SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Sefpotec 200 mg Film Coated Tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient:

1 film-coated tablet contains:

260.90 mg cefpodoxime proxetil, equivalent to 200 mg cefpodoxime. Excipients:

For a full list of excipients, see section 6.1.

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3. PHARMACEUTICAL FORM

Film-coated tablet

White, biconvex, cylindrical tablets embossed on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Cefpodoxime proxetil is indicated for the treatment of the following infections when caused by susceptible organisms.

- Sinusitis
- Tonsillitis and pharyngitis

In the above indications, cefpodoxime should be reserved for recurrent or chronic infections, or for infections where the causative organism is known or suspected to be resistant to commonly used antibiotics *or in case the commonly used antibiotic cannot be used for any reason.*

- Acute bronchitis
- Exacerbation of chronic bronchitis
- Bacterial pneumonia

Cefpodoxime is not the 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 *(see also section 5.1)* .

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2. Posology and method of administration

Posology

Adults and adolescents with normal renal function:

Sinusitis: 200 mg twice daily.

Tonsillitis and pharyngitis: 100 mg twice daily

Acute bronchitis, exacerbation of chronic bronchitis and bacterial pneumonia: 100-200 mg twice daily, dependent on the severity of the infection.

Elderly:

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

Patients with renal impairment:

The dose of cefpodoxime does not require modification if creatinine clearance exceeds 40 ml/min. Below this value, pharmacokinetic studies indicate an increase in plasma elimination half-life. Therefore, the dose should be adjusted appropriately.

CREATININE CLEARANCE (ML/MIN)	
39 - 10	Unit dose[1] administered as a single dose every 24 hours.
<10	Unit dose[1] administered as a single dose every 48 hours.
Haemodialysis Patients	Unit dose[1] administered after each dialysis session.

NOTE: [1] The unit dose is either 100 mg or 200 mg, depending on the type of infection as stated above.

Patients with hepatic impairment:

The dose does not require modification in cases of hepatic impairment

Duration

The duration of therapy depends on the patient, the indication and the causative pathogen(s).

Method of Administration

For oral administration.

The tablets should be taken with food for optimum absorption.

4.3. Contraindications

Hypersensitivity to the active substance, to any of the cephalosporins or to any of the excipients of the tablet listed in section 6.1.

Previous immediate and/or severe hypersensitivity reaction to a penicillin or to any other type of beta-lactam drug.

4.4. Special warnings and precautions for use

Hypersensitivity reactions

Before therapy with cefpodoxime is instituted, careful inquiry should be made to determine whether the patient has had any previous hypersensitivity reactions to cefpodoxime, cephalosporins, penicillins, or other beta-lactam drugs.

Cefpodoxime is contraindicated in patients who have had a previous hypersensitivity reaction to any cephalosporin.

It is also contraindicated in patients who have had a previous immediate and / or any severe hypersensitivity reaction to any penicillin or to any other beta- lactam drug.

Cefpodoxime should be given with caution to patients who have had any other type of hypersensitivity reaction to a penicillin or any other beta-lactam drug.

Hypersensitivity reactions (anaphylaxis) observed with beta-lactam antibiotics can be serious and occasionally fatal.

The onset of any manifestation of hypersensitivity indicates that treatment should be stopped.

Renal Insufficiency

In cases of severe renal insufficiency it may be necessary to reduce the dosage regimen dependent on the creatinine clearance (see section 4.2).

Gastrointestinal disease

Cefpodoxime should always be used with caution in patients with a history of gastrointestinal disease, particularly colitis. Antibiotic associated diarrhoea, colitis and pseudomembranous colitis have been reported with the use of cefpodoxime. These diagnoses should be considered in any patient who develops diarrhoea during or shortly after treatment. Cefpodoxime should be discontinued if severe and/or bloody diarrhoea occurs during treatment and appropriate therapy instituted.

Blood monitoring

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.

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

Prolonged use
As with other antibiotics, the prolonged use of cefpodoxime proxetil may result in the overgrowth of non-susceptible organisms. With oral antibiotics the normal colonic flora may be altered, allowing overgrowth by clostridia with consequent pseudomembranous colitis. Repeated evaluation of the patient is essential and if superinfection occurs during therapy, appropriate measures should be taken.

Sefpotec 200 mg Film Coated tablets contain sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

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. Cephlasporins potentially enhance the anticoagulant effect of coumarins.

Antacids and H_2 blockers
Studies have shown that bioavailability is decreased by approximately 30% when cefpodoxime is administered with drugs which neutralize 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.

Influence on laboratory diagnostic tests
A false positive reaction for glucose in the urine may occur with Benedict's or Fehling's solution or with copper sulphate test tablets, but not with tests based on enzymatic glucose oxidase reactions.

4.6. Fertility, pregnancy and lactation

For cefpodoxime proxetil no clinical data on exposed pregnancies are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development (see section 5.3).

Caution should be exercised when prescribing to pregnant women.

Studies carried out in several animal species have not shown any teratogenic or fetotoxic effects. However, the safety of cefpodoxime proxetil in pregnancy has not been established and, as with all drugs, it should be administered with caution during the early months of pregnancy.

Cefpodoxime is excreted in human milk. Mothers should stop breastfeeding during treatment with cefpodoxime.

4.7. Effects on ability to drive and use machines

Cefpodoxime proxetil has minor or moderate influence on the ability to drive and use machines.

Dizziness has been reported during treatment with cefpodoxime and may affect patients' ability to drive or operate machinery.

4.8. Undesirable effects

In this section undesirable effects are defined as follows:

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)

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

System Organ Class	**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)**
Infections and Infestations					There can be multiplication of non-sensitive microorganisms (see section 4.4).
Blood and lymphatic system disorders			Haematological disorders, such as reduction in haemoglobin, thrombocytosis, thrombocytopenia, leucopenia and eosinophilia.	Haemolytic anaemia.	
Immune system disorders					
Hypersensitivity reactions of all degrees of severity have been observed (see section 4.3 and 4.4).					
		Allergic reactions, such as mucocutaneou		Dermal reactions with blistering (erythema	

		s reactions, skin rashes, urticaria and pruritus.		multiforme, Stevens-Johnson syndrome, Lyell syndrome). The medication should be terminated if such symptoms occur. As with other cephalosporins, there have been very rare reports of anaphylactic reactions, bronchospasm, purpura and angioedema.	
Metabolism and nutrition disorders	Loss of appetite.				
Nervous system disorders		Headaches, paraesthesiae, dizziness.			
Ear and labyrinth disorders		Tinnitus.			
Gastrointestinal disorders	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 (see section 4.4).		
Hepato-biliary disorders			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.	Liver damage.	
Renal and urinary disorders				Slight increases in blood urea and creatinine.	
General disorders and administration site conditions		Asthenia or malaise.			

4.9. Overdose

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

In cases of overdose, 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: β-lactam antibiotic, 3rd generation cephalosporines,
ATC code: J01DD 13

Mechanism of action

Like other beta-lactam drugs, cefpodoxime exerts antibacterial activity by binding to and inhibiting the action of certain bacterial cell wall synthetic enzymes, namely the penicillin binding proteins. This results in the interruption of cell wall (peptidoglycan) biosynthesis, which leads to bacterial cell lysis and death.

Mechanisms of Resistance

Bacterial resistance to cefpodoxime may be due to one or more of the following mechanisms:

- hydrolysis by beta-lactamases. Cefpodoxime may be efficiently hydrolysed by certain of the extended-spectrum beta-lactamases (ESBLs) and by the chromosomally-encoded (AmpC) enzyme that may be induced or stably derepressed in certain aerobic gram-negative bacterial species
- reduced affinity of penicillin-binding proteins for cefpodoxime
- outer membrane impermeability, which restricts access of cefpodoxime to penicillin binding proteins in gram-negative organisms
- drug efflux pumps

Breakpoints:

According to the NCCLS (National Committee on Clinical Laboratory Standards) the following breakpoints have been defined for cefpodoxime:

• Enterobacteriaceae and *Staphylococcus* spp.: ≤2 μg/ml susceptible, 4 μg/ml intermediate, ≥8 μg/ml resistant
• *Haemophilus* spp.: ≤2 μg/ml susceptible
• *Neisseria gonorrhoeae* : ≤0.5 μg/ml susceptible
• *Streptococcus pneumoniae*: ≤0.5 μg/ml susceptible, 1 μg/ml intermediate, ≥2 μg/ml resistant
• Other Streptococci that are susceptible to penicillin (MIC90 ≤0.12 μg/ml) can be considered susceptible to cefpodoxime.

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 the agent in at least some types of infections is questionable.

Commonly susceptible species

Aerobes, Gram positive:

Staphylococcus aureus (methicillin susceptible)

Coagulase-negative staphylococci (methicillin-susceptible)

Streptococcus agalactiae

Streptococcus pneumoniae

Streptococcus pyogenes

Aerobes, Gram negative:

Escherichia coli

Haemophilus influenzae

Klebsiella species

Moraxella catarrhalis

Neisseria gonorrhoeae

Proteus mirabilis

Proteus rettgeri

Anaerobes:

Peptococcus species

Peptostreptococcus species

Species for which resistance may be a problem

Acinetobacter species

Citrobacter species

Enterobacter species

Morganella morganii.

Resistant

Bacteroides fragilis

Clostridium difficile

Enterococci

Listeria monocytogenes

Proteus vulgaris

Pseudomonas species

Serratia species

5.2 Pharmacokinetic properties

Cefpodoxime proxetil 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, 51.1% 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 hours 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.

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

As the majority of cefpodoxime is eliminated in the urine, the concentration is high. (Concentrations in 0-4, 4-8, 8-12 hour 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 hours after an administration of a single 200 mg dose (1.6-3.1 µg/g). Concentrations of cefpodoxime in the medullary and cortical tissues are similar.

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

5.3 Preclinical safety data

Adverse reactions not observed in clinical studies, but seen in animals at exposure levels similar to clinical exposure levels and with possible relevance to clinical use were as follows:

Acute Toxicity

The median lethal dose in mice and rats was above 8 g/kg and 4 g/kg bodyweight, respectively. In Fisher rats doses of 1 g/kg body weight and higher influenced stool consistency and weight gain. Single doses of 800 mg/kg body weight were non-toxic in dogs.

Repeat-dose toxicity

Chronic toxicity studies were carried out over 12 months in rats and 6 months in dogs. Maximum daily doses (1000 mg/kg body weight orally in rats and 400 mg/kg orally in dogs) were considerably higher than recommended therapeutic doses (3-8 mg/kg body weight). No mortality was observed in rats receiving 250, 500 or 1000 mg/kg for 12 months. Only at 1000 mg/kg, effects on the GI-tract, softened stools and dilatation of the caecum were observed.

Intestinal side effects, which were more pronounced in Fisher rats, are due to the change in intestinal flora caused by the pronounced antibacterial effect of cefpodoxime. Daily administration of 0, 25, 100, and 400 mg/kg body weight to dogs did not reveal mortality. Unchanged cefpodoxime was detected in faeces.

Reproduction toxicity

Embryotoxicity studies in rats and rabbits have not revealed any signs of teratogenic potential. Cefpodoxime had no adverse effects on fertility and peri-/postnatal toxicity studies in rats. Cefpodoxime or its metabolites cross the placenta and are excreted in breast milk in rats. No experience is available on the use of cefpodoxime during pregnancy and lactation in humans.

Mutagenicity

Extensive mutagenicity testing in different testing models was negative.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:
Microcrystalline cellulose & Carboxymethylcellulose Sodium (Avicel RC 591)
Sodium lauryl sulphate
Hydroxypropylcellulose-L (HPC-L)
Silica
Colloidal Anhydrous (Aerosil 200)
Magnesium stearate

Film Coating:
Sepifilm LP 761 Blanc*
*Film Coating material Sepifilm LP 761 Blanc consist of Anatase Titanium Dioxide (E171), Microcrystalline cellulose(E460), Stearic Acid (E570), Hydroxypropyl methylcellulose (E464)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store below 30 ºC in its own pack.

Keep out of reach and sight of children.

6.3 Nature and contents of container
Al-Al blister

(14 Film Coated Tablets/2 Blisters/1 Box)(7 Film Coated Tablets/1 blister)

(20 Film Coated Tablets/4 Blisters/1 Box)(5 Film Coated Tablets/1 blister).

6.4 Special precautions for disposal

There is no available information about the potential of the product to produce adverse environmental effects. Local regulations and procedures should be consulted prior to environmental release.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)

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9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23.03.2023

10. DATE OF REVISION OF THE TEXT

5.7.2023