105x10x40mm

1 x 10 Tablets

Nefixime®200

Cefixime Tablets USP 200 mg

NAFDAC Reg. No.: B4-7947

For :
Nectar Healthcare Ltd.
16B Residence Road,
Gbagada Estate
Phase 2, Gbagada Lagos

Manufactured by:
VAPI CARE PHARMA PVT LTD
Plot No 225/3, Nr. Morarji Circle,
GIDC, Vapi, Dist.-Valsad–396195

Dosage: As directed by the Physician.
Storage: Store in a dry place below 30°C. Read the pack insert carefully.
KEEP MEDICINE OUT OF REACH OF CHILDREN.

1 x 10 Tablets

Nefixime®200

Cefixime Tablets USP 200 mg

NAFDAC Reg. No.: B4-7947

Composition:
Each film coated tablets contains:
Cefixime (as Trihydrate) USP Eq. to Cefixime Anhydrous 200mg
Excipients Q.S.
Colour: Titanium Dioxide

(01) 18906057087136

Mfg. Lic. No.: G/28/1024
Batch No.:
Mfg. date:
Exp. Date:

1.3.1 SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE DRUG PRODUCT: NEFIXIME 200 (Cefixime Tablets USP 200 mg)

2. QUALITATIVE & QUANTITATIVE COMPOSITION

Qualitative Declaration:

Each film coated tablet contain-

Cefixime USP as Trihydrate
Eq. to Anhydrate Cefixime ….. 200mg
Excipients……Q.S.
Colour: Titanium Dioxide

Quantitative Declaration:

Batch Size: 100000 Tablets

Sr. No.	Ingredients	Spec	Qty/Tablet mg	O. A %	UOM	Qty/ Batch
Paste Preparation						
1	PVPK 30	BP	10.00	-	Kg	10.00
2	Iso Propyl Alcohol	BP	q.s	-	Lit	70.00
Granulation						
3	Cefixime Trihydrate	USP	238.00	5	Kg	238.00
4	Micro Crystalline Cellulose	BP	60.00	-	Kg	60.00
5	Colloidal Silicon Dioxide (Aerosil)	BP	3.00	-	Kg	3.00
Lubrication						
6	Magnesium Stearate	BP	3.00	-	Kg	3.000
7	Croscarmellose Sodium (Ac -Di-Sol)	BP	8.00	-	Kg	8.000
8	Purified Talc	BP	5.00	-	Kg	5.000
9	Colloidal Silicon Dioxide (Aerosil)	BP	3.00	-	Kg	3.000
Total			**330.00 mg**			**330.0 Kg**
Coating						
10	Insta coat ICS223 White	IH	10.00	-	Kg	10.00
11	Methylene Dichloride	BP	q.s	-	Lit	142.50
12	Isopropyl alcohol	BP		-	Lit	95.00
Total			**340.00**			**340.00 Kg**

3. PHARMACEUTICAL FORM

White to off white coloured circular biconvex film coated tablet, with one side plain and other side embossed with '200'.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

NEFIXIME is indicated in the treatment of the following infections caused by susceptible organisms.

- Urinary tract infections
- Upper and Lower respiratory tract infections
- Acute otitis media.
- Gonococci urethritis
- Typhoid

4.2 Posology/Dosage and method of administration:

NEFIXIME by oral administration. It can be given to the adults in the following dosages. The usual adult of Cefixime (anhydrous) is 200 - 400 mg per day administered orally, either as a single dose or in two divided doses, although lower doses may prove sufficient to treat uncomplicated urinary tract infections. For Children: 8 mg/kg daily, as either a single dose or in two divided doses, is recommended. In uncomplicated gonococcal urethritis, a single oral dose of 400 mg has been found to be effective. **OR As directed by the physician.**

Route of Administration: Oral

4.3 Contra-indications

Hypersensitivity to cefuroxime or to any of the excipients listed in 6.1. Hypersensitivity to cephalosporin antibiotic.

4.4 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 (SCARS) including toxic epidermal necrolysis (TEN), Stevens- Johnson syndrome (SJS) drug rash with eosinophilia and systemic symptoms (DRESS), and acute generalised exanthematous pustulosis (AGEP) have been reported in association with cefixime. Patients should be informed about the signs and symptoms of serious skin manifestations and monitored closely. Treatment should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of skin hypersensitivity.

NEFIXIME 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 NEFIXIME, 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

NEFIXIME should be administered with caution in patients with markedly impaired renal function.

Paediatric use

Safety of cefixime in premature or new-born infant has not been established.

Antibiotic-associated colitis

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.

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.

4.5 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.

4.6 Fertility, pregnancy and lactation

NEFIXIME should not be used in pregnancy or in nursing mothers unless considered essential by the physician.

4.7 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.

4.8 Undesirable effects:

In this section, the following convention has been used for the classification of undesirable effects in terms of frequency:

Common: ≥1/100 to <1/10,

Uncommon: ≥1/1,000 to <1/100,

Rare: ≥1/10,000 to <1/1,000 and

Very rare: <1/10,000

MedDRA System Organ Class	Adverse Drug Reaction	Frequency
Infections and infestations	Superinfections bacterial, superinfections fungal	Rare
	Antibiotic-associated colitis	Very rare
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 site conditions	Mucosal inflammation, pyrexia	Rare
Investigations	Hepatic enzyme increased (transaminase, alkaline phosphatase)	Uncommon
	Blood urea increased	Rare
	Blood creatinine increased	Very rare

4.9 Overdosage

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 NEFIXIME 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics Properties

Pharmacotherapeutic group: third generation cephalosporin, **ATC code:** J01DD08

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 methicillin-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

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 paediatric 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). No data are available on secretion of cefixime in human breast milk. Placental transfer of cefixime was small in pregnant rats dosed with labeled cefixime.

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 Cmax and AUC values were slightly greater in the elderly. Elderly patients may be given the same dose as the general population.

5.3 Preclinical safety data

There are no findings from chronic toxicity investigations suggesting that any side effects unknown to date could occur in humans. Furthermore, in-vivo and invitro studies did not yield any indication of a potential to cause mutagenicity. Long-term studies on carcinogenicity have not been conducted.
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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal Silicon dioxide
Micro Crystalline Cellulose

Magnesium Stearate
Cross Carmellose Sodium (Aerosil)
Purified Talc
PVPK 30
Insta coat ICS
Methylene Dichloride
Isopropyl Alcohol

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

36 Months

6.4 Special Precautions for Storage

Stored at temperature below 30°C in a dry place. Protect from light.

6.5 Nature and Contents of Container

1 X 10 TABLETS

10 tablets are packed in a one blister strips such a blister is packed in a Monocarton.

6.6 Special Precautions for Disposal of a used medicinal product or waste materials derived from such medicinal product and Other Handling of the Product

No special requirements

7. APPLICANT/HOLDER OF CERTIFICATE OG PRODUCT REGISTRATION

Nectar Healthcare Ltd.
16B Residence Street, Gbagada Estate, Phase 2, Gbagada Lagos.

8. DRUG PRODUCT MANUFACTURER

VAPI CARE PHARMA PVT LTD
Plot No 225/3, Nr. Morarji Circle, G.I.D.C, Vapi, Dist- Valsad – 396195.

9. NAFDAC REGISTRATION NUMBER(S)

B4-7947