National Agency for Food & Drug Administration & Control (NAFDAC)

Registration & Regulatory Affairs (R & R) Directorate

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. NAME OF THE MEDICINAL PRODUCT

Cefadox 200

2. QUALITY AND QUANTITATIVE COMPOSITION

Each film coated tablet contains:

Cefpodoxime Proxetil USP equivalent to Cefpodoxime…… 200 mg

Excipient(s) with known effect: 6.500 mg of lactose monohydrate/tablet

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets

Blue coloured, oval shaped, film-coated tablets with 200 embossed on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications:

Cefpodoxime proxetil is indicated for the treatment of patients with mild to moderate infections caused by susceptible strains of the designated microorganisms in the conditions listed below.

Recommended dosages, durations of therapy, and applicable patient populations vary among these infections.

Acute otitis media caused by Streptococcus pneumoniae (excluding penicillin-resistant strains), Streptococcus pyogenes, Haemophilus influenzae (including beta-lactamase-producing strains), or Moraxella (Branhamella) catarrhalis (including beta-lactamase-producing strains).

Pharyngitis and/or tonsillitis caused by Streptococcus pyogenes.

Community-acquired pneumonia caused by S. pneumoniae or H. Influenzae (including beta-lactamase-producing strains).

Acute bacterial exacerbation of chronic bronchitis caused by S. pneumoniae, H. influenzae (non-beta-lactamase-producing strains only), or M. catarrhalis. Data are insufficient at this time to establish efficacy in patients with acute bacterial exacerbations of chronic bronchitis caused by beta-lactamase-producing strains of H. influenzae.

Acute, uncomplicated urethral and cervical gonorrhea caused by Neisseria gonorrhoeae (including penicillinase-producing strains).

Acute, uncomplicated ano-rectal infections in women due to Neisseria gonorrhoeae (including penicillinase-producing strains).

Uncomplicated skin and skin structure infections caused by Staphylococcus aureus (including penicillinase-producing strains) or Streptococcus pyogenes. Abscesses should be surgically drained as clinically indicated.

Acute maxillary sinusitis caused by Haemophilus influenzae (including beta-lactamase-producing strains), Streptococcus pneumoniae, and Moraxella catarrhalis.

Uncomplicated urinary tract infections (cystitis) caused by Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, or Staphylococcus saprophyticus.

4.2 Posology and method of administration:

The recommended dosages, durations of treatment, and applicable patient population are as described in the following chart:

Adults and Adolescents (age 12 years and older)

Type of Infection	Total Daily Dose	Dose Frequency	Duration
Pharyngitis and/or tonsillitis	200 mg	100 mg Q 12 hours	5 to 10 days
Acute community-acquired pneumonia	400 mg	200 mg Q 12 hours	14 days
Acute bacterial exacerbations of chronic bronchitis	400 mg	200 mg Q 12 hours	10 days
Uncomplicated gonorrhea (men and women) and rectal gonococcal infections (women)	200 mg	single dose	
Skin and skin structure	800 mg	400 mg Q 12 hours	7 to 14 days
Acute maxillary sinusitis	400 mg	200 mg Q 12 hours	10 days
Uncomplicated urinary tract infection	200 mg	100 mg Q 12 hours	7 days

Patients with Renal Dysfunction

For patients with severe renal impairment (<30 mL/min creatinine clearance), the dosing intervals should be increased to Q 24 hours. In patients maintained on hemodialysis, the dose frequency should be 3 times/week after hemodialysis.

When only the serum creatinine level is available, the following formula (based on sex, weight, and age of the patient) may be used to estimate creatinine clearance (mL/min). For this estimate to be valid, the serum creatinine level should represent a steady state of renal function.

Males: (mL/min)	Weight (kg) × (140 - age) / 72 × serum creatinine (mg/100 mL)
Females: (mL/min)	0.85 × above value

Patients with Cirrhosis

Cefpodoxime pharmacokinetics in cirrhotic patients (with or without ascites) are similar to those in healthy subjects. Dose adjustment is not necessary in this population.

4.3 Contraindications:

Cefpodoxime proxetil is contraindicated in patients with a known allergy to cefpodoxime or to the cephalosporin group of antibiotics.

4.4 Special warning and precautions:

Before therapy with cefpodoxime proxetil is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cefpodoxime, other cephalosporins, penicillins, or other drugs. If cefpodoxime is to be administered 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 cefpodoxime proxetil occurs, discontinue the drug. Serious acute hypersensitivity reactions may require treatment with epinephrine and other emergency measures, including oxygen, intravenous fluids, intravenous antihistamine, and airway management, as clinically indicated.

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including cefpodoxime proxetil tablets, USP, and may range in severity from mild diarrhea 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 strains 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 antibiotic 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.
A concerted effort to monitor for C. difficile in cefpodoxime-treated patients with diarrhea was undertaken because of an increased incidence of diarrhea associated with C. difficile in early trials in normal subjects. C. difficile organisms or toxin was reported in 10% of the cefpodoxime-treated adult patients with diarrhea; however, no specific diagnosis of pseudomembranous colitis was made in these patients.
In post-marketing experience outside the United States, reports of pseudomembranous colitis associated with the use of cefpodoxime proxetil have been received.

General

In patients with transient or persistent reduction in urinary output due to renal insufficiency, the total daily dose of cefpodoxime proxetil should be reduced because high and prolonged serum antibiotic concentrations can occur in such individuals following usual doses. Cefpodoxime, like other cephalosporins, should be administered with caution to patients receiving concurrent treatment with potent diuretics.

As with other antibiotics, prolonged use of cefpodoxime proxetil may result in overgrowth of non-susceptible organisms. Repeated evaluation of the patient's condition is essential. If super infection occurs during therapy, appropriate measures should be taken.

Prescribing Cefpodoxime Proxetil Tablets, USP in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Information for Patients

Patients should be counseled that antibacterial drugs including Cefpodoxime Proxetil Tablets, USP should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When Cefpodoxime Proxetil Tablets, USP is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by Cefpodoxime Proxetil Tablets, USP or other antibacterial drugs in the future.

Diarrhea is a common problem caused by antibiotics which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with antibiotics, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months after having taken the last dose of the antibiotic. If this occurs, patients should contact their physician as soon as possible.

Excipients

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

4.5 Interactions with Other Medicaments

Antacids

Concomitant administration of high doses of antacids (sodium bicarbonate and aluminum hydroxide) or H2 blockers reduces peak plasma levels by 24% to 42% and the extent of absorption by 27% to 32%, respectively. The rate of absorption is not altered by these concomitant medications. Oral anti-cholinergics (e.g., propantheline) delay peak plasma levels (47% increase in Tmax), but do not affect the extent of absorption (AUC).

Probenecid

As with other beta-lactam antibiotics, renal excretion of cefpodoxime was inhibited by Probenecid and resulted in an approximately 31% increase in AUC and 20% increase in peak cefpodoxime plasma levels.

Nephrotoxic drugs

Although nephrotoxicity has not been noted when cefpodoxime proxetil was given alone, close monitoring of renal function is advised when cefpodoxime proxetil is administered concomitantly with compounds of known nephrotoxic potential.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are, however, no adequate and well-controlled studies of cefpodoxime proxetil use in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Lactation

Cefpodoxime is excreted in human milk. In a study of 3 lactating women, levels of cefpodoxime in human milk were 0%, 2% and 6% of concomitant serum levels at 4 hours following a 200 mg oral dose of cefpodoxime proxetil. At 6 hours post-dosing, levels were 0%, 9% and 16% of concomitant serum levels. Because of the potential for serious reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

4.7 Effects on ability to drive and use machine:

Dizziness has been reported during treatment with cefpodoxime and may affect the ability to drive and use machines.

4.8 Undesirable effects:

Adverse events thought possibly or probably related to cefpodoxime proxetil that occurred in less than 1% of patients (N=4696)

Body – fungal infections, abdominal distention, malaise, fatigue, asthenia, fever, chest pain, back pain, chills, generalized pain, abnormal microbiological tests, moniliasis, abscess, allergic reaction, facial edema, bacterial infections, parasitic infections, localized edema, localized pain.

Cardiovascular – congestive heart failure, migraine, palpitations, vasodilation, hematoma, hypertension, hypotension

Digestive – vomiting, dyspepsia, dry mouth, flatulence, decreased appetite, constipation, oral moniliasis, anorexia, eructation, gastritis, mouth ulcers, gastrointestinal disorders, rectal disorders, tongue disorders, tooth disorders, increased thirst, oral lesions, tenesmus, dry throat, toothache.
Hemic and Lymphatic – anemia.
Metabolic and Nutritional – dehydration, gout, peripheral edema, weight increase.
Musculo-skeletal – myalgia.
Nervous – dizziness, insomnia, somnolence, anxiety, shakiness, nervousness, cerebral infarction, change in dreams, impaired concentration, confusion, nightmares, paresthesia, vertigo.
Respiratory – asthma, cough, epistaxis, rhinitis, wheezing, bronchitis, dyspnea, pleural effusion, pneumonia, sinusitis.
Skin – urticaria, rash, pruritus non-application site, diaphoresis, maculopapular rash, fungal dermatitis, desquamation, dry skin non-application site, hair loss, vesiculobullous rash, sunburn.
Special Senses – taste alterations, eye irritation, taste loss, tinnitus.
Urogenital – hematuria, urinary tract infections, metrorrhagia, dysuria, urinary frequency, nocturia, penile infection, proteinuria, vaginal pain.

In clinical trials using a single dose of cefpodoxime proxetil film-coated tablets, 509 patients were treated with the recommended dosage of cefpodoxime (200 mg). There were no deaths or permanent disabilities thought related to drug toxicity in these studies.
Adverse events thought possibly or probably related to cefpodoxime in single-dose clinical trials conducted in the United States were:
Incidence Greater Than 1%

Nausea	1.4%
Diarrhea	1.2%

Incidence Less Than 1%
Central Nervous System: Dizziness, headache, syncope.
Dermatologic: Rash.
Genital: Vaginitis.
Gastrointestinal: Abdominal pain.
Psychiatric: Anxiety.

Post-marketing Experience

The following serious adverse experiences have been reported: allergic reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme and serum sickness-like reactions, pseudomembranous colitis, bloody diarrhea with abdominal pain, ulcerative colitis, rectorrhages with hypotension, anaphylactic shock, acute liver injury, in utero exposure with miscarriage, purpuric nephritis, pulmonary infiltrate with eosinophilia, and eyelid dermatitis.

One death was attributed to pseudomembranous colitis and disseminated intravascular coagulation.

4.9 Overdose:

In acute rodent toxicity studies, a single 5 g/kg oral dose produced no adverse effects.

In the event of serious toxic reaction from over dosage, hemodialysis or peritoneal dialysis may aid in the removal of cefpodoxime from the body, particularly if renal function is compromised.

The toxic symptoms following an overdose of beta-lactam antibiotics may include nausea, vomiting, epigastric distress, and diarrhea.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties:

Cefpodoxime is a bactericidal agent that acts by inhibition of bacterial cell wall synthesis. Cefpodoxime has activity in the presence of some beta-lactamases, both penicillinases and cephalosporinases, of Gram-negative and Gram-positive bacteria.

Mechanism of Resistance

Resistance to Cefpodoxime is primarily through hydrolysis by beta-lactamase, alteration of penicillin-binding proteins (PBPs), and decreased permeability.

Cefpodoxime has been shown to be active against most isolates of the following bacteria, both in vitro and in clinical infections as described in the Indications and Usage (1) section:

Gram-positive bacteria

Staphylococcus aureus (methicillin-susceptible strains, including those producing penicillinases)

Staphylococcus saprophyticus

Streptococcus pneumoniae (excluding penicillin-resistant isolates)

Streptococcus pyogenes

Gram-negative bacteria

Escherichia coli

Klebsiella pneumoniae

Proteus mirabilis
Haemophilus influenzae (including beta-lactamase producing isolates)
Moraxella catarrhalis
Neisseria gonorrhoeae (including penicillinase-producing isolates)
The following in vitro data are available, but their clinical significance is unknown. At least 90 percent of the following microorganisms exhibit an in vitro minimum inhibitory concentration (MIC) less than or equal to the susceptible breakpoint for Cefpodoxime. However, the efficacy of Cefpodoxime in treating clinical infections due to these microorganisms has not been established in adequate and well-controlled clinical trials.
Gram-positive bacteria
Streptococcus agalactiae
Streptococcus spp. (Groups C, F, G)
Gram-negative bacteria
Citrobacterdiversus
Klebsiella oxytoca
Proteus vulgaris
Providencia rettgeri
Haemophilus parainfluenzae
Anaerobic Gram-positive bacteria
Peptostreptococcusmagnus

5.2 Pharmacokinetic Properties:

Absorption and Excretion

Cefpodoxime proxetil is a prodrug that is absorbed from the gastrointestinal tract and de-esterified to its active metabolite, cefpodoxime. Following oral administration of 100 mg of cefpodoxime proxetil to fasting subjects, approximately 50% of the administered cefpodoxime dose was absorbed systemically. Over the recommended dosing range (100 to 400 mg), approximately 29 to 33% of the administered cefpodoxime dose was excreted unchanged in the urine in 12 hours. There is minimal metabolism of cefpodoxime in vivo.

Distribution

Protein binding of cefpodoxime ranges from 22 to 33% in serum and from 21 to 29% in plasma.

Effects of Decreased Renal Function

Elimination of cefpodoxime is reduced in patients with moderate to severe renal impairment (<50 mL/min creatinine clearance). In subjects with mild impairment of renal function (50 to 80 mL/min creatinine clearance), the average plasma half-life of cefpodoxime was 3.5 hours. In subjects with moderate (30 to 49 mL/min creatinine clearance) or severe renal impairment (5 to 29 mL/min creatinine clearance), the half-life increased to 5.9 and 9.8 hours, respectively. Approximately 23% of the administered dose was cleared from the body during a standard 3-hour hemodialysis procedure.

Effect of Hepatic Impairment (cirrhosis)

Absorption was somewhat diminished and elimination unchanged in patients with cirrhosis. The mean cefpodoxime T1/2 and renal clearance in cirrhotic patients were similar to those derived in studies of healthy subjects. Ascites did not appear to affect values in cirrhotic subjects. No dosage adjustment is recommended in this patient population.

Pharmacokinetics in Elderly Subjects

Elderly subjects do not require dosage adjustments unless they have diminished renal function. In healthy geriatric subjects, cefpodoxime half-life in plasma averaged 4.2 hours (vs 3.3 in younger subjects) and urinary recovery averaged 21% after a 400 mg dose was administered every 12 hours. Other pharmacokinetic parameters (Cmax, AUC, and Tmax) were unchanged relative to those observed in healthy young subjects.

5.3 Preclinical safety Data:

Long-term animal carcinogenesis studies of cefpodoxime proxetil have not been performed. Mutagenesis studies of cefpodoxime, including the Ames test both with and without metabolic activation, the chromosome aberration test, the unscheduled DNA synthesis assay, mitotic recombination and gene conversion, the forward gene mutation assay and the in vivo micronucleus test, were all negative. No untoward effects on fertility or reproduction were noted when 100 mg/kg/day or less (2 times the human dose based on mg/m2) was administered orally to rats.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients:

Lactose
Calcium CMC
Hydroxy Propyl Cellulose
Sodium Lauryl Sulphate
Crospovidone Type A
Magnesium Stearate
Colloidal silicon Dioxide
Opadry Blue 02F50896
Propylene Glycol
Talc

6.2 Incompatibilities:

Not applicable

6.3 Shelf life:

2 years

6.4 Special precautions for storage:

Store below 30°C. Keep away from the reach of children

6.5 Nature and contents of container:

Alu/alu blister of 1X 10's

6.6 Special precautions for disposal

No special requirements

7. Marketing Authorization Holder:

MICRO LABS LIMITED
31, Race course road
Bangalore-560001
INDIA

8. Marketing Authorization Numbers

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9. Date of first authorization

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10. Date of revision of the text

Jan 2021