PROFESSIONAL INFORMATION

SCHEDULING STATUS:

S4

1. NAME OF THE MEDICINE

CEFPODOXIME 40 mg / 5 ml UNICORN (powder for oral suspension)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

CEFPODOXIME 40 MG / 5 ML UNICORN:

Each 5 ml of suspension contains cefpodoxime proxetil equivalent to 40 mg cefpodoxime.

Preservative: Sodium benzoate (0,2 % *m/v*)

CEFPODOXIME 40 MG / 5 ML UNICORN contains sugar/sweetener:

Sucrose (2464,67 mg / 5 ml)

Aspartame (20,00 mg / 5 ml)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

CEFPODOXIME 40 MG / 5 ML UNICORN:

An almost white to pale yellow coloured powder forming off-white to pale yellow suspension with characteristic fruity odour on constitution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

CEFPODOXIME 40 MG / 5 ML UNICORN 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 influenzae, Streptococcus pneumoniae, Moraxella catarrhalis.*

4.2 Posology and method of administration

Posology in children:

CEFPODOXIME 40 MG / 5 ML UNICORN must not be given to children with phenylketonuria, since the formulation contains aspartame (see section 4.3 and 4.4).

The dosage of **CEFPODOXIME 40 MG / 5 ML UNICORN** 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, to be taken with meals. Shake the bottle before use.

The following table may be used as a dosage guide:

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

The use of CEFPODOXIME 40 MG / 5 ML UNICORN in children under the age of one year is currently not indicated since insufficient clinical data is available at present (see section 4.3).

Directions for reconstitution of the suspension:

See section 6.6.

Special populations

Hepatic insufficiency in children:

No dosage adjustment is necessary.

Renal insufficiency in children:

When the creatinine clearance is above 40 ml/min, it is not necessary to adjust the dose. When the creatinine clearance is 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, administered every second day for values below 10 ml/min and administered after each dialysis session for haemodialysis patients.

4.3 Contraindications

- Known sensitivity to cephalosporin antibiotics (see section 4.4) or any of the excipients listed in section 6.1.
- Safety of use in pregnancy and lactation has not been established.
- **CEFPODOXIME 40 MG / 5 ML UNICORN** must not be given to children with
- phenylketonuria since the formulation contains aspartame (20,00 mg / 5 ml).
- 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 to beta-lactam antibiotics should precede treatment with **CEFPODOXIME 40 MG / 5 ML UNICORN.**

The use of **CEFPODOXIME 40 MG / 5 ML UNICORN** is strictly contraindicated in ~~p~~atients with a previous history of immediate type hypersensitivity to cephalosporins (see section 4.3).

CEFPODOXIME 40 MG / 5 ML UNICORN should be used with extreme caution in patients sensitive to penicillin and other β-lactam antibiotics as cross-allergy may develop. Strict medical supervision is required throughout the treatment. Hypersensitivity reactions (anaphylaxis) observed with cefpodoxime can be serious and occasionally fatal. Treatment should be stopped immediately, should an allergic reaction occur.

***Clostridium difficile*-associated disease:**

Diarrhoea (particularly if severe and/or persistent) occurring during treatment or in the initial weeks following treatment with **CEFPODOXIME 40 MG / 5 ML UNICORN**, 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.

The best way to diagnose *Clostridium difficile*-associated disease is to screen faeces for this pathogen and its cytotoxin.

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

If pseudomembranous colitis is suspected, **CEFPODOXIME 40 MG / 5 ML UNICORN** should be stopped immediately and appropriate specific therapy (such as vancomycin or metronidazole) should be started without delay.

Renal impairment:

CEFPODOXIME 40 MG / 5 ML UNICORN should be used with caution in patients with renal impairment (see section 4.2). Changes in renal function have been observed with antibiotics of the same class as **CEFPODOXIME 40 MG / 5 ML UNICORN**, particularly when given concurrently with potentially nephrotoxic agents (e.g. aminoglycosides and/or potent diuretics); in such cases renal function should be monitored.

Positive Coombs' test:

CEFPODOXIME 40 MG / 5 ML UNICORN 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.

Superinfection:

The use of **CEFPODOXIME 40 MG / 5 ML UNICORN**, 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).

Aspartame:

CEFPODOXIME 40 MG / 5 ML UNICORN must not be given to children with phenylketonuria; since the formulation contains aspartame (20,00 mg / 5 ml) (see section 4.3).

Sucrose:

Contains sucrose. Patients with rare hereditary conditions such as fructose intolerance, glucose-galactose mal-absorption or sucrase-isomaltase insufficiency should not take **CEFPODOXIME 40 MG / 5 ML UNICORN**.

Sodium benzoate:

Sodium benzoate may increase jaundice (yellowing of the skin and eyes) in newborn babies (up to 4 weeks old).

4.5 Interaction with other medicines and other forms of interaction

The bioavailability of **CEFPODOXIME 40 MG / 5 ML UNICORN** is increased if the product is administered during meals (acid pH).

Histamine H_2 antagonists (such as ranitidine) and antacids reduce the bioavailability of **CEFPODOXIME 40 MG / 5 ML UNICORN**.

Probenecid slows tubular excretion of **CEFPODOXIME 40 MG / 5 ML UNICORN** and increases serum levels of this medicine.

CEFPODOXIME 40 MG / 5 ML UNICORN potentially enhances the anticoagulant effect of warfarin and reduces the contraceptive effect of oestrogens.

Potentially nephrotoxic medicines (e.g. aminoglycosides and/or potent diuretics) should be used with caution with **CEFPODOXIME 40 MG / 5 ML UNICORN** (see section 4.4).

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 of **CEFPODOXIME 40 MG / 5 ML UNICORN** in pregnant women has not been established, it is therefore not advisable to administer **CEFPODOXIME UNICORN 40 MG / 5 ML** during pregnancy (see section 4.3).

Breastfeeding

CEFPODOXIME 40 MG / 5 ML UNICORN is excreted in human breast milk, therefore either breastfeeding or treatment of the mother should be discontinued.

4.7 Effects on ability to drive and use machines

CEFPODOXIME 40 MG / 5 ML UNICORN can cause dizzy sensations, which should be taken into account when driving a vehicle or operating machinery.

4.8 Undesirable effects

a) Summary of adverse reactions

The following side effects have been reported:

Infections and infestations

Frequent: superinfections, overgrowth of non-susceptible organisms (see section 4.4), oral and vaginal candidiasis.

Less frequent: Clostridium difficile

Blood and the lymphatic system disorders

Less frequent: reduction of haemoglobin, thrombocytosis, thrombocytopenia, leucopenia, haemolytic anaemia and eosinophilia. Neutropenia and agranulocytosis may also occur.

Frequency unknown: Aplastic anaemia, pancytopenia

Immune system disorders

Less frequent: anaphylactic reactions: e.g. angioedema, bronchospasm, malaise, possibly culminating in shock may occur (see section 4.4).

Nervous system disorders

Less frequent: headache, dizzy sensations, paraesthesia.

Frequency unknown: asthenia, seizures, especially with high doses and in patients with renal function impairment.

Ear and labyrinth disorders

Less frequent: tinnitus.

Frequency unknown: hearing loss.

Gastrointestinal disorders

Frequent: diarrhoea, nausea, vomiting, abdominal pains.

Less frequent: dyspepsia, flatulence, pseudomembranous colitis.

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).

Hepato-biliary disorders

Less frequent: increases in 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, rash, pruritus, 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 **CEFPODOXIME 40 MG / 5 ML UNICORN**, particularly when co-prescribed with nephrotoxic agents (see section 4.4).

Frequency unknown: toxic nephropathy

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.

Adverse reactions must also be reported to Unicorn Pharmaceuticals (Pty) Ltd to enquiries@unicornpharma.co.za

4.9 Overdose

Treatment of overdose should be symptomatic and supportive.

In cases of overdosage, particularly in patients with renal insufficiency, there is a risk of encephalopathy. Convulsions have also been reported with very high doses especially in patients with renal impairment.

5. PHARMACOLOGICAL PROPERTIES

PHARMACOLOGICAL CLASSIFICATION:

A 20.1.1 Broad and medium spectrum antibiotics

5.1 Pharmacodynamic properties

Cefpodoxime proxetil is a semisynthetic β-lactam antibiotic belonging to the third generation oral cephalosporin group. Cefpodoxime proxetil is the prodrug of the bactericidal antibiotic cefpodoxime. Cefpodoxime possesses *in vitro* bactericidal activity against a broad spectrum of Gram-positive and Gram-negative bacteria. *In vitro* sensitivity does not necessarily imply

in vivo efficacy, therefore sensitivity tests must be performed. The mechanism of action is bactericidal through inhibition of bacterial cell wall biosynthesis enhanced by a high affinity for proteins at the cytoplasmic membrane.

The following organisms are not sensitive

Group D streptococci, Methicillin-resistant *staphylococci* (*S. aureus* and *S. epidermidis), Staphylococcus saprophyticus, Corynebacteria group's J and K, Listeria monocytogenes, Pseudomonas aeruginosa* and *Pseudomonas spp., Acinetobacter baumanii, Clostridium difficile, Bacteroides fragilis* and related species.

5.2 Pharmacokinetic properties

The bioavailability of cefpodoxime proxetil is increased when the medicine is administered with meals, or when there is a decrease in gastric pH. An increase in gastric pH results in decreased bioavailability.

Absorption:

After oral administration, cefpodoxime proxetil is absorbed in the gastrointestinal tract and rapidly hydrolysed by non-specific esterases in the gastrointestinal wall to cefpodoxime, the active acid.

Distribution:

In children:

After oral administration of a single 5 mg/kg dose (200 mg maximum) of cefpodoxime to children between 4 and 12 years of age, the maximum plasma concentration (Cmax) is on average 2,6 mg/l. The time taken to reach the maximum concentration (Tmax) is 2 to 4 hours. The average plasma concentrations observed 8 and 12 hours after administration (residual) are 0,39 and 0,08 mg/l respectively.

Diffusion in fluids and tissues:

Cefpodoxime proxetil diffuses well into the lung parenchyma, bronchial mucosa, pleural fluid and tonsils.

Biotransformation:

The main metabolite is cefpodoxime, resulting from the hydrolysis of cefpodoxime proxetil.

Elimination:

The elimination half-life of cefpodoxime is 2,4 hours. 80 % of unchanged cefpodoxime is excreted in the urine.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Anhydrous citric acid,

carboxymethyl cellulose sodium,

silica (colloidal anhydrous),

hydroxypropyl cellulose,

maize starch,

microcrystalline cellulose,

spectracol yellow iron oxide (E172) and

artificial banana flavour spray dry (containing modified starch (E1450), nature identical flavoring substances, propylene glycol (E1520), natural flavoring substances and artificial flavoring substances)

Contains sugar / sweetener:

Sucrose (2464.67 mg / 5 ml) and aspartame (20,00 mg / 5 ml).

Contains preservative:

Sodium benzoate 0,2 % *m/v*).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

CEFPODOXIME 40 MG / 5 ML UNICORN:

Before reconstitution:

Store at or below 25 °C. Protect from light and humidity.

After reconstitution:

Use within 10 days. Store in a refrigerator (2 - 8 °C). Do not freeze.

Shake well before use.

Keep the bottle tightly closed.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6.5 Nature and contents of container

CEFPODOXIME 40 MG / 5 ML UNICORN:

is packed into a 75 ml or 150 ml round, translucent, HDPE bottle. The closure is a white, ribbed polypropylene child resistant closure with liner. The bottle is packed into an outer printed cardboard carton.

The 75 ml or 150 ml bottles contain powder for reconstitution up to 50 ml or 100 ml of suspension, respectively.

6.6 Special precautions for disposal <and other handling>

Directions and for reconstitution of the suspension:

Remove the screw-cap by simultaneously pushing and turning it. Remove the desiccant plug by pulling the tear-tab, and discard.

Add 27,0 ml water into the dry powder for the 50 ml suspension.

Add 54,0 ml water in two equally divided portions to the dry powder for the 100 ml suspension. Shake well after each addition.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Unicorn Pharmaceuticals (Pty) Ltd

Cnr. Searle & Pontac Streets,

Cape Town,

South Africa, 8001

8. REGISTRATION NUMBER(S)

49/20.1.1/0595

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

07/12/2021

10. DATE OF REVISION OF THE TEXT

Not applicable