APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

DYNACEF SUSPENSION (powder for oral suspension)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

DYNACEF SUSPENSION contains sugar (sucrose 2,46 g/5 mL). Contains sweetener (aspartame 20 mg/5 mL).

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Powder for oral suspension.

Powder: Almost white to pale yellow coloured powder.

Reconstituted solution: Off-white to pale yellow suspension with characteristic fruity odour.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

In Children:

DYNACEF SUSPENSION is indicated for use in the short-term treatment of upper and lower respiratory tract infections caused by susceptible micro-organisms:

- Acute 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

Paediatric population

The dosage depends on the weight of the child being treated. The average dose is 8 mg/kg/day.

The following may be used as a dosage guide:

- Children weighing between 10 and 15 kg the dose is 5 mL (40 mg) every 12 hours.
- Children weighing 15 kg or more, the dose is 10 mL (80 mg) every 12 hours.

The use of DYNACEF SUSPENSION in children under one year of age has not been established (see section 4.3).

DYNACEF SUSPENSION must not be given to children with phenylketonuria, since the formulation contains aspartame (see section 4.3).

Refer to section 6.6 for reconstitution instructions.

Special populations

Renal Insufficiency in 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. For values 10 - 39 mL/min DYNACEF SUSPENSION should be administered as a single daily dose and every second day for values below 10 mL/min. DYNACEF SUSPENSION should be administered after each dialysis session for haemodialysis patients.

Hepatic insufficiency in children:

No dosage adjustment necessary.

Method of administration

Oral use.

DYNACEF SUSPENSION is administered in two doses at 12 hourly intervals with meals. Shake the bottle before use.

Refer to section 6.6. for reconstitution instructions.

Missed dose:

Doctors should advise patients who forget to take DYNACEF SUSPENSION to take a dose as soon as possible and then continue with the normal dose. Patients should not take a double dose to compensate for the missed dose.

4.3 Contraindications

- Known sensitivity to cephalosporin antibiotics, penicillin's, any other beta-lactam class of antibiotics, or to any of the ingredients of DYNACEF SUSPENSION (see section 6.1)
- DYNACEF SUSPENSION must not be given to children with phenylketonuria since the

formulation contains aspartame.

- Children below 1 year of age (see section 4.2).

4.4 Special warnings and precautions for use

Hypersensitivity reactions:

Before initiating therapy with DYNACEF SUSPENSION, careful enquiry should be made concerning an allergic diathesis and previous hypersensitivity reactions to penicillin and other beta-lactam antibiotics.

The use of DYNACEF SUSPENSION is strictly contraindicated in subjects with a previous history of immediate type hypersensitivity to cephalosporins (see section 4.3).

There have been reports of serious and occasionally fatal hypersensitivity reactions which progressed to Kounis syndrome (acute allergic coronary arterio-spasm that can result in myocardial infarction) (see section 4.8). If an allergic reaction occurs, treatment should be stopped immediately.

***Clostridium difficile*–associated disease:**

Prolonged use may result in overgrowth of non-susceptible organisms.
Pseudomembranous colitis may develop. It is important to consider its diagnosis in patients who develop diarrhoea, particularly if severe and/or persistent in association with the use of DYNACEF SUSPENSION. Such colitis may range in severity from mild to life threatening. Treatment should be discontinued if symptoms suggestive of pseudomembranous colitis arise. Mild cases of pseudomembranous colitis usually respond to discontinuance of the medicine alone.

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.

When the colitis or suspected pseudomembranous colitis, does not improve after the medicine has been discontinued, or when it is severe, oral vancomycin or metronidazole therapy should be started without delay.

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

Renal impairment:

DYNACEF SUSPENSION should be given with caution to patients with renal impairment. In patients with severe renal failure, it may be necessary to adjust the daily dose based on creatinine clearance (see section 4.2).

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

Interactions with laboratory tests:

DYNACEF SUSPENSION may interfere with Jaffè method of measuring creatinine concentrations and may produce falsely high values.

Positive Coombs' test:

DYNACEF SUSPENSION 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 DYNACEF SUSPENSION, 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).

Encephalopathy:

Beta-lactam antibiotics, including cefpodoxime (as in DYNACEF SUSPENSION), predispose patients to encephalopathy risk (which may include convulsions, confusion, impairment of consciousness or movement disorders), particularly in case of overdose or if they have impaired renal function.

Information on excipients of DYNACEF SUSPENSION:

DYNACEF SUSPENSION contains aspartame (20 mg/5 mL), and sucrose.

Excessive use of aspartame should be avoided by patients with phenylketonuria since one of its metabolic products is phenylalanine (see section 4.3).

Sucrose:

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

4.5 Interaction with other medicines and other forms of interaction

- Probenecid slows tubular excretion of DYNACEF SUSPENSION and increases serum levels

thereof

- the bioavailability increases if DYNACEF SUSPENSION is administered during meals (acid pH)
- absorption of DYNACEF SUSPENSION is decreased by concurrent ingestion of antacids or histamine H_2-receptor antagonists such as ranitidine. Therefore, mineral antacids (aluminium hydroxide, sodium bicarbonate) and histamine blocking H_2 blockers, which cause an increase in gastric pH, should be taken 2 or 3 hours after DYNACEF SUSPENSION administration. In contrast, a decrease in gastric pH (pentagastrin) will increase bioavailability
- enhanced nephrotoxicity with a loop diuretic (e.g. furosemide) may occur
- changes in renal function have been observed with antibiotics of the same class, particularly when given concurrently with potentially nephrotoxic medicines such as aminoglycosides (e.g. gentamicin) and/or potent diuretics. In such cases, renal function should be monitored (see section 4.2)
- as with other cephalosporins, isolated cases showing development of a positive Coombs' test have been reported (see section 4.4)

  In patients treated with DYNACEF SUSPENSION, a false positive reaction for glucose in the urine may occur with Benedict's or Fehling's solutions or with copper sulphate test tablets, but not with tests based on enzymatic glucose oxidase reactions
- concurrent use with anticoagulants, such as warfarin, may increase the risk of bleeding.

Special INR imbalance issues

Numerous cases of increased oral anticoagulant activity have been reported in patients receiving

antibiotics. The severity of the infection or inflammation, age and general health status of the patient appear to be risk factors. Under these circumstances, it seems difficult to determine to what extent the infection itself or its treatment play a role in the INR imbalance. However, certain classes of antibiotics are more involved, particularly fluoroquinolones, macrolides, cyclines, cotrimoxazole and certain cephalosporins.

4.6 Fertility, pregnancy and lactation

Not applicable.

4.7 Effects on ability to drive and use machines

If adverse effects occur, such as dizziness or encephalopathy (which can include seizure, confusion, consciousness disorders or abnormal movements), (see sections 4.4, 4.8, 4.9), patients should not drive or use machines.

4.8 Undesirable effects

Summary of the safety profile

Tabulated list of adverse effects

System Organ Class	**Frequency**	**Side effects**
Infections and Infestations	Frequent	Oral and vaginal candidiasis, superinfections, overgrowth of non-susceptible organisms

Blood and lymphatic system disorders	Less frequent	Thrombocytopenia, leucopenia, neutropenia, hypoprothrombinaemia, haemolytic anaemia, reduction of haemoglobin, thrombocytosis and agranulocytosis, aplastic anaemia, pancytopenia, eosinophilia, lymphocytosis, anaemia, leukocytosis eosinophilia,
Immune system disorders	Less frequent	Hypersensitivity reactions, anaphylactic reactions, angioedema, bronchospasm, malaise, shock
Metabolism and nutrition disorders	Frequent	Appetite loss
Nervous system disorders	Frequent Less frequent	Headache Dizziness, paraesthesia, asthenia, seizures, CNS toxicity
Ear and labyrinth disorders	Less frequent	Tinnitus, hearing loss
Cardiac disorders	Frequency unknown	Kounis syndrome
Gastrointestinal disorders	Frequent Less frequent	Diarrhoea, nausea, vomiting and abdominal pain Dyspepsia, flatulence, pseudomembranous colitis, blood in stools, acute pancreatitis, fever
Hepato-biliary disorders	Less frequent	Hepatic dysfunction including cholestasis, elevated liver enzymes (elevations of AST, ALT and alkaline phosphatase), bilirubinaemia, liver injury, hepatitis, cholestatic jaundice

Skin and subcutaneous tissue disorders	Less frequent	Pruritus and urticaria, toxic epidermal necrolysis, erythema multiforme, rash, Stevens-Johnson syndrome, bullous eruptions, cutaneous eruptions, purpura, Linear IgA bullous dermatosis (LABD)
Renal and urinary disorders	Less frequent	Renal dysfunction, toxic nephropathy, increase in blood urea and creatinine
General disorders and administrative site conditions	Less frequent	Fatigue and asthenia
Investigations	Less frequent	Positive response to the Coombs' test

a. Description of selected adverse reactions

Beta-lactam antibiotics, including cefpodoxime (as in DYNACEF SUSPENSION, predispose patients to encephalopathy (which can include seizure, confusion, consciousness disorders or abnormal movements), particularly if they have had an overdose or if they have renal failure.

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. Healthcare professionals are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.
An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za, to ensure safety of the product.

4.9 Overdose

Signs and symptoms:

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

Convulsions and other signs of CNS toxicity have been associated with high doses, especially in patients with severe renal impairment. There is a risk of encephalopathy, particularly in patients with renal insufficiency.

Management of overdose:

There is no specific antidote for DYNACEF SUSPENSION.

Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antibacterials for systemic use

ATC code: J01DD13

Pharmacological classification: A.20.1.1 Broad and medium spectrum antibiotics.

Mechanism of action

Cefpodoxime proxetil is a semi-synthetic beta-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 viv*o efficacy. The antibacterial action of cefpodoxime is through inhibition of bacterial cell wall biosynthesis most likely by acylation of membrane bound transpeptidase enzymes. This prevents cross linkage of

peptidoglycan chains, which is necessary for bacterial cell wall strength and rigidity.

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 baumannii, Clostridium difficile, Bacteroides fragilis* and related species.

5.2 Pharmacokinetic properties

The bioavailability of cefpodoxime proxetil is increased when the product is administered with meals, or when there is a decrease in gastric pH. Absorption is decreased in conditions of low gastric acidity.

Absorption:

Cefpodoxime proxetil is absorbed orally and rapidly hydrolysed by non-specific esterases in the gastrointestinal wall to cefpodoxime, the active acid.

Paediatric population:

After oral administration of a single 5 mg/kg dose (200 mg maximum) of cefpodoxime to subjects between 4 and 12 years of age, the maximum plasma concentration (C_{max}) is on average 2,6 mg/L. The time taken to reach maximum concentration (T_{max}) 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 in lung parenchyma, bronchial mucosa, pleural fluid and tonsils.

Metabolism and elimination:

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

serum half-life is about 2,4 hours. Clearance is about 2,4 mL/min/kg. Approximately 80 % of cefpodoxime is excreted unchanged in the urine.

5.3 Preclinical safety data

Not applicable

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Anhydrous citric acid

Artificial banana flavour spray dry

Aspartame

Hydroxypropyl cellulose

Maize starch

Microcrystalline cellulose & carboxymethyl cellulose sodium

Silica colloidal anhydrous

Sodium benzoate (preservative 0,2 % m/v)

Spectracol yellow iron oxide

Sucrose.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 years

APPROVED PROFESSIONAL INFORMATION

6.4 Special precautions for storage

***Before reconstitution*:**

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

After reconstitution:

Use within 10 days. Store in a refrigerator (2 to 8 °C).

Shake well before use.

Keep the bottle tightly closed. Discard any unused portion. Do not freeze.

6.5 Nature and contents of container

Translucent HDPE bottle with a white polypropylene 28 mm cap (child resistant, with foil seal peelable liner), containing powder for reconstitution up to 50 mL or 100 mL of suspension, contained in a printed outer carton.

6.6 Special precautions for disposal <and other handling>

Directions 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 THE CERTIFICATE OF REGISTRATION

Pharma Dynamics (Pty) Ltd

1st Floor, Grapevine House, Steenberg Office Park

Silverwood Close

Westlake, Cape Town

7945, South Africa

8. REGISTRATION NUMBER(S)

RSA: 43/20.1.1/1084

9. DATE OF FIRST AUTHORISATION

30 September 2011

10. DATE OF REVISION OF THE TEXT

06 December 2024

NAM: NS2 12/20.1.1/0173

MOZ: 4771