## SUMMARY OF PRODUCT CHARACTERISTICS (SMPC)

### CEFDOXIM-200

**1.Name of The Product**
CEFDOXIM-200

**2. Qualitative & Quantitative Composition**
Each film coated tablet contains:
Cefpodoxime Proxetil USP 200 mg

**3. Pharmaceutical Form**
Film Coated Tablets

**4. Clinical Particulars**

**4.1 Therapeutic indications**
Cefpodoxime is indicated for the treatment of the following infections when caused by susceptible pathogens in adults:

• **Upper respiratory tract infections**

- Acute bacterial sinusitis

- Tonsillitis [For 100mg Tablets only]

• **Lower respiratory tract infections**

- Acute exacerbation of chronic bronchitis

- Bacterial pneumonia - Cefpodoxime might not be suitable option depending on the pathogen involved. Consideration should be given to the official guidance on the appropriate use of antibacterial agents.

**4.2 Posology and method of administration**
Route of administration: oral.

The tablets should be taken with food for optimum absorption.

**Adults and adolescents with normal renal function**:

***Upper respiratory tract infections:***

Acute bacterial sinusitis: 200 mg twice daily.

Tonsillitis: 100 mg twice daily. (For 100mg Tablets only)

***Lower respiratory tract infections:***

Acute exacerbation of chronic bronchitis: 200mg twice daily

Bacterial pneumonia: 200mg twice daily

**Elderly**:

It is not necessary to modify the dose in elderly patients with normal renal function.

**Children:**

Pediatric formulation of cefpodoxime is available for infants and children.

**Hepatic Impairment:**

The dosage does not require modification in cases of hepatic impairment.

**4.3 Contraindications**

• Hypersensitivity to cefpodoxime, any other cephalosporins or to any of the excipients.

• Previous history of immediate and / or severe hypersensitivity reaction (anaphylaxis) to penicillin or other beta-lactam antibiotic.

**4.4 Special warnings and precautions for use**

Cefpodoxime is not a preferred antibiotic for the treatment of staphylococcal pneumonia and should not be used in the treatment of atypical pneumonia caused by organisms such as *Legionella, Mycoplasma* and *Chlamydia.* Cefpodoxime is not recommended for the treatment of pneumonia due to *S. pneumonia*.

As with all beta-lactam antibacterial agents, serious and occasionally fatal hypersensitivity reactions have been reported. In case of severe hypersensitivity reactions, treatment with cefpodoxime 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 cefpodoxime, to other cephalosporins or to any other type of beta-lactam agent. Caution should be used if cefpodoxime is given to patients with a history of non-severe hypersensitivity to other beta-lactam agents.

In cases of severe renal insufficiency it may be necessary to reduce the dosage regimen dependent on the creatinine clearance.

Antibacterial agent-associated colitis and pseudo-membranous colitis have been reported with nearly all anti-bacterial agents, including cefpodoxime, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea during or subsequent to the administration of cefpodoxime. Discontinuation of therapy with cefpodoxime and the administration of specific treatment for *Clostridium difficile* should be considered. Medicinal products that inhibit peristalsis should not be given.

Cefpodoxime should always be prescribed with caution in patients with a history of gastrointestinal disease, particularly colitis.

As with all beta-lactam antibiotics, neutropenia and more rarely agranulocytosis may develop particularly during extended treatment. For cases of treatment lasting longer than 10 days, the blood count should be monitored and treatment discontinued if neutropenia is found.

Cephalosporins may be absorbed onto the surface of red cell membranes and react with antibodies directed against the drug. This can produce a positive Coomb's test and very rarely, haemolytic anaemia. Cross-reactivity may occur with penicillin for this reaction.

Changes in renal function have been observed with cephalosporin antibiotics, particularly when given concurrently with potentially nephrotoxic drugs such as aminoglycosides and/or potential diuretics. In such cases, renal function should be monitored.

As with other antibiotics, prolonged use of cefpodoxime may result in the overgrowth of non-susceptible organisms (candida and C lostridium difficile), which may require interruption of treatment.

**Interaction with laboratory tests:**

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.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Sunset yellow (E110) may cause allergic reactions.

**4.5 Interaction with other medicinal products and other forms of interaction**

No clinically significant drug interactions have been reported during the course of clinical studies.

Histamine $H_2$-antagonists and antacids reduce the bioavailability of cefpodoxime. Probenecid reduces the excretion of cephalosporins. Cephalosporins potentially enhance the anticoagulant effect of coumarins and reduce the contraceptive effect of oestrogens.

**Oral anticoagulants:** Simultaneous administration of cefpodoxime with warfarin may augment its anti-coagulant effects. There have been many reports of increases in oral anti-coagulant activity in patients receiving antibacterial agents, including cephalosporins. The risk may vary with the underlying infection, age and general status of the patient so that the contribution of the cephalosporins to the increase in INR (international normalised ratio) is difficult to assess. It is recommended that the INR should be monitored frequently during and shortly after co-administration of cefpodoxime with an oral anti-coagulant agent.

Studies have shown that bioavailability is decreased by approximately 30% when cefpodoxime is administered with drugs which neutralise gastric pH or inhibit acid secretions. Therefore, such drugs as antacids of the mineral type and $H_2$ blockers such as

ranitidine, which can cause an increase in gastric pH, should be taken 2 to 3 hours after Cefpodoxime administration.

**4.6 Fertility, pregnancy and lactation**

**Pregnancy:**

There are no or limited amount of data from the use of cefpodoxime in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. Due to the benefit of antibiotic treatment, the use of cefpodoxime may be considered during pregnancy if necessary.

Caution should be exercised when prescribing to pregnant women.

**Lactation:**

Cefpodoxime is excreted in breast milk in small amounts. Cefpodoxime may be used during breast-feeding. Continuation of breast-feeding should be questioned in case of diarrhoea or mucosal fungus infection in the breastfed infant. The possibility of sensitisation should be borne in mind.

**4.7 Effects on ability to drive and use machines**

Dizziness has been reported during treatment with **CEFDOXIM-200** and may affect the ability to drive and use machines.

**4.8 Undesirable effects**

Adverse drug reactions are listed below by system organ class and frequency. Frequencies are defined as:

Very common (≥1/10)

Common (≥1/100 to <1/10)

Uncommon (≥1/1,000 to <1/100)

Rare (≥1/10,000 to <1/1,000)

Very rare (<1/10,000), not known (cannot be estimated from the available data)

**Blood and lymphatic system disorders**

| | |
|---|---|
| *Rare:* | Haematological disorders such as reduction in haemoglobin, thrombocytosis, thrombocytopenia, leucopenia and eosinophilia |
| *Very rare:* | Haemolytic anaemia. |

**Nervous system disorders**

| | |
|---|---|
| *Uncommon:* | Headache, paraesthesia, dizziness |

**Ear and labyrinth disorders**

| | |
|---|---|
| *Uncommon:* | Tinnitus |

**Gastrointestinal disorders**

| | |
|---|---|
| *Common:* | Gastric pressure, nausea, vomiting, abdominal pain, flatulence, diarrhoea. |

Bloody diarrhoea can occur as a symptom of enterocolitis.
The possibility of pseudomembranous enterocolitis should be considered if severe or persistent diarrhoea occurs during or after treatment.

**Metabolism and nutrition disorders**

| | |
|---|---|
| Common: | Loss of appetite |

**Immune system disorders**

Hypersensitivity reactions of all degrees of severity have been observed.

| | |
|---|---|
| Very rare: | anaphylactic reactions, bronchospasm, purpura and angioedema. |

**Renal and urinary disorders**

| | |
|---|---|
| *Very rare:* | Slight increases in blood urea and creatinine |

**Hepato-biliary disorders**

| | |
|---|---|
| Rare: | Transient moderate elevations of ASAT, ALAT and alkaline phosphatase and/or bilirubin. These laboratory abnormalities which may be explained by the infection, may rarely exceed twice the upper limit of the named range and elicit a pattern of liver injury, usually cholestatic and most often asymptomatic. |
| Very rare: | liver damage |

**Skin and subcutaneous tissue disorders**

| | |
|---|---|
| *Uncommon:* | Hypersensitivity mucocutaneous reactions, rash, urticaria, pruritus |
| *Very rare:* | Stevens- Johnson syndrome, toxic epidermal necrolysis and erythema multiforme |

**Infections and infestations**

There can be multiplication of non-sensitive micro-organisms

**General disorders and administration site conditions**

| | |
|---|---|
| *Uncommon:* | Asthenia or malaise |

### 4.9 Overdose

In the event of overdosage with cefpodoxime, supportive and symptomatic therapy is indicated.

In cases of overdosage, particularly in patients with renal insufficiency, encephalopathy may occur. The encephalopathy is usually reversible once cefpodoxime plasma levels have fallen.

## 5. Pharmacological properties

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Beta-lactam antibacterial, a 3rd generation cephalosporin.

# CEFDOXIM-200

ATC Code: J01DD13

**Mode of Action:**

Cefpodoxime 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.

**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 that the unbound concentration remains above the minimum inhibitory concentration (MIC) of cefpodoxime for individual target species (i.e. %T>MIC).

**Mechanism(s) of resistance:**

Resistance to cephalosporins results from a variety of mechanisms:

1) alteration of the cell-wall permeability of gram-negative bacteria.

2) alteration of the penicillin binding proteins (PBPs)

3) β-lactamase production

4) bacterial efflux pumps

**Break points:**

European Committee on Antimicrobial Susceptibility Testing (EUCAST) clinical breakpoints for MIC testing are presented below. EUCAST clinical MIC breakpoints for cefpodoxime (2011-01-05, v 1.3)

| Organism | Susceptible (S) (mg/l) | Resistant (R) (mg/l) |
|---|---|---|
| *Enterobacteriaceae (uncomplicated UTI only)* | ≤ 1 | >1 |
| *Staphylococcus spp.* | Note[1] | Note[1] |
| *Streptococcus groups A, B, C and G* | Note[2] | Note[2] |
| *Streptococcus pneumoniae* | ≤ 0.25 | >0.5 |
| *Haemophilus influenzae* | ≤ 0.25<br>Note[3] | >0.5 |
| *Moraxella catarrhalis* | ≤ 0.25<br>Note[3] | >0.5 |
| *Neisseria gonorrhoeae* | IE | IE |
| *Non-species related breakpoint* | IE | IE |

1 Susceptibility of staphylococci to cephalosporins is inferred from the cefoxitin susceptibility.

2 The beta-lactam susceptibility of beta-haemolytic streptococcus groups A, B, C and G is inferred from the penicillin susceptibility.

3 Strains with MIC values above the susceptible breakpoint are very rare or not yet reported. The identification and antimicrobial susceptibility tests on any such isolate must be repeated and if the result is confirmed the isolate must be sent to a reference laboratory.

| Antibacterial spectrum |
|---|
| **Commonly Susceptible species** |
| ***Aerobic Gram positive organisms:*** |
| *Staphylococcus aureus* (Methicillin-susceptible) |
| *Streptococcus pyogenes* |
| ***Aerobic Gram negative organisms:*** |
| *Haemophilus influenzae* |
| *Moraxella catarrhalis* |
| *Proteus mirabilis*[%] |
| **Species for which acquired resistance may be a problem** |
| ***Aerobic Gram positive organisms*** |
| *Streptococcus pneumoniae* |
| ***Aerobic Gram negative organisms*** |
| *Citrobacter freundi*[$] |
| *Enterobacter cloacae*[$] |
| *Escherichia coli*[%] |
| *Klebsiella pneumoniae*[%] |
| *Serratia marcescens*[$] |
| **Inherently resistant organisms** |
| ***Aerobic Gram positive organisms*** |
| *Enterococcus spp.* |
| *Staphylococcus aureus (methicillin resistant)* |
| ***Aerobic Gram negative organisms*** |
| *Morganella morganii* |
| *Pseudomonas aeruginosa.* |
| ***Others*** |
| *Chlamydia* spp. |
| *Chlamydophila* spp. |
| *Legionella pneumophila* |
| *Mycoplasma* spp. |

**Susceptibility:**

The pr evalence of ac quired resistance m ay va ry geographically and with time for *selected* species and local i nformation on resistance i s de sirable, particularly when

treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

$ natural intermediate susceptibility

+Resistance rates >50% in at least 1 region

% ESBL producing species are always resistant

**5.2 Pharmacokinetic properties**

Cefpodoxime is taken up in the intestine and is hydrolysed to the active metabolite cefpodoxime. When cefpodoxime proxetil is administered orally to fasting subjects as a tablet corresponding to 100 mg of cefpodoxime, 51.5% is absorbed and absorption is increased by food intake. The volume of distribution is 32.3 L and peak levels of cefpodoxime occur 2 to 3 hrs after dosing. The maximum plasma concentration is 1.2 mg/L and 2.5 mg/L after doses of 100 mg and 200 mg respectively. Following administration of 100 mg and 200 mg twice daily over 14.5 days, the plasma pharmacokinetic parameters of cefpodoxime remain unchanged.

Serum protein binding of cefpodoxime, 40% principally to albumin. This binding is non saturable in type.

Concentrations of cefpodoxime in excess of the minimum inhibitory levels (MIC) for common pathogens can be achieved in lung parenchyma, bronchial mucosa, pleural fluid, tonsils, interstitial fluid and prostate tissue.

As the majority of cefpodoxime is eliminated in the urine, the concentration is high. (Concentrations in 0-4, 4-8, 8-12 hr fractions after a single dose exceed $MIC_{90}$ of common urinary pathogens). Good diffusion of cefpodoxime is also seen into renal tissue, with concentrations above $MIC_{90}$ of the common urinary pathogens, 3-12 hrs after an administration of a single 200 mg dose (1.6-3.1µg/g). Concentrations of cefpodoxime in the medullary and cortical tissues is similar.

Studies in healthy volunteers show median concentrations of cefpodoxime in the total ejaculate 6-12 hrs following administration of a single 200 mg dose to be above the $MIC_{90}$ of *N. gonorrhoeae*.

The main route of excretion is renal, 80% is excreted unchanged in the urine, with an elimination half-life of approx 2.4 hours

**5.3 Preclinical safety data**

Preclinical data based on conventional studies on acute toxicity, repeated dose toxicity, reproduction toxicity and genotoxicity reveal no special hazard for humans not already considered in other sections of the SPC.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of Excipients

Calcium carboxymethyl cellulose, L-HPC, Sodium Lauryl sulphate, Magnesium Steratae, Lactose, Colour Coat FC4S. Isopropyl alcohol, Methylene dichloride, Titanium dioxide, PVPK-30

### 6.2 Incompatibilities

Not applicable

### 6.3 Shelf life

3 Years

### 6.4 Special precautions for storage

Store at a temperature below 30°C.

### 6.5 Nature and contents of container

10 x 1 x 10 Alu alu Blister

### 6.6 Special precautions for disposal

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

### 6.7 Manufactured By

Lark Laboratories (India) Ltd.
SP-1192 E, RIICO Indl. Area, Phase-IV,
Bhiwadi - 301019, Distt. Alwar (Raj.)

### 6.8 Marketed By

Digitall Healthcare Ltd.
Plot E, First Avenue Festac Town Lagos, Nigeria