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

PROFESSIONELE INLIGTING

SKEDULERINGSTATUS: S4

1. NAAM VAN DIE MEDISYNE

Cepodem 100 Tablets (Filmbedekte tablette)

Cepodem 200 Tablets (Filmbedekte tablette)

Cepodem Suspension 40 mg/5 mL (Poeier vir Orale Suspensie)

2. KWALITATIEWE EN KWANTITATIEWE SAMESTELLING

Cepodem 100 Tablets

Elke filmbedekte tablet bevat:

Kefpodoksiemproksetiel gelykstaande aan kefpodoksiem 100 mg.

Bevat suiker: Anhidriese laktose 10,0 mg

Cepodem 200 Tablets

Elke filmbedekte tablet bevat:

Kefpodoksiemproksetiel gelykstaande aan kefpodoksiem 200 mg.

Bevat suiker: Anhidriese laktose 20,0 mg

Vir die volledige lys van onaktiewe bestanddele, sien afdeling 6.1.

Cepodem Suspension 40 mg/5 mL

Elke 5 mL van die hersaamgestelde suspensie bevat:

Kefpodoksiemproksetiel gelykstaande aan kefpodoksiem 40 mg

Preserveermiddel: Natriumbensoaat 0,2 % m/v

Bevat suiker: Sukrose 2,7 g; anhidriese laktose 7,23 mg

Vir die volledige lys van onaktiewe bestanddele, sien afdeling 6.1.

3. FARMASEUTIESE VORM

Filmbedekte tablette

Cepodem 100 Tablets*:* Wit gekleurde, kapsulevormige, filmbedekte tablette gedruk met `RX520' op een kant in swart eetbare ink.

Cepodem 200 Tablets: Wit gekleurde, kapsulevormige, filmbedekte tablette gedruk met RX521' op een kant in swart eetbare ink.

Suspensie

Cepodem Suspension 40 mg/5 mL: Naaswit tot geel granulêre poeier wat ‘n naaswit tot geel suspensie vorm na hersamestelling met water. Die hersaamgestelde suspensie het ‘n kenmerkende vrugtige geur.

4. KLINIESE BESONDERHEDE

4.1 Terapeutiese indikasies

In Volwassenes

Cepodem 100 Tablets en Cepodem 200 Tablets word aangedui vir gebruik in die korttermyn behandeling van boonste en onderste lugweginfeksies as gevolg van vatbare mikro-oraganismes (sensitiwiteitstoetse moet uitgevoer word):

Akute brongitis en akute verergering van chroniese brongitis as gevolg van:

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

Faringitis en tonsillitis as gevolg van: *Streptococcus pyogenes*

Bakteriële pneumonie en gemeenskapsverworwe brongopneumonie as gevolg van: *Haemophilus influenza, Streptococcus pneumoniae, Moraxella catarrhalis.*

Akute sinusitis as gevolg van: *Haemophilus influenzae (nie-tipeerbaar), Streptococcus pneumoniae, Methicillin-sensitive Staphylococcus aureus, Moraxella catarrhalis.*

In Kinders

Cepodem Suspension 40 mg/5 mL word aangedui vir gebruik in die korttermyn behandeling van infeksies as gevolg van vatbare mikro-organismes:

Boonste en onderste lugweginfeksies

Otitis media as gevolg van: *Haemophilus influenzae* (nie-tipeerbaar), *Streptococcus pneumoniae, Moraxella catarrhalis.*

Tonsillitis en faringitis as gevolg van: *Streptococcus pyogenes.*

Pneumonie as gevolg van: *Haemophilus influenza, Streptococcus pneumoniae, Moraxella catarrhalis.*

4.2 Posologie and metode van toediening

Posologie

In Volwassenes

Elke filmbedekte tablet bevat 100 mg of 200 mg van kefpodoksiem.

Die dosering van Cepodem 100 Tablets en Cepodem 200 Tablets hang af van die toestand wat behandel word.

Tonsillitis, faringitis en akute brongitis

Een Cepodem 100 Tablet (100 mg) elke 12 uur saam met etes (200 mg/dag).

In die behandeling van beta-hemolitiese streptokokkale infeksies, moet 'n terapeutiese dosis vir ten minste 10 dae toegedien word.

Akute sinusitis, akute verergering van chroniese brongitis, pneumonie

Een Cepodem 200 Tablet (200 mg) elke 12 uur saam met maaltye (400 mg/dag).

Spesiale populasies

Bejaarde pasiënte

Dit is nie nodig om die dosis aan te pas waar die nierfunksie normaal is nie.

Hepatiese ontoereikendheid in volwassenes en kinders:

Geen dosisaanpassing is nodig nie.

Renale ontoereikendheid in volwassenes en kinders:

Dit is nie nodig om die dosis aan te pas wanneer die kreatinienopruiming bo 40 mL/min is nie.

Vir waardes onder 40 mL/min, moet die daaglikse doseringsregimen met die helfte verlaag word en as 'n enkeldosis toegedien word vir waardes van 10-39 mL/min, elke tweede dag vir waardes onder 10 mL/min, en na elke dialise-sessie vir hemodialise-pasiënte.

In Kinders

Elke 5 mL van die hersaamgestelde suspensie bevat 40 mg van kefpodoksiem.

Preserveermiddel: Natriumbensoaat 0,2 % m/v

Die dosis hang af van die gewig van die kind wat behandel word. Die gemiddelde dosis is is 8 mg/kg/dag toegedien in twee dosisse met 12-uurlikse intervalle saam met maaltye. Skud die bottel voor gebruik.

Die volgende tabel kan gebruik word as dosisriglyn:

Gewig (kg)	**Dosis**
Tussen 10 en 15 kg	5 mL (40 mg) elke 12 uur
≥ 15 kg	10 mL (80 mg) elke 12 uur

Cepodem Suspension 40 mg/5 mL word huidiglik nie vir gebruik in kinders onder die ouderdom van een jaar aangedui nie, aangesien onvoldoende kliniese data tans beskikbaar is (sien afdeling 4.3).

Metode van toediening

Oraal.

Cepodem 100/200 filmbedekte tablette saam met maaltye geneem.

CEPODEM Suspension 40 mg/5 mL toegedien saam met maaltye.

Aanwysings vir hersamestelling van die suspensie: Skud die bottel om die granules los te maak. Voeg 33 mL en 66 mL water vir 50 mL en 100 mL verpakkings, respektiewelik, in twee verdeelde porsies by die droë mengsel in die bottel. Skud goed na elke byvoeging.

4.3 Kontra-indikasies

Hipersensitiwiteit teen kefpodoksiem, die kefalosporiengroep van antibiotika (sien afdeling 4.4) of vir enige van die onaktiewe bestanddele gelys in afdeling 6.1.

Swangerskap en laktasie (sien afdeling 4.6).

Kinders onder 1-jarige ouderdom (sien afdeling 4.2)

4.4 Spesiale waarskuwings en voorsorgmaatreëls vir gebruik

Anafilaktiese reaksies:

Voorbereidende navraag oor ‘n allergiese diatese en veral hipersensitiwiteit vir beta-laktaam antibiotika moet behandeling met CEPODEM voorafgaan.

Die gebruik van CEPODEM word sterk teenaangedui in persone met 'n vorige geskiedenis van onmiddellike tipe hipersensitiwiteit teen kefalosporiene.

CEPODEM moet met uiterste sorg gebruik word in pasiënte wat sensitief is vir penisillien en ander ß-laktaam antibiotika aangesien kruis-allergie kan ontwikkel. Streng mediese toesig word deurentyds benodig gedurende behandeling.

Hipersensitiwiteitsreaksies (anafilakse) wat met CEPODEM waargeneem word, kan ernstig en soms fataal wees. As 'n allergiese reaksie voorkom, moet behandeling onmiddellik gestaak word.

Langdurige gebruik kan lei tot oorgroei van nie-vatbare organismes en, soos met ander breëspektrum antibiotika, kan pseudomembraneuse kolitis ontwikkel. Dit is belangrik om so 'n diagnose te oorweeg in pasiënte wat diaree ontwikkel in assosiasie met die gebruik van antibiotika. Sulke kolitis kan wissel in ernstigheid van lig tot lewensbedreigend. Behandeling moet gestaak word as simptome voortspruit aanduidend van pseudomembraneuse kolitis. Ligte gevalle van pseudomembraneuse kolitis reageer gewoonlik op slegs onttrekking van die geneesmiddel. Wanneer die kolitis nie verbeter nadat die medisyne gestaak is nie, of wanneer dit ernstig is, is orale vankomisien die medisyne van keuse vir antibiotika-geassosieerde pseudomembraneuse kolitis aangebring deur *C. difficile*.

***Clostridium difficile* – geassosieerde siekte:**

Diaree, veral as dit ernstig is en/of aanhoudend voorkom gedurende die behandeling of in die opeenvolgende weke na behandeling met CEPODEM, kan dit moontlik simptomaties wees van *Clostridium difficile*-geassosieerde siekte, die mees ernstige vorm daarvan is pseudomembraneuse kolitis. Die diagnose van hierdie moontlike fatale toestand word bevestig deur endoskopie en/of histologie. Sifting van feses vir hierdie patogeen,en sy sitotoksien is die beste manier om *Clostridium difficile*-geassosieerde siekte te diagnoseer.

As 'n diagnose van pseudomembraneuse kolitis vermoed word, moet CEPODEM onmiddellik gestaak word en moet sonder uitstel met toepaslike spesifieke terapie begin word (bv. vankomisien of metronidasool).

Clostridium difficile-geassosieerde siekte kan deur fekale stase bevorder word.

Superinfeksie:

Die gebruik van CEPODEM, veral as dit langdurig is, kan lei tot die oorgroei van nie-vatbare organismes. Herhaaldelike evaluering van die pasiënt se toestand is noodsaaklik. As superinfeksie tydens terapie voorkom, moet toepaslike maatreëls getref word (sien afdeling 4.8: Infeksies en Infestasies).

Renale inkorting:

Kefalosporiene moet met omsigtigheid toegedien word aan pasiënte met renale inkorting. Veranderinge in renale funksie is waargeneem met antibiotika van dieselfde klas as CEPODEM, veral wanneer gelyktydig toegedien word met potensieel nefrotoksiese middels soos aminoglikosiede en/of kragtige diuretika. In sulke gevalle, moet nierfunksie gemonitor word.

Positiewe Coombs se toets:

Daar mag 'n positiewe respons wees op die Coombs se toets tydens behandeling met kefalosporiene. CEPODEM kan op die oppervlak van rooiselmembrane geabsorbeer word en reageer met antibiotika gerig teen die medisyne. Dit kan 'n positiewe antiglobulientoets en hemolitiese anemie veroorsaak. Kruis-reaktiwiteit kan voorkom met penisillien vir hierdie reaksie.

Pediatriese pasiënte: Geen pediatries-spesifieke probleme is tot nou toe aangeteken vir die gebruik van kefpodoksiemproksetiel nie. Die veiligheid en doeltreffendheid van Cepodem is nie vasgestel in kinders onder die ouderdom van een jaar nie (sien afdeling 4.3).

Geriatriese pasiënte: Cepodem kan teen die normale aanbevole dosisse in bejaarde pasiënte, selfs met ligte tot matige nierinkorting gebruik word; toepaslike modifikasie in dosering word egter aangeraai in pasiënte met ernstige renale inkorting (sien afdeling 4.2).

Onaktiewe bestanddele: Sukrose/Laktose Cepodem 100 Tablets, 200 Tablets en Suspension 40 mg/5 mL bevat laktose. Cepodem Suspension 40 mg/5 mL bevat ook sukrose. Pasiënte met seldsame oorerflike probleme van galaktose onverdraagsaamheid, totale laktase tekort of glukose-galaktose wanabsorpsie moet nie Cepodem gebruik nie.

4.5 Interaksie met ander medisyne en ander vorme van interaksie

Absorpsie van kefpodoksiem word verlaag deur teensuurmiddels of histamien H_2-reseptor antagoniste.

Probenesied verlaag die renale uitskeiding van kefpodoksiem.

Die biobeskikbaarheid van CEPODEM word verhoog as die produk tydens maaltye (suur pH) toegedien word.

Daar is 'n moontlikheid dat CEPODEM die antikoagulant-effek van warfarien verhoog en die kontraseptiewe effek van estrogene verlaag.

Gevalle wat dui op die ontwikkeling van 'n positiewe Coombs se toets is aangemeld (sien afdeling 4.4).

'n Vals positiewe reaksie vir glukose in die urine kan voorkom met Benedict se of Fehling se oplossing of met kopersulfaat-toetstablette, maar nie met toetse gebaseer op ensiematiese glukose-oksidase reaksies nie.

4.6 Fertiliteit, swangerskap en laktasie

Swangerskap:

Veiligheid is nie vasgestel in swangerskao nie (sien afdeling 4.3).

Laktasie:

Veiligheid is nie vasgestel in laktasie nie (sien afdeling 4.3).

4.7 Effekte op die vermoë om te bestuur of masjinerie te hanteer

Duiseligheid kan voorkom, wat in ag geneem moet word wanneer 'n motor bestuur word of masjinerie hanteer word. Pasiënte moet daarom aangeraai word om nie te bestuur of masjinerie te hanteer totdat hulle bekend is met hulle individuele vatbaarheid nie.

4.8 Ongewenste effekte

Getabulleerde lys van ongunstige reaksies

MedDRA Stelsel orgaanklas	**Voorkoms**	**Ongunstige reaksies**
Infeksies en Infestasies	*Minder dikwels*	Superinfeksies, oorgroei van nie-vatbare organismes (sien afdeling 4.4).
Bloed- en limfatiese stelselversteurings	*Dikwels*	Eosinofilie.
	Minder dikwels	Leukopenie, trombositopenie, verlaging van hemoglobien, trombositose, leukopenie, hemolitiese anemie en

		eosinofilie. Neutropenie en agranulositose kan voorkom tydens behandeling met CEPODEM.
Immuunstelselversteurings	*Minder dikwels*	Anafilaktiese reaksies bv. angio-edeem, brongospasma, malaise, wat moontlik kulmineer in skok, kan voorkom (sien afdeling 4.4).
Oor-en labirintversteurings	*Minder dikwels*	Tinnitus.
Gastroïntestinale versteurings	*Dikwels*	Naarheid, braking, abdominale pyne
	Minder dikwels	Abdominale versteurings, diaree kan somtyds 'n simptoom wees van enterokolitis, wat, in sommige gevalle saamgaan met bloed in die stoelgange. 'n Sekere vorm van enterocolitis wat kan voorkom met antibiotika is pseudomembraneuse kolitis (in meeste gevalle as gevolg van *Clostridium difficile*) (sien afdeling 4.4), smaakversteurings, stomatitis, droë mond.
Hepato-biliêre versteurings	*Minder dikwels*	Verhogings van lewerensieme (AST, ALT en alkaliese fosfatase), en/of bilirubien. Hierdie laboratoriumabnormaliteite oorskry die boonste limiet van die normale reeks twee maal en lok 'n patroon van geneesmiddel-geïnduseerde hepatitis, gewoonlik cholestatiese, uit.

Vel- en subkutane weefselversteurings	*Minder dikwels*	Kutaneuse uitbarstings en pruritus, uitslag, urtikarie en purpura. Gevalle van blasie-agtige uitbarstings (veelvuldige eriteem, Stevens-Johnson Sindroom, toksiese epidermale nekrolise) is aangemeld.
Renale en urinêre versteurings	*Minder dikwels*	Verhogings van bloedureum en kreatinien.
Veranderinge in nierfunksie is waargeneem met antibiotika van dieselfde groep as CEPODEM, veral wanneer gelyktydig met aminoglikosiede en/of kragtige diuretika voorgeskryf word (sien afdeling 4.4).		
Algemene versteurings en toedienplektoestande	*Minder dikwels*	Astenie

Aanmelding van vermoedelike ongunstige reaksies

Aanmelding van vermoedelike ongunstige reaksies na goedkeuring van die medisyne is belangrik. Dit verseker volgehoue monitering van die voordeel/risiko balans van die medisyne. Gesondheidsorgvoorsieners word versoek om enige vermoedelike ongunstige reaksie aan te meld by SAHPRA *via* die "**6.04 Adverse Drug Reactions Reporting Form**", wat aanlyn beskikbaar is onder SAHPRA se publikasies: https://www.sahpra.org.za/Publications/Index/8.

4.9 Oordosis

Oordosis met Cepodem kan in enige van die simptome wat onder afdeling 4.8 beskryf word manifesteer.

Behandeling is simptomaties en ondersteunend.

Konvulsies en ander tekens van SSS-toksisiteit is geassosieer met hoë dosisse, veral in pasiënte met renale inkorting.

5. FARMAKOLOGIESE EIENSKAPPE

5.1 Farmakodinamiese eienskappe

A. 20.1.1 Breë en medium spektrum antibiotika.

Meganisme van werking

Kefpodoksiemproksetiel is 'n semi-sintetiese ß-laktaam antibiotikum wat aan die derde generasie van orale kefalosporiengroep-antibiotika behoort. Kefpodoksiemproksetiel is die voorlooper-geneesmiddel van die bakterisidiese antibiotikum, kefpodoksiem.

Die antibakteriële werking van kefpodoksiem is deur inhibisie van bakteriële selwandsintese moontlk deur asitilering van membraangebonde transpeptidase ensieme; dit verhoed kruisverbinding van peptidoglikaankettings, wat noodsaaklik is vir bakteriële selwandsterkte en rigiditeit.

Antibakteriële spektrum

In vitro studies het die vatbaarheid van meeste stamme van die volgende mikro-organismes vir kefpodoksiemproksetiel aangetoon. Sulke *in vitro* aktiwiteit impliseer egter nie noodwendig *in vivo* doeltreffendheid nie.

Gram-positiewe organismes

Streptococcus pneumoniae, S. pyogenes, S. agalactiae, S. mitis, S. sanguis en S. salivarius; Propionibacterium acnes; Corynebacterium diphtheriae; metisillien-sensitiewe penisillinase en nie-penisillinase produserende stamme van *S. aureus.*

Gram negatiewe organismes

ß-laktamase en nie-ß-laktamase produserende stamme van *Haemophilus influenzae, Haemophilus para-influenzae, Moraxella catarrhalis (Branhamella catarrhalis)* en *Neisseria gonorrhoea; Escherichia coli; Klebsiella pneumoniae; Klebsiella oxytoca; Proteus mirabilis.*

Die volgende organismes is nie sensitief nie: Groep-D streptokokki, metisillien-weerstandige stafilokokki *(S. aureus en S. epidermidis), Staphylococcus saprophyticus, Corynebacteria,* groepe J en K, *Listeria monocytogenes, Pseudomonas aeruginosa* en *Pseudomonas* spp., *Acinetobacter baumanii, Clostridium difficile, Bacteroides fragilis* en verwante spesies.

5.2 Farmakokinetiese eienskappe

Absorpsie:

Kefpodoksiemproksetiel word oraal geabsorbeer en vinnig gehidroliseer deur nie-spesifieke esterases in die spysverteringskanaalwand na kefpodoksiem, die aktiewe suur. Absorpsie word verlaag in toestande van lae maagsuur.

Verspreiding:

Na orale toediening van 'n enkel 5 mg/kg (200 mg maksimum) dosis van kefpodoksiemproksetiel-suspensie in kinders, is die maksimum plasmakonsentrasie (C_{maks}) met 'n gemiddeld van 2,6 mg/l behaal.

Met kefpodoksiemproksetiel tablette is die tyd wat dit neem om maksimumkonsentrasie (T_{maks}) te bereik, ongeveer 2,7 uur.

Met die suspensie is die tyd wat dit neem om maksimumkonsentrasie (T_{maks}) te bereik ongeveer 2 tot 4 uur.

Die geneesmiddel versprei goed in die respiratoriese weefsels.

Die serum halfleeftyd is ongeveer 2,46 uur.

Ongeveer 27 % van kefpodoksiem in die plasma is aan plasmaproteïene gebind.

Die volume van verspreiding is ongeveer 0,46 l/kg.

Eliminasie:

Die opruiming is rondom 2,4 mL/min/kg.

Ongeveer 81 % van die onveranderde kefpodoksiem word in die urine uitgeskei.

6. FARMASEUTIESE BESONDERHEDE

6.1 Lys van onaktiewe bestanddele

Cepodem Tablets

Tabletkern

Kalsium-karboksimetielsellulose

Hidroksipropielsellulose

Anhidriese laktose

Magnesiumstearaat

Natriumlourielsulfaat

Filmbedekking

Propileenglikool

Opadry Wit 03H58987 bestaande uit:

Hipromellose

Titaniumdioksied

Propileenglikool

Drukkersink:

Opacode-S-1-17823 bestaande uit:

Shellakglans

Swart ysteroksied

N-Butielalkohol

Propileenglikool

Cepodem Suspension 40 mg/5 ml

Natriumkarboksimetielsellulose

Karrageenan

Sitroensuur

Anhidriese kolloïdale silika

Natriumkroskarmellose

Hidroksipropielsellulose

Anhidriese laktose

Natrium-mikrokristallyne sellulose

Natriumbensoaat 0,2 % *m/v* (as preserveermiddel)

Natriumsitraat

Sukrose

Geurmiddel: Kersiegeur; Vrugtegomgeur.

Kleurstof: Geel ysteroksied

6.2 Onverenigbaarhede

Nie van toepassing nie.

6.3 Rakleeftyd

Cepodem 100 Tablets/ Cepodem 200 Tablets: 24 maande.

Cepodem Suspension 40 mg/5 mL: 18 maande

6.4 Spesiale voorsorgmaatreëls vir bewaring

Bewaar by of onder 25 °C, beskerm teen lig en vog.

Na hersamestelling van die suspensie, moet die houer teen 2-8 °C in 'n yskas bewaar word. Die hersaamgestelde suspensie moet binne 10 dae na voorbereiding gebruik word. Gooi enige ongebruikte gedeelte van die hersaamgestelde suspensie na 10 dae weg. Skud goed voor dosering.

6.5 Aard en inhoud van die verpakking

Cepodem 100 Tablets: Aluminiumstulpverpakking van 10 tablette elk.

Cepodem 200 Tablets: Aluminiumstulpverpakking van 10 tablette elk.

Cepodem Suspension 40 mg/5 mL: Natuurlike deursigtige HDPE bottelverpakking van 50 mL en 100 mL.

6.6 Spesiale voorsorgmaatreëls vir vernietiging

Geen spesiale vereistes nie.

7. HOUER VAN DIE REGSITRASIESERTIFIKAAT

Ranbaxy Pharmaceuticals (Pty) Ltd

'n Sun Pharma maatskappy

Lautreweg 14, Stormill Uitbreiding 1

Roodepoort, 1724

Suid-Afrika

8. REGISTRASIENOMMERS

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. DATUM VAN EERSTE GOEDKEURING/HERNUWING VAN DIE GOEDKEURING

11 Desember 2003

10. DATUM VAN HERSIENING VAN DIE TEKS

26 September 2022

Namibië
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