nor peritoneal dialysis removes significant amounts of drug from the body.

Administration

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

ZIPRAX DT

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

ZIPRAX 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 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.

Special Warnings and Precautions for Use

Hypersensitivity Reactions

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 and patient is to be treated with appropriate agents if necessary.

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.

Clostridium difficile-Associated Diarrhoea

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*.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing isolates of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibacterial drug use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

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.

Dose Adjustment in Renal Impairment

The dose of cefixime should be adjusted in patients with renal impairment as well as those undergoing CAPD and haemodialysis. Patients on dialysis should be monitored carefully.

Coagulation Effects

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.

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.

Development of Drug-Resistant Bacteria

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.

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. The administration of cefixime may result in a false-positive reaction for glucose in the urine using Benedict's solution, or Fehling's solution. It is recommended that glucose tests based on enzymatic glucose oxidase reactions be used. A false-positive direct Coombs test has been reported during treatment with other cephalosporins; therefore, it should be recognized that a positive Coombs test may be due to the drug.

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.

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.

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.

Use in Special Population

Patients with Renal Impairment

The dose of cefixime should be adjusted in patients with renal impairment as well as those undergoing CAPD and haemodialysis. Patients on dialysis should be monitored carefully.

Patients with Hepatic Impairment

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

Pregnant Women

Pregnancy Category B

Reproduction studies have been performed in mice and rats at doses upto 40 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. Cefixime should, therefore, not be used in pregnancy or in nursing mothers unless considered essential by the physician.

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

Lactating Women

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 Patients

Safety and effectiveness of cefixime in children aged less than 6 months old have not been established. 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 hepatic function. **Please refer to DOSAGE AND ADMINISTRATION**.

Geriatric Patients

Clinical studies did not include sufficient numbers of subjects aged 65 years and older to determine whether they respond differently than younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and

younger patients. A pharmacokinetic study in the elderly detected differences in pharmacokinetic parameters. These differences were small and do not indicate a need for dosage adjustment of the

drug in the elderly.

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

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, convulsion and seizures. Beta-lactams, including cefixime, 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).

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. Anaphylactic/anaphylactoid reactions (including shock and fatalities), skin rashes, urticaria, drug fever, pruritus, angioedema, pyrexia, facial oedema, genital pruritis and vaginitis. Erythema multiforme, Stevens-Johnson syndrome, drug rash with eaosinophillia and systemic symptoms (DRESS) and serum sickness-like reactions have been reported.

Hemic and Lymphatic System

Thrombocytosis, transient thrombocytopenia, leucopenia, granulocytopenia hypereosinophilia, haemolytic anaemia, prolongation in prothrombin time, elevated LDH, neutropenia and agranulocytosis have been reported.

Hepatic Disorders

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

Renal Disorders

Transient elevations in BUN or creatinine, acute renal failure

Respiratory, thoracic and mediastinal disorders

Dyspnoea

Renal and urinary disorders

Renal failure acute including tubulointerstitial nephritis as an underlying pathological condition.

Investigations

Increases aspartate aminotransferase increased, alanine aminotransferase, blood bilirubin, blood urea and blood creatinine.

Miscellaneous

Acute generalized exanthematous pustulosis (AGEP) as an adverse drug reaction. Other possible reactions include genital pruritus and vaginitis, candidiasis and toxic epidermal necrolysis.

If you experience any side effects, talk to your doctor or pharmacist or write to drugsafety@cipla.com. You can also report side effects directly via the National Pharmacovigilance Programme of India by calling on 1800 267 7779 (Cipla number) or you can report to PvPI on 1800 180 3024. By reporting side effects, you can help provide more information on the safety of this product.

Overdose

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 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. General supportive measures are recommended.

Pharmacological Properties

Mechanism of Action

Cefixime is a semisynthetic cephalosporin antibacterial drug. As with other cephalosporins, the bactericidal action of cefixime results from inhibition of cell wall synthesis. Cefixime is stable in the presence of certain beta-lactamase enzymes. As a result, certain organisms resistant to penicillins

and some cephalosporins due to the presence of betalactamases may be susceptible to cefixime.

Pharmacodynamic Properties

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.

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), *Klebsiella species* and *Enterobacter* species. It is highly stable in presence of beta-lactamase enzymes.

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

Citrobacter amalonaticus

Citrobacter diversus

Serratia marcescens

Pharmacokinetic Properties

Absorption

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 is to 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.

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.

Distribution

Cefixime is almost exclusively bound to the albumin fraction, the mean free fraction being approximately 30%. 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.

Metabolism and Excretion

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.

Special Populations

Geriatric

Average AUCs at steady state in elderly patients are approximately 40% higher than average AUCs in other healthy adults. Differences in the pharmacokinetic parameters between 12 young and 12 elderly subjects who received 400 mg of cefixime once daily for 5 days are summarized as follows:

Pharmacokinetic Parameters (mean ± SD) for Cefixime in Both Young & Elderly Subjects		
Pharmacokinetic parameter	Young	Elderly
Cmax (mg/L)	4.74 ± 1.43	5.68 ± 1.83
Tmax (h)*	3.9 ± 0.3	4.3 ± 0.6
AUC (mg.h/L)*	34.9 ± 12.2	49.5 ± 19.1
T½ (h)*	3.5 ± 0.6	4.2 ± 0.4
Cave (mg/L)*	1.42 ±0.50	1.99 ± 0.75

*- Difference between age groups was significant ($p<0.05$)

However, these increases were not clinically significant.

Renal Impairment

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.

Nonclinical Properties

Animal Toxicology or Pharmacology

Carcinogenesis, Mutagenesis, Impairment of Fertility

Lifetime studies in animals to evaluate carcinogenic potential have not been conducted. Cefixime did not cause point mutations in bacteria or mammalian cells, DNA damage, or chromosome damage in vitro and did not exhibit clastogenic potential in vivo in the mouse micronucleus test. In rats, fertility

and reproductive performance were not affected by cefixime at doses up to 25 times the adult therapeutic dose.

Description

Cefixime is a semisynthetic, cephalosporin antibacterial for oral administration. Chemically, it is (6R,7R)-7-[2-(2-Amino-4-thiazolyl)glyoxylamido]-8-oxo-3-vinyl-5-thia-1-azabicyclo [4.2.0] oct-2-en--2-carboxylic acid, 72-(Z)-[O-(carboxy methyl) oxime] trihydrate. Molecular weight = 507.50 as the trihydrate. Chemical Formula is C16H15N5O7S2.3H2O.

Pharmaceutical Particulars

Incompatibilities

Not applicable

Shelf-life

As on the pack.

Packaging Information

ZIPRAX-50 DT: Strip pack of 10 dispersible tablets

ZIPRAX-100 DT: Strip pack of 10 dispersible tablets

ZIPRAX-200 DT: Strip pack of 10 dispersible tablets

ZIPRAX-50 Dry Syrup: Bottle of 30 ml dry syrup

ZIPRAX-100 Dry Syrup: Bottle of 30 ml dry syrup

Storage and Handling Instructions

ZIPRAX DT

Store below 30°C. Protect from light.

ZIPRAX 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.

Patient Counselling Information

1. What is Cefixime and what it is used for?

Cefixime belongs to a group of antibiotics called ‘cephalosporins’ which is used to treat infections caused by bacteria. These include infections of the:

- Ear
- Nose, sinuses (such as sinusitis)
- Throat (such as tonsillitis, pharyngitis)
- Chest and lungs (such as bronchitis, pneumonia)
- Urinary system (such as cystitis and kidney infections)

2. What you need to know before you take Cefixime?

Do not take cefixime: if you are allergic to cefixime, any other cephalosporin antibiotics including penicillin or to any of the other ingredients of this medicine. Signs of an allergic reaction include: a rash, swallowing or breathing problems, swelling of the lips, face, throat and tongue. Do not take this medicine if the above applies to you. If you are not sure, talk to your doctor or pharmacist before taking cefixime.

Warnings and precautions

Talk to your doctor before taking cefixime:

If you have ever had colitis

If you have kidney problems

If you are not sure if any of the above apply to you, talk to your doctor before taking this medicine.

Other medicines and cefixime

Tell your doctor if you are taking, have recently taken or might take any other medicines. This includes medicines you buy without a prescription, including herbal medicines. This is because cefixime can affect the way some other medicines work. Also some medicines can affect the way cefixime works. In particular, tell your doctor if you are taking the following:

- **Medicines to thin the blood such as warfarin**

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines

This medicine can cause symptoms including fits (convulsions), feeling confused, feeling less alert or aware of things than usual, unusual muscle movements or stiffness. If you experience any of these effects don’t drive or use machinery.

Medical Tests

If you require any tests (such as blood or urine tests) while taking this medicine, please make sure your doctor knows that you are taking cefixime.

3. How to take cefixime?

Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

- Take this medicine by mouth
- If you feel the effect of the medicine is too weak or too strong, do not change the dose yourself, but ask your doctor. The medicine should be taken for the prescribed number of days.

The recommended dose is:

Adults

A dosage of 200 to 400 mg daily according to the severity of infection, may be given given either as a single dose or in two divided doses.

Elderly patients

Elderly patients may be given the same dose as recommended for adults.

People with kidney problems

Your doctor may prescribe a lower dose.

Children

Cefixime can be given to children aged 6 months and older.

If you take more cefixime than you should

If you have too much of this medicine, talk to your doctor straight away.

If you forget to take cefixime.

If you forget to take a dose, take it as soon as you remember it. However, if it is nearly time for the next dose, skip the missed dose. Do not take a double dose to make up for a forgotten dose.

If you stop taking cefixime

Do not stop taking this medicine without talking to your doctor. You should not stop

taking cefixime just because you feel better. This is because the infection may come

back or get worse again. If you have any further questions on the use of this medicine, ask your doctor.

4. Possible Side Effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Tell your doctor straight away or go to the nearest hospital casualty department if you notice any of the following serious side effects – you may need urgent medical treatment:

- **You have an allergic reaction.** The signs may include: a rash, joint pain, swallowing or breathing problems, swelling of your lips, face, throat or tongue
- **Blistering or bleeding** of the skin around the lips, eyes, mouth, nose and genitals. Also flu-like symptoms and fever. This may be something called ‘Stevens-Johnson’ syndrome.

- Severe blistering rash where layers of the skin may peel off to leave large areas of raw
- exposed skin over the body. Also a feeling of being generally unwell, fever, chills and
- aching muscles. This may be something called 'Toxic epidermal necrolysis'
- You have a skin rash or skin lesions with a pink/red ring and a pale centre which may be itchy, scaly or filled with fluid. The rash may appear especially on the palms or soles of your feet. These could be signs of a serious allergy to the medicine called 'erythema multiforme'
- You get infections more easily than usual. This could be because of a blood disorder. This normally gets better after stopping the medicine
- You bruise or bleed more easily than normal. This could be because of a blood disorder. This normally gets better after stopping the medicine
- If your child gets nose bleeds, bleeding gums, chills, tiredness, pale skin (often with a yellow tinge), shortness of breath. This may be due to haemolytic anaemia.
- Changes in the way the kidneys are working or blood in your child's urine
- Fits (convulsions) - Frequency not known
- A brain condition with symptoms including fits (convulsions), feeling confused, feeling less alert or aware of things than usual, unusual muscle movements or stiffness. This may be something called encephalopathy. This side effect is more likely if you have taken an overdose or you already have a problem with your kidneys
- Stop taking this medicine and contact your doctor without delay if you get:
- Severe watery diarrhoea that will not stop and you are feeling weak and have a fever. This may be something called 'Pseudomembranous colitis' Tell your doctor if any of the following side effects get serious or lasts longer than a few days:
- Feeling sick (nausea) or being sick (vomiting)
- Stomach pains, indigestion or wind
- Headaches
- Feeling dizzy
- Feeling itchy in the genital or vaginal area
- Tell your doctor if any of the side effects gets serious or lasts longer than a few days, or if you notice any side effects not listed in this leaflet.

Blood tests

Cefixime can cause blood clots or small changes to the way the liver and kidney work. This would be shown up in blood tests. This is not common and goes back to normal after stopping this medicine.

Reporting of side effects

If you get any side effects talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Cefixime?

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the pack.

Store cefixime dispersible tablet below 30°C.

Store cefixime dry syrup below 25°C, before reconstitution. 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.

Do not throw away medicines via wastewater or household waste. Ask your chemist how to throw away medicines you no longer use. These measures will help protect the environment.

Details of Manufacturer

Mfd. By Cipla Ltd.

Registered Office:

Cipla House, Peninsula Business Park,

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Details of Permission or License Number with Date

ZIPRAX 50 mg and 100 mg Dry Syrup

PD/475A 03/02/2015

ZIPRAX 100 mg Dry Syrup

PD/135 03/02/2015

ZIPRAX 50 DT, ZIPRAX 100 DT and ZIPRAX 200 DT

PD/135 05/03/2018

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