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CIN NO: U24231GJ1992PLC018237

MODULE 1- ADMINISTRATIVE PARTICULARS OF THE PRODUCT

1.3 Product Information

1.3.1 Summary of Product Characteristics (SmPC)

Enclosed



Summary of product characteristics (SmPC)

1. NAME OF THE MEDICINAL PRODUCT

AFRIXIME 200 (Cefixime Tablets USP 200 mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains:

Cefixime Trihydrate USP

eq. to. Cefixime Anhydrous 200 mg

Excipients.....q.s.

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Film coated tablet

Visual & Physical characteristics of the product: An orange coloured, round shape, biconvex, film coated tablets having embossed “CHCL” mark on one side and embossed symbol of “CHANRAI” on other side of the tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Cefixime is indicated for the treatment of the following infections when caused by susceptible organisms. (Pharmacodynamic properties & special warnings and precautions for use)

Acute exacerbations of chronic bronchitis

Community-acquired Pneumonia

Lower urinary tract infections

Pyelonephritis

In the treatment of:

Otitis media

Sinusitis

Pharyngitis

The use of cefixime should be reserved for infections in which the causative organism is known or suspected to be resistant to other commonly used antibacterial agents or when treatment failure with other commonly used antibacterial agents may carry significant risk.



4.2 Posology and Method of Administration

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

Posology

Adults and Children over 10 Years or weighing more than 50 kg:

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.

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

Method for administration

For oral administration. Pediatric Data: Cefixime Tablets are not recommended for use in children under 10 years old.

The safety and efficacy of cefixime has not been established in children less than 6 months.

4.3 Contraindications

Hypersensitivity to cephalosporin antibiotics or to any of the excipients listed in section 6.1.

Previous, immediate and/or severe hypersensitivity reaction to penicillin or any beta lactam antibiotic.

4.4 Special Warnings and Precautions for Use

Cefixime should be given with caution to patients who have shown hypersensitivity to other drugs. Cephalosporins should be given with caution to penicillin-sensitive patients, 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. Special care is indicated in patients who have experienced any allergic reaction to penicillins or any other beta-lactam antibiotics as cross-reactions may occur. (Contraindications)



If severe hypersensitivity reactions or anaphylactic reactions occur after administration of cefixime, the use of cefixime should be discontinued immediately and appropriate emergency measures should be initiated.

Renal insufficiency

Cefixime should be administered with caution in adult patients with creatinine clearance < 20 ml / min. (Posology and method of administration & Pharmacokinetic) There are insufficient data regarding use of cefixime in the pediatric and adolescent age group in the presence of renal insufficiency: the use of cefixime in these patient-groups is not recommended. Prolonged use of cefixime may result in the overgrowth of non-susceptible organisms.

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 including cefixime); it is therefore important to consider its diagnosis in patients who develop diarrhoea in association with the use of antibiotics. In patients who develop severe diarrhoea during or after use of cefixime, the risk of life threatening pseudo-membranous colitis should be considered (Undesirable effects). The use of cefixime should be discontinued and appropriate treatment measures should be established. 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 use of medicinal products inhibiting the intestinal peristalsis is contraindicated.

4.5 Interaction with other Medicinal Products and 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.

In common with other cephalosporins, increases in prothrombin time have been noted in a few patients. Care should therefore be taken in patients receiving anticoagulation therapy.



4.6 Pregnancy, Lactation and Fertility

Pregnancy: Caution should be exercised when prescribing to pregnant women. Cefixime should not be used in pregnant mothers unless considered essential by the physician.

Lactation: It is unknown whether cefixime is excreted in human breast milk. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with cefixime should be made considering the benefit of breast-feeding to the child and the benefit of cefixime therapy to the woman. However, until further clinical experience is available, cefixime should not be prescribed to breast-feeding mothers.

4.7 Effects on Ability to Drive and Use Machines

Cefixime has no known influence on the ability to drive and use machines. However, side effects may occur (See also section Undesirable effects), which may influence the ability to drive and use machines.

4.8 Undesirable Effects

In this section, the following convention has been used for the classification of undesirable effects in terms of frequency: Common: $\geq 1/100$ to $< 1/10$, Uncommon: $\geq 1/1,000$ to $< 1/100$, Rare: $\geq 1/10,000$ to $< 1/1,000$ and Very rare: $< 1/10,000$:

MedDRA System Organ Class	Adverse Drug Reaction	Frequency
Infections and infestations	Superinfection bacterial, Superinfection fungal	Rare
	Antibiotic-associated colitis	Very rare
	(see section special warnings)	
Blood and lymphatic system disorders	Eosinophilia	Rare
	Leucopenia, agranulocytosis, pancytopenia, thrombocytopenia, haemolytic anaemia	Very rare
Immune system disorders	Hypersensitivity	Rare
	Anaphylactic shock, serum sickness	Very rare
Metabolism and nutrition disorders	Anorexia	Rare
Nervous system disorders	Headache	Uncommon
	Vertigo	Rare
	Psychomotor hyperactivity	Very rare
Gastrointestinal disorders	Diarrhoea	Common
	Abdominal pain, nausea, vomiting	Uncommon
	Flatulence	Rare
Hepatobiliary disorders	Hepatitis, cholestatic jaundice	Very rare
Skin and subcutaneous tissue disorders	Rash	Uncommon
	Angioneurotic oedema, pruritus	Rare
	Stevens-Johnson syndrome, toxic epidermal necrolysis	Very rare
Renal and urinary disorders	Interstitial nephritis	Very rare



General disorders and administration conditions	Mucosal inflammation, pyrexia	Rare
Investigations	Hepatic enzyme increased (transaminase, alkaline phosphatase)	Uncommon
	Blood urea increased	Rare
	Blood creatinine increased	Very rare

4.9 Overdose

There is no experience with overdoses with cefixime.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Third generation Cephalosporin

ATC Code: J01DD08

Mode of Action

Cefixime is an antibacterial agent of the cephalosporin class. Like other cephalosporins, cefixime exerts antibacterial activity by binding to and inhibiting the action of penicillin-binding proteins involved in the synthesis of bacterial cell walls. This leads to bacterial cell lysis and cell death.

PK/PD relationship

The time that the plasma concentration of cefixime exceeds the MIC of the infecting organism has been shown to best correlate with efficacy in PK/PD studies.

Mechanisms of resistance

- Bacterial resistance to cefixime may be due to one or more of the following mechanisms: Hydrolysis by extended-spectrum beta-lactamases and / or by chromosomally-encoded (AmpC) enzymes that may be induced or depressed in certain aerobic gram-negative bacterial species.
- Reduced affinity of penicillin-binding proteins
- Reduced permeability of the outer membrane of certain gram-negative organisms restricting access to penicillin-binding proteins
- Drug efflux pumps

More than one of these mechanisms of resistance may co-exist in a single bacterial cell. Depending on the mechanism(s) present, bacteria may express cross-resistance to several or all other beta-lactams and / or antibacterial drugs of other classes.

5.2 Pharmacokinetic Properties

Absorption



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.

Distribution:

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.

From in vitro studies, serum or urine concentrations of 1 mg/L 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 mg/L. Little or no accumulation of cefixime occurs following multiple dosing.

Metabolism and elimination:

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. 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).

Special age groups:

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 (see section Posology and method of administration).

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**

Pregelatinized Maize Starch

Sodium Starch Glycolate (Type - A)

Colloidal anhydrous Silica

Purified Talc.



Magnesium Stearate

Crospovidone

Dichloromethane

Col. Elegance Coat-EL-MBS-1094 Orange

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf Life:

24 months

6.4 Special Precautions for Storage

Store below 30°C & dry place. Protect from light & moisture.

Keep out of reach of children.

6.5 Nature and Contents of Container

Primary Packing: 10 tablets are packed in Alu-Alu blister pack.

Secondary Packing: Such one Alu-Alu blister packed in monocarton along with package insert.

6.6 Special Precautions for Disposal:

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. APPLICANT:

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