PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1 NAME OF THE MEDICINE

NITROFURANTOIN 50 PHARMC, 50 mg, hard capsules.

NITROFURANTOIN 100 PHARMC, 100 mg, hard capsules.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

NITROFURANTOIN 50 PHARMC

Each hard gelatin capsule contains 50 mg of nitrofurantoin macrocrystals.

Contains sugar: lactose monohydrate 113 mg per capsule.

NITROFURANTOIN 100 PHARMC

Each hard gelatin capsule contains 100 mg of nitrofurantoin macrocrystals.

Contains sugar: lactose monohydrate 226 mg per capsule.

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Hard capsules.

NITROFURANTOIN 50 PHARMC

Hard gelatin capsule size ‘3’ with “A9” imprint on opaque yellow cap and plain opaque white body containing pale yellow granular powder.

NITROFURANTOIN 100 PHARMC

Hard gelatin capsule size ‘2’ with “A8” imprint on opaque yellow cap and plain opaque yellow body containing pale yellow granular powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

NITROFURANTOIN PHARMC is indicated for the treatment and prevention of recurrence of uncomplicated lower urinary tract infections, e.g. pyelonephritis, pyelitis and cystitis.

It is not indicated for the treatment of associated renal, cortical or perinephric abscesses.

4.2 Posology and method of administration

Posology

Adults

Acute urinary tract infections: 50 mg to 100 mg four times a day, with meals and at bedtime.

To prevent recurrences: 50 mg to 100 mg per day.

Children

Acute urinary tract infections: Should be calculated on the basis of 5 mg/kg to 7 mg/kg of body mass per 24 hours to be given in divided doses four times a day (contraindicated for children under one month).

To prevent recurrences: 1 mg/kg/day for long-term therapy. NITROFURANTOIN PHARMC may be given with food or milk to further minimise gastric upset.

Therapy should be continued for at least one week and for at least 3 days after sterility of the urine is obtained. Continued infection indicates need for re-evaluation.

NITROFURANTOIN PHARMC is highly soluble in urine, to which it may impart a brown colour,

Method of administration

NITROFURANTOIN PHARMC is for oral use.

4.3 Contraindications

- Hypersensitivity to nitrofurantoin or to any of the excipients (see section 6.1)
- Anuria, oliguria and renal impairment are contraindications to therapy with NITROFURANTOIN PHARMC.
- Treatment of this type of patient carries an increased risk of toxicity because of impaired

excretion of NITROFURANTOIN PHARMC.

- Pregnant women at term, as well as infants under one month of age, because of the possibility of haemolytic anaemia due to immature enzyme systems (glutathione instability).
- Safe use in earlier pregnancy has not been established.
- Patients with a deficiency of glucose-6-phosphate dehydrogenase or nursing mothers of infants with this deficiency.
- Patients suffering from renal dysfunction with an eGFR below 45 ml/minute.
- Acute porphyria.

4.4 Special warnings and precautions for use

A course of therapy should not exceed 14 days, and repeated courses should be separated by rest periods.

NITROFURANTOIN PHARMC is not effective for the treatment of parenchymal infections of unilaterally non-functioning kidney. A surgical cause for infection should be excluded in recurrent or severe cases.

Since pre-existing conditions may mask adverse reactions, NITROFURANTOIN PHARMC should be used with caution in patients with renal impairment, pulmonary disease, hepatic dysfunction, neurological disorders, and allergic diathesis.

Neuropathy

Peripheral neuropathy and susceptibility to peripheral neuropathy, which may become severe or irreversible, has occurred and may be life threatening. Therefore, treatment should be stopped at the first signs of neural involvement (paraesthesia).

Care is required in patients with predisposing pulmonary, hepatic, neurological or allergic disorders. NITROFURANTOIN PHARMC should be used with caution in patients with

anaemia, diabetes mellitus, electrolyte imbalance, debilitating conditions and vitamin B (particularly folate) deficiency which may predispose to peripheral neuropathy.

Patients with renal impairment

NITROFURANTOIN PHARMC should be used with caution in patients with renal impairment, Patients with mild to moderate renal dysfunction will require adequate monitoring, as they may experience an increase in pulmonary adverse events when taking NITROFURANTOIN PHARMC (see section 4.8).

NITROFURANTOIN PHARMC is not recommended for use in patients with severe renal impairment (see section 4.3).

Pulmonary reactions

Patients with a history of asthma may experience acute asthmatic attacks. Elderly patients and patients undergoing prolonged therapy should be monitored for changes in pulmonary function.

Acute, subacute and chronic pulmonary reactions have been observed in patients treated with nitrofurantoin, as in NITROFURANTOIN PHARMC. If these reactions occur, NITROFURANTOIN PHARMC should be discontinued immediately. Acute pulmonary reactions occur within the first week of treatment and are reversible. If any of the following respiratory reactions occur NITROFURANTOIN PHARMC should be discontinued. Acute pulmonary reactions are commonly manifested by fever, chills, cough, chest pain, dyspnoea, pulmonary infiltration with consolidation or pleural effusion on chest x-ray, and eosinophilia. In subacute pulmonary reactions, fever and eosinophilia occur less often than in the acute form.

Chronic pulmonary reactions occur less frequently in patients who have received continuous therapy for six months or longer and are more frequent in elderly patients.

Chronic pulmonary reactions (including pulmonary fibrosis and diffuse interstitial pneumonitis) can develop insidiously and may occur frequently in elderly patients. Close monitoring of the pulmonary conditions of patients receiving long-term therapy is warranted (especially in the elderly).

Changes in ECG have occurred, associated with pulmonary reactions. Minor symptoms such as fever, chills, cough and dyspnoea may be significant. Collapse and cyanosis have been reported less frequently. The severity of chronic pulmonary reactions and their degree of resolution appear to be related to the duration of therapy after the first clinical signs appear. It is important to recognise symptoms as early as possible. Pulmonary function may be impaired permanently, even after cessation of therapy.

Lupus-like syndrome associated with pulmonary reactions to nitrofurantoin has been reported (see section 4.8).

Laboratory Tests

Urine may be coloured yellow or brown after taking NITROFURANTOIN PHARMC. Patients on NITROFURANTOIN PHARMC are susceptible to false positive urinary glucose (if tested for reducing substances).

Haematologic Effects

Cases of haemolytic anaemia of the primaquine sensitivity type have been induced by nitrofurantoin as in NITROFURANTOIN PHARMC

Nitrofurantoin may cause haemolysis in patients with glucose-6-phosphate dehydrogenase deficiency (ten percent of black patients and a variable percentage of ethnic groups of Mediterranean, Near Eastern and Asian origin). Haemolysis ceases when the medicine is discontinued. Agranulocytosis, leukopenia, granulocytopenia, haemolytic anaemia, thrombocytopenia, glucose-6-phosphatedehydrogenase deficiency anaemia, megaloblastic anaemia and eosinophilia have occurred. Aplastic anaemia has been reported less frequently. Cessation of therapy has generally returned the blood picture to normal.

Clostridium difficile associated diarrhoea (CDAD)

Gastrointestinal reactions may be minimised by taking NITROFURANTOIN PHARMC with food or milk, or by adjustment of dosage. *Clostridium difficile* associated diarrhoea (CDAD) has been reported with use of NITROFURANTOIN PHARMC and may range in severity from mild diarrhoea to fatal colitis. Treatment with antibacterial medicines alters the normal flora of the colon leading to overgrowth of *C. difficile*.

Hepatotoxicity

Hepatic reactions including hepatitis, autoimmune hepatitis, cholestatic jaundice chronic active hepatitis and hepatic necrosis, occur less frequently. Fatalities have been reported. The onset of chronic active hepatitis may be insidious, and patients should be monitored periodically for changes in biochemical tests that would indicate liver injury. Cholestatic jaundice is generally associated with short-term therapy (usually up to two weeks). Chronic active hepatitis, occasionally leading to hepatic necrosis is generally associated with long-term therapy (usually after six months). The onset may be insidious. Treatment should be stopped at the first sign of hepatotoxicity. If hepatitis occurs, NITROFURANTOIN PHARMC should be withdrawn immediately and appropriate measures should be taken. Less frequently liver failure (which maybe fatal) have been reported after nitrofurantoin usage. For long term treatment, monitor patient closely for appearance of hepatitis (or liver damage), pulmonary or neurological symptoms and other evidence of toxicity. Discontinue treatment with NITROFURANTOIN PHARMC if otherwise unexplained pulmonary, hepatotoxic, haematological or neurologic syndromes occur.

Carcinogenicity

There has been limited evidence of carcinogenic effects of nitrofurantoin in experimental animals, but NITROFURANTOIN PHARMC has not been shown to be carcinogenic in humans.

Antimicrobial medicines

As with other antimicrobial medicines, superinfections by fungi or resistant organisms such as *Pseudomonas* may occur. However, these are limited to the genitourinary tract because suppression of normal bacterial flora does not occur elsewhere in the body.

Excipients

Patients with rare hereditary problems of galactose intolerance total lactase deficiency or glucose-galactose malabsorption should not take NITROFURANTOIN PHARMC.

4.5 Interaction with other medicines and other forms of interaction

Concomitant administration of magnesium trisilicate reduces absorption of nitrofurantoin.

Uricosuric medicines such as probenecid and sulphinpyrazone may reduce the excretion of nitrofurantoin and should not be given concomitantly. The resulting increase in serum levels may increase toxicity. Decreased urinary levels could reduce efficacy as a urinary tract antibacterial.

Antagonism between NITROFURANTOIN PHARMC and nalidixic acid, and NITROFURANTOIN PHARMC and oxolinic acid has been demonstrated *in-vitro*. Concurrent use with quinolones is not recommended.

There may be decreased antibacterial activity for nitrofurantoin in the presence of carbonic anhydrase inhibitors and urine alkalinising medicines.

As a result of the presence of nitrofurantoin when tested for reducing substances, a false positive reaction for glucose in the urine may occur.

The presence of food or medicines delaying gastric emptying can result in increased absorption of nitrofurantoin.

As nitrofurantoin belongs to the group of antibacterials, it will have the following resulting interactions:

Oestrogens: Antibacterials that do not induce liver enzymes possibly reduce contraceptive effect of oestrogens (risk probably small, Interactions of combined oral contraceptives may also apply to combined contraceptive patches).

Typhoid fever vaccine (oral): Antibacterials inactivate oral typhoid fever vaccine.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safe use in earlier pregnancy has not been established (see section 4.3)

Breastfeeding

Caution should be exercised while breast feeding an infant known or suspected to have any erythrocyte enzyme deficiency as nitrofurantoin is detected in trace amounts in breast milk.

Fertility

In men at supra-therapeutic doses, a temporary stoppage in spermatogenesis and reduced sperm counts. Clinical doses are not associated with male infertility. No reduced fertility was observed in animal studies.

4.7 Effects on ability to drive and use machines

NITROFURANTOIN PHARMC may cause dizziness and drowsiness. Patients should be advised not to drive or operate machinery if affected in this way until such symptoms go away.

4.8 Undesirable effects

A tabulated list of undesirable effects is outlined below:

The undesirable effects are listed according to organ systems and following frequencies: Frequent, Less frequent and Frequency unknown (cannot be estimated from available data).

System organ class	Frequency	Adverse reactions
Infections and infestations	Frequency unknown	Superinfections by fungi or resistant organisms such as *Pseudomonas*. However, these are limited to the genitourinary tract
Blood and lymphatic system disorders	Less frequent	Aplastic anaemia
	Frequency unknown	Agranulocytosis, leukopenia, granulocytopenia, haemolytic anaemia, thrombocytopenia, glucose 6-phosphatedehydrogenase deficiency anaemia, megaloblastic anaemia and eosinophilia
Immune system disorders	Frequency unknown	Allergic skin reactions, angioneurotic oedema and anaphylaxis, cutaneous vasculitis

System organ class	Frequency	Adverse reactions
Psychiatric disorders	Frequency unknown	Depression, euphoria, confusion, psychotic reactions
Nervous system disorders	Frequency unknown	Peripheral neuropathy including optic neuritis (sensory as well as motor involvement), nystagmus, vertigo, dizziness, headache and drowsiness. Benign intracranial hypertension
Cardiac disorders	Less frequent	Collapse and cyanosis
Respiratory, thoracic and mediastinal disorders	Frequency unknown	Acute pulmonary sensitivity reactions, subacute pulmonary reactions*, chronic pulmonary reactions, cough, dyspnoea, permanent impairment of pulmonary function, pulmonary fibrosis; possible association with lupus-erythematous-like syndrome, bronchiolitis obliterans organising pneumonia.
Gastrointestinal disorders	Frequency unknown	Sialadenitis, pancreatitis, nausea and vomiting, anorexia, emesis, abdominal pain and diarrhoea.
Hepato-biliary disorders	Less frequent	Liver failure (which maybe fatal)
	Frequency unknown	Cholestatic jaundice, chronic active hepatitis and hepatocellular damage (fatalities have been reported), hepatic necrosis, autoimmune hepatitis
Skin and subcutaneous tissue disorders (see section 4.4)	Frequency unknown	Transient alopecia, exfoliative dermatitis and erythema multiforme (including Stevens-Johnson Syndrome), maculopapular, erythematous or eczematous eruptions,

System organ class	Frequency	Adverse reactions
		urticaria, rash, and pruritus. Lupus-like syndrome associated with pulmonary reaction. Drug Rash with Eosinophilia and Systemic Symptoms (DRESS syndrome), cutaneous vasculitis
Renal and urinary disorders	Frequency unknown	Yellow or brown discolouration of urine, interstitial nephritis
Congenital, familial and genetic disorders	Frequency unknown	Acute porphyria
General disorders and administration site conditions	Frequency unknown	Asthenia, fever, chills, drug fever and arthralgia
Investigations	Frequency unknown	False positive urinary glucose

* Acute pulmonary reactions usually occur within the first week of treatment and are reversible with cessation of therapy. Acute pulmonary reactions are frequently manifested by fever, chills, cough, chest pain, dyspnoea, pulmonary infiltration with consolidation or pleural effusion on chest x-ray, and eosinophilia. In subacute pulmonary reactions, fever and eosinophilia occur less often than in the acute form. Chronic pulmonary reactions occur rarely in patients who have received continuous therapy for six months or longer and are more frequent in elderly patients. Changes in ECG have occurred, associated with pulmonary reactions.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of NITROFURANTOIN PHARMC is important. It allows continued monitoring of the benefit/risk balance of NITROFURANTOIN

PHARMC. Health care providers 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.

In addition, side effects can also be reported to info@pharmacorp.co.za.

4.9 Overdose

Symptoms

Symptoms and signs of overdose include gastric irritation, nausea and vomiting.

Management

There is no known specific antidote. Nitrofurantoin can be haemodialysed. Treatment is symptomatic and supportive. Monitoring of full blood count, liver function tests and pulmonary function are recommended. A high fluid intake should be maintained to promote urinary excretion of NITROFURANTOIN PHARMC.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and Class: A 18.5 Urinary tract antiseptics

Pharmacotherapeutic group: Antibacterial. ATC Code: J01XE01.

Nitrofurantoin is an antibacterial medicine for specific urinary tract infections.

Nitrofurantoin exerts bacteriostatic activity against many strains of:

Escherichia coli

Enterococci

Anti-bacterial activity is higher in acidic urine.

Many strains of *Enterobacter* species and *Klebsiella* species are resistant to nitrofurantoin.

It is not active against most strains of *Proteus* and *Pseudomonas* species.

5.2 Pharmacokinetic properties

Absorption

Nitrofurantoin is rapidly and completely absorbed from the gastrointestinal tract. Intake with food or milk increases absorption.

Distribution

Nitrofurantoin is highly soluble in urine, but plasma concentrations are low with peak levels usually less than 1 microgram/ml.

Biotransformation

Nitrofurantoin is loosely bound to plasma albumin (60 – 70 %). The molecule is readily distributed into intra and extracellular compartments. However, substantial tissue concentrations are not expected since the medicine is rapidly excreted and readily degraded by tissue enzymes. The medicine crosses the placenta in small amounts.

Elimination

Anti-bacterial concentration is not achieved in plasma following ingestion of recommended doses because of rapid elimination. Maximum urinary excretion usually occurs 2 – 4 hours after administration of nitrofurantoin. Urinary medicine dose recoveries of about 40 – 45 % are obtained. It has an elimination half-life of about 30 minutes and after oral administrations of macrocrystals, less than 60 minutes.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule fill contents

Lactose monohydrate

Maize starch

Talc (E553b)

Capsule shell

Gelatin

Iron oxide yellow (E104)

Sodium Lauryl sulphate

Titanium Dioxide (E171)

Printing ink

Black Iron Oxide (E172)

Shellac (E904)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at or below 25 °C.

Keep the blisters in the outer carton until required for use.

6.5 Nature and contents of container

10 capsules are packed in a blister strip of aluminium foil with VMCH coating (25 micron) and PVC white opaque film (250 micron). 3 or 5 blister strips are packaged in a cardboard box along with a leaflet.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACORP (PTY) LTD

29 Victoria Link

Route 21 Corporate Park

Irene, 0178, RSA

8 REGISTRATION NUMBERS

NITROFURANTOIN 50 PHARMC: 55/18.5/0862

NITROFURANTOIN 100 PHARMC: 55/18.5/0863

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

27 February 2024

10 DATE OF REVISION OF THE TEXT

04 September 2026