## 1.3.1 SUMMARY OF PRODUCT CHARACTERISTICS

***1. NAME OF THE DRUG PRODUCT:*** NECTAR CEFUROXIME (Cefuroxime Axetil Tablets USP 500 mg)

***2. QUALITATIVE & QUANTITATIVE COMPOSITION***

**Qualitative Declaration:**

**Each film coated tablet contain-**

Cefuroxime Axetil USP

Eq. to cefuroxime……..500 mg

Excipients……q.s Colour: Titanium Dioxide BP

**Quantitative Declaration:**

**Batch Size:** 100000 Tablets

| Sr. No. | Ingredients | Spec. | Input (mg/tab) | O.A. | Std. qty. for 1.0 Lac Tab. (kg) (lit) |
|---|---|---|---|---|---|
| 1. | Cefuroxime Axetil | USP | 635.25 | - | 63.525 |
| 2. | Indion Resin 234 | IH | 80.00 | - | 8.000 |
| 3. | Aerosil | BP | 12.00 | - | 1.200 |
| 4. | Cross Carmellose Sodium | BP | 70.00 | - | 7.000 |
| 5. | Sodium Lauryl Sulphate | BP | 8.00 | - | 0.800 |
| 6. | Talcum | BP | 16.00 | - | 1.600 |
| 7. | MCC 102- vivapur | BP | 16.75 | - | 1.675 |
| 8. | Magnesium Stearate | BP | 4.00 | - | 0.400 |
| | | Total | 842.00 MG | | |
| | **COATING** | | | | |
| 9. | Ready Mix Powder ICS 223 White | IH | 25.65 | - | 2.565 |
| 10. | Methylene Dichloride | BP | 0.170 | - | 17.00 Lit |
| 11. | Isopropyl Alcohol | BP | 0.100 | - | 10.00 Lit |
| | | | 867.92 MG | | |

***3. PHARMACEUTICAL FORM***

White coloured, standard concave, film coated tablets embossed '500' on one side.

***4. CLINICAL PARTICULARS***

**4.1 Therapeutic Indications**

Nectar® Cefuroxime Axetil Tablets are indicated or the treatment of the following infections caused by sensitive bacteria:

Lower respiratory tract infection e.g. acute bronchitis, acute exacerbations of chronic bronchitis and pneumonia. Upper respiratory tract infections: e.g. ear, nose, throat infections such as otitis media, sinusitis, tonsillitis and pharyngitis.

Uncomplicated genito-urinary tract infections e.g. Pyelo-nephritis, cystitis and urethritis, Uncomplicated Skin and Soft Tissue infections e.g. furunculosis, pyoderma, and impetigo.

Gonorrhea e.g. acute uncomplicated gonococcal urethritis and cervicitis.

Treatment of early Lyme disease and subsequent prevention of late Lyme disease in adults and children over 12 years.

## 4.2 Posology/Dosage and method of administration:

**Posology/Dosage:**

**Adults:**
In pharyngitis, acute sinusitis; 250 mg b.d.

In acute exacerbations of chronic bronchitis, acute bronchitis skin and skin structure infections, 250 mg - 500 mg b.d. is recommended.

For uncomplicated urinary tract infections, 125 - 250 mg b.d.
In uncomplicated gonorrhoea, single dose of 1 g.

**Children:**

The recommended dose of Nectar® Cefuroxime 10 mg/kg (to a maximum of 125 mg) to 15 mg/kg (to a maximum of 250 mg) twice daily depending on the severity and type of infection.

**Route of Administration:** Oral

## 4.3 Contra-indications

Hypersensitivity to cefuroxime or to any of the excipients/component.

## 4.4 Special Warnings and Precautions for Use

Hypersensitivity reactions
Special care is indicated in patients who have experienced an allergic reaction to penicillin's or other beta lactam antibiotics because there is a risk of cross-sensitivity. As with all beta-lactam anti- bacterial agents, serious and occasionally fatal hypersensitivity reactions have been reported. In case of severe Hypersensitivity reactions, treatment with cefuroxime must be discontinued immediately and adequate Emergency measures must be initiated.
Before beginning treatment, it should be established whether the patient has a history of severe Hypersensitivity reactions to cefuroxime, to other cephalosporin's or to any other type of beta lactam agent.

## 4.5 Interaction with other Medicinal products and other forms of Interaction

Drugs which reduce gastric acidity may result in a lower bioavailability of cefuroxime axetil compared with that of the fasting state and tend to cancel the effect of enhanced absorption after food. Cefuroxime is excreted by glomerular filtration and tubular secretion. Concomitant use of probenecid is not recommended. Concurrent administration of probenecid significantly increases the peak concentration, area under the serum concentration time curve and elimination half-life of cefuroxime.
Concomitant use with oral anticoagulants may give rise to increased INR.

## 4.6 Fertility, pregnancy and lactation Pregnancy

There are limited data from the use of cefuroxime in pregnant women. Studies in animals have shown no harmful effects on pregnancy, embryonic or foetal development, parturition or postnatal development. There is no clear evidence of congenital and related teratogenicity to Cefuroxime but like any drug administration of cefuroxime should be done with caution during the first three months of pregnancy.
Cefuroxime axetil should be prescribed to pregnant women only if the benefit outweighs the risk.

**Breastfeeding**

Cefuroxime is excreted in human milk in small quantities. Adverse effects at therapeutic doses are not expected, although a risk of diarrhoea and fungus infection of the mucous membranes cannot be excluded. Breastfeeding might have to be discontinued due to these effects. The possibility of sensitization should be taken into account. Cefuroxime should only be used during breastfeeding after benefit/risk assessment by the physician in charge.
Cefuroxime is excreted in human milk therefore, caution needs be taken when administering to a breast feeding mother.

**Fertility**

There are no data on the effects of cefuroxime axetil on fertility in humans. Reproductive studies in animals have shown no effects on fertility.

## 4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, as this medicine may cause dizziness, patients should be warned to be cautious when driving or Operating machinery.

## 4.8 Undesirable effects:

Haematological: Eosinophilia
Neurological: Headache
Gastrointestinal: Nausea, vomiting, abdominal pain, diarrhoea, in some cases accompanied by blood in stools, which may be a symptom of enterocolitis.
Kidney/Genitourinary: Vaginal candidiasis
Liver: Transient increases in hepatic enzyme levels
Skin: Erythema multiforme, Stevens Johnson syndrome, toxic epidermal necrolysis
Other: Hypersensitivity reactions including skin rashes, urticaria, pruritus, bronchospasm, drug fever, serum sickness and anaphylaxis.

## 4.9 Overdosage

**Symptoms:** Seizures have been reported.
**Treatment:** Treatment is symptomatic and supportive.
Serum levels of Cefuroxime can be reduced by haemodialysis or peritoneal dialysis.

## *5. PHARMACOLOGICAL PROPERTIES*

### 5.1 Pharmacodynamics Properties

**Pharmacotherapeutic group:** Antibacterial for systemic use, second-generation cephalosporins.

**Mechanism of action:** Cefuroxime axetil undergoes hydrolysis by esterase enzymes to the active antibiotic, cefuroxime. Cefuroxime inhibits bacterial cell wall synthesis following attachment to penicillin binding proteins (PBPs). This results in the interruption of cell wall (peptidoglycan) biosynthesis, which leads to bacterial cell lysis and death. Mechanism of resistance Bacterial resistance to cefuroxime may be due to one or more of the following mechanisms: hydrolysis by beta-lactamases; including (but not limited to) by extended spectrum beta- lactamases (ESBLs), and AmpC enzymes that may be induced or stably depressed in certain aerobic Gram-negative bacteria species reduced affinity of penicillin-binding proteins for cefuroxime outer membrane impermeability, which restricts access of cefuroxime to penicillin binding proteins in Gram-negative bacteria bacterial efflux pumps Organisms that have acquired resistance to other injectable cephalosporins are expected to be resistant to cefuroxime. Depending on the mechanism of resistance, organisms with acquired resistance to penicillins may demonstrate reduced susceptibility or resistance to cefuroxime.

**Microbiological susceptibility:** The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of cefuroxime axetil in at least some types of infections is questionable. Cefuroxime is usually active against the following microorganisms in vitro.

**Commonly susceptible species**

Gram-positive aerobes: Staphylococcus aureus (methicillin susceptible)*, Streptococcus pyogenes, Streptococcus agalactiae.

Gram-negative aerobes: Haemophilus influenza, Haemophilus parainfluenzae, Moraxella catarrhalis Spirochetes: Borrelia burgdorferi

**Microorganisms for which acquired resistance may be a problem**

Gram-positive aerobes: Streptococcus pneumonia

Gram-negative aerobes: Citrobacter freundii, Enterobacter aerogenes, Enterobacter cloacae, Escherichia coli, Klebsiella pneumonia, Proteus mirabilis, Proteus spp. (other than P. vulgaris), Providencia spp. Gram-positive anaerobes: Peptostreptococcus spp., Propionibacterium spp.

Gram-negative anaerobes: Fusobacterium spp., Bacteroides spp.

**Inherently resistant microorganisms**

Gram-positive aerobes: Enterococcus faecalis, Enterococcus faecium

Gram-negative aerobes: Acinetobacter spp., Campylobacter spp., Morganella morganii, Proteus vulgaris, Pseudomonas aeruginosa, Serratia marcescens Gram-negative anaerobes: Bacteroides fragilis

Others: Chlamydia spp., Mycoplasma spp., Legionella spp.

***** All methicillin-resistant S. aureus are resistant to cefuroxime.

### 5.2 Pharmacokinetic properties

**Absorption:** After oral administration cefuroxime axetil is absorbed from the gastrointestinal tract and rapidly hydrolysed in the intestinal mucosa and blood to release cefuroxime into the circulation. Optimum absorption occurs when it is administered shortly after a meal.

Following administration of cefuroxime axetil tablets peak serum levels (2.9 µg/mL for a 125 mg dose, 4.4 µg/mL for a 250 mg dose, 7.7 µg/mL for a 500 mg dose and 13.6 µg/mL for a 1000 mg dose) occur approximately 2.4 hours after dosing when taken with food. The rate of absorption of cefuroxime from the suspension is reduced compared with the tablets, leading to later, lower peak serum levels and reduced systemic bioavailability (4 to 17% less). Cefuroxime axetil oral suspension was not bioequivalent to cefuroxime axetil tablets when tested in healthy adults and therefore is not substitutable on a milligram-per-milligram basis (see section 4.2).The pharmacokinetics of cefuroxime is linear over the oral dosage range of 125 to 1000 mg. No accumulation of cefuroxime occurred following repeat oral doses of 250 to 500 mg.

**Distribution:** Protein binding has been stated as 33 to 50% depending on the methodology used. Following a single dose of cefuroxime axetil 500 mg tablet to 12 healthy volunteers, the apparent volume of distribution was 50 L (CV%=28%). Concentrations of cefuroxime in excess of the minimum inhibitory levels for common pathogens can be achieved in the tonsilla, sinus tissues, bronchial mucosa, bone, pleural fluid, joint fluid, synovial fluid, interstitial fluid, bile, sputum and aqueous humor. Cefuroxime passes the blood-brain barrier when the meninges are inflamed.

**Biotransformation:** Cefuroxime is not metabolised.

**Elimination:** The serum half-life is between 1 and 1.5 hours. Cefuroxime is excreted by glomerular filtration and tubular secretion. The renal clearance is in the region of 125 to 148 mL/min/1.73 $m^2$.

**Special patient populations**

Gender: No differences in the pharmacokinetics of cefuroxime were observed between males and females.

Elderly: No special precaution is necessary in the elderly patients with normal renal function at dosages up to the normal maximum of 1 g per day. Elderly patients are more likely to have decreased renal function; therefore, the dose should be adjusted in accordance with the renal function in the elderly (see section 4.2).

Pediatrics: In older infants (aged >3 months) and in children, the pharmacokinetics of cefuroxime are similar to that observed in adults. There is no clinical trial data available on the use of cefuroxime axetil in children under the age of 3 months.

Renal impairment: The safety and efficacy of cefuroxime axetil in patients with renal failure have not been established. Cefuroxime is primarily excreted by the kidneys. Therefore, as with all such antibiotics, in patients with markedly impaired renal function (i.e. C1cr <30 mL/minute) it is recommended that the dosage of cefuroxime should be reduced to compensate for its slower excretion. Cefuroxime is effectively removed by dialysis.

Hepatic impairment: There are no data available for patients with hepatic impairment. Since cefuroxime is primarily eliminated by the kidney, the presence of hepatic dysfunction is expected to have no effect on the pharmacokinetics of cefuroxime.

PK/PD relationship: For cephalosporins, the most important pharmacokinetic-pharmacodynamic index correlating with in vivo efficacy has been shown to be the percentage of the dosing interval (%T) that the unbound concentration remains above the minimum inhibitory concentration (MIC) of cefuroxime for individual target species (i.e. %T>MIC).

### 5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on studies of safety pharmacology, repeated dose toxicity, genotoxicity and toxicity to reproduction and development. No carcinogenicity studies have been performed; however, there is no evidence to suggest carcinogenic potential. Gamma glutamyl transpeptidase activity in rat urine is inhibited by various cephalosporins, however the level of inhibition is less with cefuroxime. This may have significance in the interference in clinical laboratory tests in humans.

## *6. PHARMACEUTICAL PARTICULARS*

### 6.1 List of excipients

| |
|---|
| Indion Resin 234 |
| Aerosil |
| Cross Carmellose Sodium |
| Sodium Lauryl Sulphate |
| Talcum |
| MCC 102- vivapur |
| Magnesium Stearate |

| |
|---|
| Ready Mix Powder ICS 223 White |
| 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)*

B4-7497