APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS: S4

1. NAME OF THE MEDICINE

Cepodem 100 Tablets (Film-coated tablets)

Cepodem 200 Tablets (Film-coated tablets)

Cepodem Suspension 40 mg/5 ml (Powder for Oral Suspension)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Cepodem 100 Tablets

Each film coated tablet contains:

Cefpodoxime proxetil equivalent to cefpodoxime 100 mg.

Contains sugar: Lactose anhydrous 10,0 mg

Cepodem 200 Tablets

Each film coated tablet contains: Cefpodoxime proxetil equivalent to cefpodoxime200 mg.

Contains sugar: Lactose anhydrous 20,0 mg

For the full list of excipients, see section 6.1.

Cepodem Suspension 40 mg/5 ml

Each 5 ml of the constituted suspension contains:

Cefpodoxime proxetil equivalent to cefpodoxime 40 mg

Preservative: Sodium benzoate 0,2 % m/v

Contains sugar: Sucrose 2,7 g; lactose anhydrous 7, 23 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets

Cepodem 100 Tablets*:* White coloured, capsule shaped, film coated tablets imprinted with `RX520' on one side in black edible ink.

Cepodem 200 Tablets: White coloured, capsule shaped, film coated tablets imprinted with `RX521' on one side in black edible ink.

Suspension

Cepodem Suspension 40 mg/5 ml: Off-white to yellow granular powder forming an off-white to yellow suspension on constitution with water. The resulting suspension has a characteristic fruity flavour.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

In Adults

Cepodem 100 Tablets and Cepodem 200 Tablets are indicated for use in the short-term treatment of upper and lower respiratory tract infections due to susceptible micro-organisms (sensitivity tests must be performed):

Acute bronchitis and acute exacerbations of chronic bronchitis due to:

Haemophilus influenzae, *Streptococcus pneumoniae*, *Moraxella catarrhalis.*

Pharyngitis and tonsillitis due to: *Streptococcus pyogenes*

Bacterial pneumonia and community-acquired bronchopneumonia due to: *Haemophilus influenza, Streptococcus pneumoniae, Moraxella catarrhalis.*

Acute sinusitis due to: *Haemophilus influenzae (non-typeable), Streptococcus pneumoniae, Methicillin-sensitive Staphylococcus aureus, Moraxella catarrhalis.*

In Children

Cepodem Suspension 40 mg/5 ml is indicated for use in the short-term treatment of infections due to susceptible micro-organisms:

Upper and lower respiratory tract infections

Otitis media due to: *Haemophilus influenzae* (non-typeable), *Streptococcus pneumoniae, Moraxella catarrhalis.*

Tonsillitis and pharyngitis due to: *Streptococcus pyogenes.*

Pneumonia due to: *Haemophilus influenza, Streptococcus pneumoniae, Moraxella catarrhalis.*

4.2 Posology and method of administration

Posology

In Adults

Each film-coated tablet contains 100 mg or 200 mg of cefpodoxime.

The dosage of Cepodem 100 Tablets and Cepodem 200 Tablets depends on the condition being treated.

Tonsillitis, pharyngitis and acute bronchitis

One Cepodem 100 Tablet (100 mg) every 12 hours with meals (200 mg/day).

In the treatment of beta-haemolytic streptococcal infections, a therapeutic dose should be administered for at least 10 days.

Acute sinusitis, acute exacerbations of chronic bronchitis, pneumonia

One Cepodem 200 Tablet (200 mg) every 12 hours with meals (400 mg/day).

Special populations

Elderly patients

Where renal function is normal, it is not necessary to adjust the dose.

Hepatic insufficiency in adults and children:

No dosage adjustment necessary.

Renal insufficiency in adults and children:

When the creatinine clearance is above 40 ml/min, it is not necessary to adjust the dose.

For values below 40 ml/min, the daily dosage regimen should be reduced by half and administered as a single daily dose for values 10-39 ml/min, every second day for values below 10 ml/min, and after each dialysis session for haemodialysis patients.

In Children

Each 5 ml of the constituted suspension contains 40 mg of cefpodoxime.

Preservative: Sodium benzoate 0,2 % m/v

The dosage depends on the weight of the child being treated. The average dose is 8 mg/kg/day administered in two doses at 12 hourly intervals withmeals. Shake the bottle before use.

The following table may be used as a dosage guide:

Weight (kg)	**Dose**

Between 10 and 15 kg	5 ml (40 mg) every 12 hours
≥ 15 kg	10 ml (80 mg) every 12 hours

Cepodem Suspension 40 mg/5 ml is currently not indicated for use in children under one year of age since insufficient clinical data is available at present (see section 4.3).

Method of administration

Oral.

Cepodem 100/200 film-coated tablet taken with meals.

CEPODEM Suspension 40 mg/5 ml administered with meals.

Directions for reconstitution of the suspension: Shake the bottle to loosen the granules. Add 33 ml and 66 ml water for 50 ml and 100 ml packs respectively in two divided portions to the dry mixture in the bottle. Shake well after each addition.

4.3 Contraindications

Hypersensitivity to cefpodoxime, the cephalosporin group of antibiotics (see section 4.4) or any of the excipients listed in section 6.1.

Pregnancy and lactation (see section 4.6).

Children below 1 year of age (see section 4.2)

4.4 Special warnings and precautions for use

Anaphylactic reactions:

Preliminary enquiry as to an allergic diathesis and particularly hypersensitivity of beta-lactam antibiotics should precede treatment with CEPODEM.

The use of CEPODEM is strictly contraindicated in subjects with a previous history of immediate type hypersensitivity to cephalosporins.

CEPODEM should be used with extreme caution in patients sensitive to penicillin and other ß-lactam antibiotics as cross-allergy may develop. Strict medical supervision is required throughout the treatment.

Hypersensitivity reactions (anaphylaxis) observed with CEPODEM can be serious and occasionally fatal.

If an allergic reaction occurs, treatment should be stopped immediately.

Prolonged use may result in overgrowth of non-susceptible organisms and, as with other broad spectrum antibiotics, pseudomembranous colitis may develop. It is important to consider its diagnosis in patients who develop diarrhoea in association with the use of antibiotics. Such colitis may range in severity from mild to life threatening. Treatment should be discontinued if symptoms suggestive of psuedomembranous colitis arise. Mild cases of pseudomembranous colitis usually respond to drug discontinuance alone. When the colitis does not improve after the medicine has been discontinued, or when it is severe, oral vancomycin is the medicine of choice for antibiotic associated pseudomembranous colitis produced by C. difficile.

Clostridium difficile – associated disease:

Diarrhoea, particularly if severe and/or persistent, occurring during treatment or in the initial weeks following treatment with CEPODEM, may be symptomatic of Clostridium difficile-associated disease, the most severe form of which is pseudomembranous colitis. The diagnosis of this possibly fatal condition is confirmed by endoscopy and/or histology. Screening of faeces for this pathogen, and its cytotoxin is the best way to diagnose Clostridium difficile associated disease.

If a diagnosis of pseudomembranous colitis is suspected, CEPODEM should be stopped immediately and appropriate specific therapy should be started without delay (e.g. vancomycin or metronidazole).

Clostridium difficile-associated disease can be favoured by faecal stasis.

Superinfection:

The use of CEPODEM, especially if prolonged, may result in overgrowth of non-susceptible organisms. Repeated evaluation of the patient's condition is essential. If superinfection occurs during therapy, appropriate measures should be taken (see section 4.8: Infections and Infestations).

Renal impairment:

Cephalosporins should be given with caution to patients with renal impairment.

Changes in renal function have been observed with antibiotics of the same class as CEPODEM, particularly when given concurrently with potentially nephrotoxic agents such as aminoglycosides and/or potent diuretics. In such cases, renal function should be monitored.

Positive Coombs' test:

There may be a positive response to the Coombs' test during treatment with cephalosporins. CEPODEM may be absorbed onto the surface of red cell membranes and react with antibiotics directed against the medicine. This can produce a positive antiglobulin test and haemolytic anaemia. Cross-reactivity may occur with penicillin for this reaction.

Paediatrics: No paediatrics-specific problems have been documented with the use of cefpodoxime proxetil to date. The safety and efficacy of Cepodem have not been established in children under one year of age (see section 4.3).

Geriatrics: Cepodem may be used at the normal recommended dosage in elderly patients even with mild to moderate renal impairment; however, appropriate modification in dosage is advised in patients with severe renal impairment (See section 4.2).

Excipients: Sucrose/Lactose Cepodem 100 Tablets, 200 Tablets and Suspension 40 mg/5 ml contain lactose. Cepodem Suspension 40 mg/5 ml also contains sucrose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take Cepodem.

4.5 Interaction with other medicines and other forms of interaction

Absorption of cefpodoxime is decreased by antacids or histamine H2-receptor antagonists.

Probenecid reduces the renal excretion of cefpodoxime.

The bioavailability of CEPODEM is increased if the product is administered during meals (acid pH).

CEPODEM potentially enhances the anticoagulant effect of warfarin and reduces the contraceptive effect of oestrogens.

Cases showing development of a positive Coombs' test have been reported (see section 4.4).

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

Pregnancy:

Safety in pregnancy has not been established (see section 4.3).

Lactation:

Safety in Lactation has not been established (see section 4.3).

4.7 Effects on ability to drive and operate machines

Dizziness may occur, which should be taken into account when driving a vehicle or operating machines. Patients should therefore be advised not to drive or operate machinery until their individual susceptibility is known.

4.8 Undesirable effects

Tabulated list of adverse reactions

MedDRA System organ class	**Frequency**	**Adverse reactions**
Infections and Infestations	*Less frequent*	Superinfections, overgrowth of non-susceptible organisms (see section 4.4).
Blood and lymphatic system disorders	*Frequent*	Eosinophilia.
	Less frequent	Leucopenia, thrombocytopenia, reduction of haemoglobin, thrombocytosis, leucopenia, haemolytic anaemia and eosinophilia. Neutropenia and agranulocytosis may occur during treatment with CEPODEM.
Immune system disorders	*Less frequent*	Anaphylactic reactions e.g. angioedoema, bronchospasm, malaise, possibly culminating in shock may occur (see section 4.4).
Ear and labyrinth disorders	*Less frequent*	Tinnitus.
Gastrointestinal disorders	*Frequent*	Nausea, vomiting, abdominal pains

	Less frequent	abdominal disorders, diarrhoea may sometimes be a symptom of enterocolitis, which may, in some cases, be accompanied by blood in stools. A particular form of enterocolitis that can occur with antibiotics is pseudomembranous colitis (in most cases due to Clostridium difficile) (see section 4.4), taste disturbances, stomatitis, dry mouth.
Hepato-biliary disorders	*Less frequent*	Elevations of liver enzymes (AST, ALT and alkaline phosphatase), and/or bilirubin. These laboratory abnormalities exceed twice the upper limit of the normal range and elicit a pattern of drug induced hepatitis, usually cholestatic.
Skin and subcutaneous tissue disorders	*Less frequent*	Cutaneous eruptions and pruritus, rash, urticaria and purpura. Cases of bullous eruptions (erythema multiforme, Stevens-Johnson Syndrome, toxic epidermal necrolysis) have been reported.
Renal and urinary disorders	*Less frequent*	Increase of blood urea and creatinine.
Changes in renal function have been observed with antibiotics from the same group as CEPODEM, particularly when co-prescribed with aminoglycosides and/or potent diuretics (see section 4.4).		
General disorders and administrative site conditions	*Less frequent*	Asthenia

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

Overdosage with Cepodem may manifest in any of the symptoms described under section 4.8.

Treatment is symptomatic and supportive.

Convulsions and other signs of CNS toxicity have been associated with high doses, especially in patients with renal impairment.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A. 20.1.1 Broad and medium spectrum antibiotics.

Mechanism of action

Cefpodoxime proxetil is a semi-synthetic ß-lactam antibiotic belonging to the third generation oral cephalosporin group. Cefpodoxime proxetil is the prodrug of the bactericidal antibiotic cefpodoxime.

The antibacterial action of cefpodoxime is through inhibition of bacterial cell wall synthesis probably by acylation of membrane bound transpeptidase enzymes; this prevents cross linkage of peptidoglycan chains, which is necessary for bacterial cell wall strength and rigidity.

Antibacterial spectrum

In vitro studies have demonstrated the susceptibility of most strains of the following micro-organisms to cefpodoxime proxetil. However, such in vitro activity does not necessarily imply in vivo efficacy.

Gram-positive organisms

Streptococcus pneumoniae, S. pyogenes, S. agalactiae, S. mitis, S. sanguis and S. salivarius; Propionibacterium acnes; Corynebacterium diphtheriae; methicillin-sensitive penicillinase and non-penicillinase producing strains of *S. aureus.*

Gram negative organisms

ß-lactamase and non-ß-lactamase producing strains of *Haemophilus influenzae, Haemophilus para-influenzae, Moraxella catarrhalis (Branhamella catarrhalis)* and *Neisseria gonorrhoea; Escherichia coli; Klebsiella pneumoniae; Klebsiella oxytoca; Proteus mirabilis.*

The following organisms are not sensitive: Group D streptococci, Methicillin-resistant staphylococci *(S. aureus and S. epidermidis), Staphylococcus saprophyticus, Corynebacteria,* groups J and K, *Listeria monocytogenes, Pseudomonas aeruginosa* and *Pseudomonas* spp., *Acinetobacter baumanii, Clostridium difficile, Bacteroides fragilis* and related species.

5.2 Pharmacokinetic properties

Absorption:

Cefpodoxime proxetil is absorbed orally and rapidly hydrolysed by non-specific esterases in the gastro-intestinal wall to cefpodoxime, the active acid. Absorption is decreased in conditions of low gastric acidity.

Distribution:

After oral administration of a single 5 mg/kg (200 mg maximum) dose of cefpodoxime proxetil suspension in children, the maximum plasma concentration (Cmax) obtained is on average 2,6 mg/l.

With cefpodoxime proxetil tablets the time taken to reach the maximum concentration (Tmax) is about 2,7 hours.

With the suspension the time taken to reach the maximum concentration (Tmax) is about 2 to 4 hours.

The drug diffuses well into respiratory tissues.

The serum half-life is about 2,46 hours.

About 27 % of cefpodoxime in the plasma is bound to plasma proteins

The volume of distribution is about 0,46 l/kg.

Elimination:

The clearance is around 2,4 ml/min/kg.

About 81 % of unchanged cefpodoxime is excreted in the urine.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cepodem Tablets

Tablet core

Carboxymethyl cellulose calcium

Hydroxypropylcellulose

Lactose anhydrous

Magnesium stearate

Sodium lauryl sulphate

Film-coat

Propylene glycol

Opadry White 03H58987 consisting of:

Hypromellose

Titanium dioxide

Propylene glycol

Printing Ink:

Opacode-S-1-17823 consisting of :

Shellac Glaze

Iron oxide black

N-Butyl Alcohol

Propylene glycol

Cepodem Suspension 40 mg/5 ml

Carboxymethyl cellulose sodium

Carrageenan

Citric acid

Colloidal anhydrous silica

Croscarmellose sodium

Hydroxypropyl cellulose

Lactose anhydrous

Microcrystalline cellulose sodium

Sodium benzoate

Sodium citrate

Sucrose

Flavourant: Flavour Cherry; Flavour Fruit Gum

Colourant: Ferric Oxide Yellow

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Cepodem 100 Tablets/ Cepodem 200 Tablets: 24 months.

Cepodem Suspension 40 mg/5 ml: 18 months

6.4 Special precautions for storage

Store at or below 25 °C, protected from light and moisture.

After constitution of the suspension, the pack must be stored at 2-8 °C in a refrigerator. The constituted suspension should be consumed within 10 days of preparation. Discard any unused portion of the constituted suspension after 10 days. Shake well before dosing.

6.5 Nature and contents of container

Cepodem 100 Tablets: Aluminium strip pack of 10 tablets.

Cepodem 200 Tablets: Aluminium strip pack of 10 tablets.

Cepodem Suspension 40 mg/5 ml: Natural translucent HDPE bottle pack of 50 ml and 100 ml.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Ranbaxy Pharmaceuticals (Pty) Ltd

a Sun Pharma Company

14 Lautre Road, Stormill Ext 1

Roodepoort, 1724

South Africa

8. REGISTRATION NUMBERS

Cepodem 100 Tablets: 36/20.1.1/0225

Cepodem 200 Tablets: 36/20.1.1/0226

Cepodem Suspension 40 mg/5 ml: 36/20.1.1/0227

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

11 December 2003

10. DATE OF REVISION OF THE TEXT

26 September 2022

Namibia:

Cepodem 100 NS2 07/20.1.1/0024

Cepodem 200 NS2 07/20.1.1/0025

Cepodem Suspension 40 mg/5 ml NS2 07/20.1.1/0026