**APPROVED PROFESSIONAL INFORMATION**

## SCHEDULING STATUS

S4

## 1. NAME OF THE MEDICINE

**DYNACEF 100 mg** film coated tablet

**DYNACEF 200 mg** film coated tablet

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

DYNACEF 100 mg

Each film coated tablet contains cefpodoxime proxetil equivalent to

100 mg cefpodoxime. Each 100 mg tablet contains sugar (lactose monohydrate, 9 mg).

DYNACEF 200 mg

Each film coated tablet contains cefpodoxime proxetil equivalent to

200 mg cefpodoxime. Each 200 mg tablet contains sugar (lactose monohydrate, 18 mg).

For the full list of excipients, see section 6.1

## 3. PHARMACEUTICAL FORM

Film coated tablets

DYNACEF 100 mg**:** White to off white, round biconvex film coated tablets with “100” debossed on one side and plain on the other side.

DYNACEF 200 mg**:** White to off white, round biconvex film coated tablets with “200” debossed on one side and plain on the other side.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

**In Adults**

DYNACEF 100 mg and 200 mg tablets are indicated for use in the short-term treatment of upper and lower respiratory tract infections when caused by susceptible organisms (sensitivity tests must be performed):

- acute bronchitis due to *Haemophilus influenzae, Streptococcus pneumoniae, Moraxella catarrhalis*
- pharyngitis and tonsillitis due to *Streptococcus pyogenes*
- acute exacerbations of chronic bronchitis due to: *Haemophilus influenzae, Streptococcus pneumoniae, Moraxella catarrhalis*
- bacterial pneumonia and community acquired bronchopneumonia due to *Haemophilus influenzae, Streptococcus pneumoniae, Moraxella catarrhalis*
- acute sinusitis due to *Haemophilus influenzae* (non-typeable)*, Streptococcus pneumoniae,* Methicillin-sensitive *Staphylococcus aureus, Moraxella catarrhalis*

### 4.2 Posology and method of administration

**Posology**

**Adults**

Each film coated tablet of DYNACEF contains either 100 mg or 200 mg cefpodoxime. The dosage is dependent on the condition being treated.

***Tonsillitis, pharyngitis and acute bronchitis***

One DYNACEF 100 mg tablet every 12 hours with meals (200 mg/day).

As is the case with all beta lactam antibiotics in the treatment of beta-haemolytic streptococcal infections, therapeutic doses should be administered for at least ten days.

***Acute sinusitis, acute exacerbations of chronic bronchitis, pneumonia***

One DYNACEF 200 mg tablets every 12 hours (400 mg/day), to be taken with meals.

**Special populations**

**Elderly patients**

No dose adjustments are necessary with normal renal function.

**Renal insufficiency in adults**

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 tablets should be administered as a single daily dose and every second day for values below 10 mL/min. DYNACEF tablets should be administered after each dialysis session for haemodialysis patients.

**Hepatic insufficiency in adults**

No dose adjustments are necessary.

**Method of administration**

DYNACEF tablets are for oral use and must be swallowed whole with half a glass of water and should be taken with meals.

## 4.3 Contraindications

- hypersensitivity to cefpodoxime proxetil, the cephalosporin group of antibiotics, penicillin's or to any of the ingredients of DYNACEF.
- safety in pregnancy and lactation has not been established.

## 4.4 Special warnings and precautions for use

Prescribers must adhere to the principles of antibiotic stewardship.

Before initiating therapy with DYNACEF, careful enquiry should be made concerning previous hypersensitivity reactions to penicillin and other β-lactam antibiotics.

The use of DYNACEF 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 allergic hypersensitivity reactions which progressed to Kounis syndrome (acute 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:***

Diarrhoea, particularly if severe and/or persistent, occurring during treatment or in the initial weeks following treatment with DYNACEF may be symptomatic of *Clostridium difficile*-associated disease, (CDAD) 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.

It is important to consider its diagnosis in patients who develop diarrhoea in association with the use of DYNACEF. Such colitis may range in severity from mild to life threatening.

Treatment should be discontinued if symptoms suggestive of pseudomembranous colitis arise.

When the colitis does not improve after the medicine has been discontinued, or when it is severe, appropriate specific therapy should be started without delay. *Clostridium difficile*-associated disease can be favoured by faecal stasis.

**Renal impairment:**

DYNACEF should be given with caution to patients with renal impairment, dosage reduction may be necessary. Renal and haematological status should be monitored, especially during prolonged and high-dose therapy.

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

As with all beta-lactam antibiotics, neutropenia and less frequently agranulocytosis may develop particularly during extended treatments. For cases of treatment lasting longer than 10 days, blood count should therefore be monitored, and treatment discontinued if neutropenia is found.

**Superinfection:**

Overgrowth of non-susceptible organisms may result during DYNACEF treatment, especially if

prolonged. Repeated evaluation of the patient's condition is essential. If superinfection occurs during therapy, appropriate measures should be taken (see section 4.8).

**Interference with laboratory testing:**

Positive results to the antiglobulin direct Coombs' test and haemolytic anaemia have been found during treatment with cefpodoxime, such as in DYNACEF, and these can interfere with blood-cross-matching. Cross-reactivity may occur with penicillin for this reaction. The urine of patients being treated with DYNACEF may give false-positive reactions for glucose using copper-reduction reactions.
DYNACEF may interfere with Jaffè method of measuring creatinine concentrations and may produce falsely high values.

**Encephalopathy:**

Beta-lactams, including cefpodoxime, predispose the patient to encephalopathy risk (which may include convulsions, confusion, impairment of consciousness, movement disorders), particularly in case of overdose or renal impairment.

**Lactose:**

DYNACEF 100 mg and 200 mg tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

**Paediatric population**

Safety and efficacy of DYNACEF have not been established in children under one year of age.

## 4.5 Interaction with other medicines and other forms of interaction

The bioavailability of cefpodoxime is increased if DYNACEF is administered during meals (acid pH).

Absorption of cefpodoxime is decreased by concurrent ingestion of antacids and histamine $H_2$-receptor antagonists such as ranitidine. Therefore, mineral antacids and histamine blocking $H_2$ blockers, which cause an increase in gastric pH, should be taken 2 or 3 hours after DYNACEF administration. In contrast, a decrease in gastric pH (pentagastrin) will increase bioavailability.

Probenecid slows tubular excretion of DYNACEF and increases serum levels thereof.

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. Enhanced nephrotoxicity with a loop diuretic (e.g. furosemide) may occur. In such cases, renal function should be monitored (see section 4.4).

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, 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 warfarin may increase resulting in an enhanced anticoagulant effect.

DYNACEF may reduce the contraceptive effect of oestrogens.

## 4.6 Fertility, pregnancy and lactation

### Pregnancy

Safety and efficacy in pregnancy have not been established (see section 4.3)

### Breastfeeding

Cefpodoxime is excreted into breast milk. It is recommended that either breastfeeding should be ceased, or treatment of the mother should be discontinued.

### Fertility

There is no data on fertility with DYNACEF.

## 4.7 Effects on ability to drive and use machines

DYNACEF tablets can lead to dizziness and patients should be aware how they react to DYNACEF tablets and exercise caution before driving, operating hazardous machinery or performing hazardous tasks.

## 4.8 Undesirable effects

### Summary of the safety profile

The most frequent reported adverse effects of DYNACEF are gastrointestinal disturbances, especially diarrhoea.

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## Tabulated list of adverse effects

| System Organ Class | Frequency | Side effects |
|---|---|---|
| Infections and infestations | Frequent<br><br><br>Less frequent | Oral and vaginal candidiasis, superinfections, overgrowth of non-susceptible organisms.<br>*Clostridium difficile* |
| Blood and lymphatic system disorders | Less frequent | Thrombocytopenia, leucopoenia, neutropenia, hypoprothrombinaemia, haemolytic anaemia, reduction of haemoglobin, thrombocytosis, agranulocytosis, aplastic anaemia, pancytopenia, eosinophilia, lymphocytosis, anaemia, leucocytosis |
| Immune system disorders | Less frequent | Hypersensitivity reactions, anaphylactic reactions, angioedema, bronchospasm, malaise, shock |
| Metabolism and nutrition disorders | Frequent | Appetite loss |
| Nervous system disorders | Less frequent<br><br>Frequency unknown | Headache, dizziness, paraesthesia<br>Asthenia, convulsions and signs of CNS toxicity especially in patients with severe renal impairment |
| Ear and labyrinth disorders | Less frequent | Tinnitus, hearing loss |

| | | |
|---|---|---|
| Cardiac disorders | Frequency unknown | Kounis syndrome |
| Gastrointestinal disorders | Frequent<br><br>Less frequent | Diarrhoea, nausea, vomiting, abdominal pain<br>Dyspepsia, flatulence, enterocolitis, pseudomembranous colitis, blood in stools, acute pancreatitis |
| Hepatobiliary disorders | Less frequent<br><br>Frequency unknown | Bilirubinaemia, liver injury, acute hepatitis, cholestatic jaundice<br>Hepatic dysfunction including cholestasis |
| Skin and subcutaneous tissue disorders | Less frequent | Pruritus and urticaria, bullous eruptions (erythema multiforme, rash, Stevens-Johnson syndrome, toxic epidermal necrolysis), cutaneous eruptions, purpura, Linear IgA bullous dermatosis (LABD) |
| Renal and urinary disorders | Less frequent | Renal dysfunction, toxic nephropathy, acute renal insufficiency, increase in blood urea and creatinine |
| General disorders and administrative site conditions | Less frequent | Asthenia, fatigue, malaise |
| Investigations | Less frequent | Positive response to the Coombs test, elevations of AST, ALT and alkaline phosphatase, increase of blood urea and creatinine |

### a. Description of selected adverse reactions

Increased liver enzymes (AST, ALT and alkaline phosphatase) and/or bilirubin are less frequently

observed; however, these laboratory abnormalities exceed twice the upper limit of the normal range and elicit a pattern of drug-induced hepatitis, usually cholestatic.

Changes in renal function have been observed with antibiotics from the same group as DYNACEF, particularly when co-prescribed with aminoglycosides and/or potent diuretics (see section 4.4).

Diarrhoea may sometimes be a symptom of enterocolitis, which may, in some cases, be accompanied by blood in stools. A particular form of enterocolitis than can occur with antibiotics is pseudomembranous colitis (in most cases due to *Clostridium difficile*) (see section 4.4).

*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 asked to report any suspected adverse 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 may manifest in any of the symptoms described under undesirable side effects (see section 4.8). Convulsions and other signs of CNS toxicity and encephalopathy have been associated with high doses, especially in patients with severe renal impairment.

**Management of overdose:**

There is no specific antidote for DYNACEF. Treatment should be symptomatic and supportive.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Third generation cephalosporins

ATC code: J01DD13

Pharmacological classification: A 20.1.1 Broad and medium spectrum antibiotics

**Mechanism of action**

Cefpodoxime proxetil is a semi-synthetic 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. Cefpodoxime is stable in the presence of the majority of beta-lactamases. The antibacterial action of cefpodoxime is through inhibition of bacterial cell wall synthesis.

**Resistance:**

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 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 in the gastrointestinal tract when taken orally, and rapidly hydrolysed by non-specific esterases in the gastrointestinal wall to cefpodoxime, the active acid.

**Distribution:**

Adults:

After oral administration of a single dose of 100 mg of cefpodoxime, the maximum plasma concentration ($C_{max}$) obtained is 1 to 1,2 mg/L and after administration of a dose of 200 mg of cefpodoxime, the maximum plasma concentration ($C_{max}$) obtained is 2,2 to 2,5 mg/L. In both cases the time taken to reach the maximum concentration ($T_{max}$) is 2 – 3 hours.

Following administration of 100 mg twice daily for 14,5 days, the pharmacokinetic parameters of cefpodoxime remain unchanged, indicating that there is no accumulation of the active principle.

The binding of cefpodoxime to plasma proteins is about 40 %. This binding is principally to albumin and is of the non-saturable type.

Cefpodoxime diffuses well in lung parenchyma, bronchial mucosa, pleural fluid and tonsils.

**Biotransformation 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

*Cores:*

Carmellose calcium

Hydroxypropyl cellulose

Lactose monohydrate

Magnesium stearate

Sodium lauryl sulphate

*Coating:*

Opadry White (as the colourant) 03A28718 which includes:

Hypromellose

Titanium dioxide

Talc

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

Dynacef 100 mg: 24 months

Dynacef 200 mg: 24 months

### 6.4 Special precautions for storage

DYNACEF 100 mg and DYNACEF 200 mg:

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

Keep blister strip in the carton until required for use.

### 6.5 Nature and contents of container

DYNACEF 100 mg: One silver aluminium/aluminium lidding foil blister strip containing 10 tablets in a printed outer carton.

DYNACEF 200 mg: One or two silver aluminium/aluminium lidding foil blister strip containing 10 or 20 tablets in a printed outer carton.

Not all pack sizes are marketed

### 6.6 Special precautions for disposal and other handling

No special requirements.

## 7. HOLDER OF CERTIFICATE OF REGISTRATION

Pharma Dynamics (Pty) Ltd

1st Floor Grapevine House, Steenberg Office Park

Silverwood Close

Westlake, Cape Town

7945, South Africa

Tel: +27 21 707 7000

or 0860-PHARMA (742 762)

## 8. REGISTRATION NUMBER(S)

DYNACEF 100 mg**:** 44/20.1.1/0012

DYNACEF 200 mg**:** 48/20.1.1/0583

## 9. DATE OF FIRST AUTHORISATION

DYNACEF 100 mg**:** 05 August 2011

DYNACEF 200 mg**:** 23 February 2021

## 10. DATE OF REVISION OF THE TEXT

28 March 2025

DYNACEF 100 MG:

NAM: NS2 12/20.1.1/0058

MOZ: J5227