SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

RENOFTRA 100 (hard gelatin capsules)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 100 mg nitrofurantoin.

Excipients with known effect:

Contains Lactose Monohydrate 234 mg.

For the full list of excipients, (see section 6.1).

3. PHARMACEUTICAL FORM

Capsules

Blue opaque cap and blue opaque body, hard gelatin size "2" capsules imprinted with "LS" on cap and "412" on body with black ink containing light yellow to yellow colored powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

RENOFTRA 100 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.

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.

Method of administration

For oral use

This medicine should always be taken with food or milk to further minimise gastric upset. Taking Nitrofurantoin Capsules with a meal improves absorption and is important for optimal efficacy

4.3 Contraindications

- Hypersensitivity to Nitrofurantoin, other nitrofurans or to any of the excipients listed in section 6.1.
- Anuria, oliguria and renal impairment are contraindications to therapy with this medicine.
- Treatment of this type of patient carries an increased risk of toxicity because of impaired excretion of the medicine.
- Acute porphyria
- 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).
- Patients with a deficiency of glucose-6-phosphate dehydrogenase or nursing mothers of infants with this deficiency

4.4 Special warnings and precautions for use

A course of therapy should not exceed 14 days and repeated courses should be separated

25 by rest periods.

Patients with a history of asthma may experience acute asthmatic attacks.

Prescribers must adhere to the principles of antibiotic stewardship

RENOFTRA 100 is not effective for the treatment of parenchymal infections of unilaterally nonfunctioning kidney. A surgical cause for infection should be excluded in recurrent or severe cases.

RENOFTRA 100 may be used with caution as short-course therapy only for the treatment of uncomplicated lower urinary tract infection in individual cases with an eGFR between 30-44 mL/min to treat resistant pathogens, when the benefits are expected to outweigh the risks.

Since pre-existing conditions may mask adverse reactions, RENOFTRA 100 should be used with caution in patients with pulmonary disease, hepatic dysfunction, neurological disorders, and allergic diathesis.

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 (paraesthesiae).

RENOFTRA 100 should be used in caution with patients with anaemia, diabetes mellitus, electrolyte imbalance, debilitating conditions and vitamin B (particularly folate) deficiency.

Acute, subacute and chronic pulmonary reactions have been observed in patients treated with nitrofurantoin. If these reactions occur, nitrofurantoin should be discontinued immediately.

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

Patient should be monitored closely for signs of hepatitis (particularly in long term use). Urine may be coloured yellow or brown after taking RENOFTRA 100. Patients on Nitrofurantoin are susceptible to false positive urinary glucose (if tested for reducing substances).

RENOFTRA 100 should be discontinued at any sign of haemolysis in those with suspected glucose-6-phosphate dehydrogenase deficiency.

Discontinue treatment with RENOFTRA 100 if otherwise unexplained pulmonary, hepatic, haematological or neurological syndromes occur.

Hepatotoxicity

Hepatic reactions, including hepatitis, autoimmune hepatitis, cholestatic jaundice, chronic active hepatitis, and hepatic necrosis, occur rarely. 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. If hepatitis occurs, the medicine should be withdrawn immediately and appropriate measures should be taken.

Pulmonary adverse reactions

Acute, subacute and chronic pulmonary reactions have been observed in patients treated with nitrofurantoin. If these reactions occur, nitrofurantoin should be discontinued immediately. Signs of pulmonary damage include difficulty and or pain when breathing, shortness of breath and coughing up blood or mucus.

Chronic pulmonary reactions

Chronic pulmonary reactions (including pulmonary fibrosis and diffuse interstitial pneumonitis) can develop insidiously and can often occur in elderly patients. Close monitoring of the lung disease of patients receiving long-term therapy is indicated (especially in the elderly).

Acute pulmonary reactions

Pulmonary reactions may be acute and usually occur within the first week of treatment. Increased vigilance for respiratory symptoms in patients who have just started therapy is warranted (especially in the elderly).

Capsules contain lactose and sodium:

Patients with rare hereditary problems of galactose intolerance, the total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

This medicine contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicines and other forms of interaction

- Increased absorption with food or medicines delaying gastric emptying.
- Decreased absorption with magnesium trisilicate.
- Decreased renal excretion of Nitrofurantoin by probenecid and sulphinpyrazone.
- Decreased anti-bacterial activity by carbonic anhydrase inhibitors and urine alkalisation.
- Anti-bacterial antagonism by quinolone anti-infectives.

- RENOFTRA 100 may cause false positive reactions in urine tests for glucose using copper reduction methods.
- As Nitrofurantoin belongs to the group of Antibacterials, it will have the following interactions:
- Typhoid Vaccine (oral):
    - Antibacterials inactivate oral typhoid vaccine.
- Antagonism between RENOFTRA 100 and nalidixic acid, and RENOFTRA 100 and oxolinic acid has been demonstrated *in-vitro* and RENOFTRA 100 should not be given concomitantly with quinolones.

4.6 Fertility, pregnancy and lactation

Pregnancy

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

Breastfeeding

RENOFTRA 100 is contraindicated in infants less than one month old (see section 4.3) because of the possible risk of haemolysis of the infants' immature red blood cells. Therefore, nursing mothers should not breastfeed their infants while being treated with RENOFTRA 100.

Fertility

There are no data on fertility in humans.

4.7 Effects on ability to drive and use machines

Nitrofurantoin may cause dizziness and drowsiness and the patient should not drive or operate machinery if affected this way until such symptoms go away.

4.8 Undesirable effects

Summary of the safety profile

Tabulated summary of adverse reactions:

System organ class	Frequency	Adverse reaction
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, leucopenia, 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
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 reactions, subacute pulmonary reactions* chronic pulmonary reactions cough, dyspnoea, pulmonary fibrosis; possible association with lupus-erythematous-like syndrome.
Gastrointestinal disorders	Frequency unknown	Sialadenitis, pancreatitis, nausea, anorexia, emesis, abdominal pain and diarrhoea.
Hepatic disorders	Frequency unknown	Cholestatic jaundice, chronic active hepatitis (fatalities have been reported), hepatic necrosis, autoimmune hepatitis

Skin and subcutaneous tissue disorders	Frequency unknown	Transient alopecia, exfoliative dermatitis and erythema multiforme (including Stevens-Johnson Syndrome), maculopapular, erythematous or eczematous eruptions, 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
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 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 common in elderly patients. Changes in ECG have occurred, associated with pulmonary reactions.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine are 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 Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

Symptoms

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

Management

Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 18.5 Urinary tract antiseptics

Pharmacotherapeutic group: Antibacterials for systemic use, Nitrofuran derivatives

ATC code: J01XE01.

Mechanism of action

Nitrofurantoin is a broad-spectrum antibacterial medicine, active against the majority of urinary pathogens. Anti-bacterial activity is higher in acidic urine. The wide range of organisms sensitive to the bactericidal activity include:

Enterococcus Faecalis

Escherichia coli

Citrobacter Species

Staphylococcus Species, e.g. *S.Aureus, S.Saprophyticus, S.Epidermidis*

Resistance

Most strains of *Proteus*

Most strains of *Serratia* are resistant.

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

All *pseudomonas* strains are resistant.

5.2 Pharmacokinetic properties

The nitrofurantoin macrocrystals are specially formulated.

The controlled crystal size is designed to control the speed of absorption and thus reduce the incidence of nausea. Clinical and animal studies indicate that Nitrofurantoin therapy decreases the likelihood of nausea in patients who might experience these symptoms on Nitrofurantoin

therapy. This special formulation of Nitrofurantoin had not caused any decrease in antibacterial efficacy.

Absorption

Orally administered Nitrofurantoin is readily, absorbed in the upper gastrointestinal tract at a slower rate and to reduced extent when compared to microcrystalline Nitrofurantoin. Blood concentrations at therapeutic dosage are usually low.

Elimination

Maximum urinary excretion usually occurs 4-5 hours after administration of macrocrystalline Nitrofurantoin. Urinary drug dose recoveries of about 25-30 % are obtained. It has an elimination half-life of about 30 minutes or less.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose Monohydrate (Tablettose 80)

Corn Starch (Maize starch extra white pharma grade)

Talc (Luzenac Pharma M)

6.2 Incompatibilities

Not known

6.3 Shelf life

24 months

6.4 Special precautions for storage

- Store at or below 30 °C.
- Protect from light.
- Keep the blisters in the carton until required for use
- KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of the container

Alu-Alu blister:

The blister consist of cold formable aluminium foil (OPA/Aluminium/PVC) and 25µ hard tempered aluminium foil coated with heat seal lacquer (HSL) as lidding foil.

Pack size: 28s in a carton (14 tablets packed in blister and such 2 blisters in a carton.

6.6 Special precautions for disposal and other handling

Nitrofurantoin Capsules should be used as directed by physician.

A patient information leaflet is provided with details of use and handling of the product.

7. HOLDER OF CERTIFICATE OF REGISTRATION

RBC PHARMACEUTICALS (PTY) LTD.

23 Kiaat Street, ERF 926, Extension 7,

Noordwyk, Midrand, Gauteng,

South Africa, 1687

8. REGISTRATION NUMBERS

59/18.5/0553

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

26 May 2026.

10. DATE OF REVISION OF TEXT

TBA