SCHEDULING STATUS: S4

1 NAME OF THE MEDICINE

PREVURO 50 (hard gelatine capsules)

PREVURO 100 (hard gelatine capsules)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

PREVURO 50: Each hard gelatine capsule contains 50 mg of nitrofurantoin macrocrystals.

Contains sugar: Lactose monohydrate 103,50 mg.

PREVURO 100: Each hard gelatine capsule contains 100 mg of nitrofurantoin macrocrystals.

Contains sugar: Lactose monohydrate 207,00 mg.

3 PHARMACEUTICAL FORM

Hard gelatine capsules

PREVURO 50: A size 3 hard gelatine capsule with a yellow cap and white body. Within each hard gelatine capsule is a yellow powder.

PREVURO 100: A size 1 hard gelatine capsule with a yellow cap and yellow body. Within each hard gelatine capsule is a yellow powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

PREVURO 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.

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.

PREVURO is highly soluble in urine, to which it may impart a brown colour.

Special populations

Elderly population

Provided there is no significant renal impairment, in which PREVURO is contraindicated, the dosage should be that for any normal adult. See precaution and risks to elderly patients associated with long-term therapy (see section 4.8).

Paediatric population

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.

Method of administration

For oral use.

PREVURO may be given with food or milk to further minimise gastric upset.

Taking PREVURO with a meal improves absorption and is important for optimal efficacy.

4.3 Contraindications

- In patients with known sensitivity to nitrofurantoin microcrystals and any of the excipients of PREVURO (listed in section 6.1).
- Anuria and oliguria and renal impairment are contraindications to therapy with PREVURO. Treatment of this type of patient carries an increased risk of toxicity because of impaired excretion of PREVURO.
- In patients with a deficiency of glucose 6-phosphate dehydrogenase or nursing mothers of infants with this deficiency or nursing mothers of infants with this deficiency.
- 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 early pregnancy has not been established (see section 4.6).
- Acute porphyria.
- Patients suffering from renal impairment with an eGFR of less than 45 mL/min.

4.4 Special warnings and precautions for use

- Prolonged use of PREVURO is not recommended.
- A course of therapy should not exceed 14 days, and repeated courses should be separated by rest periods.
- Patients with a history of asthma may experience acute asthmatic attacks.
- Cases of haemolytic anaemia of the primaquine sensitivity type have been induced by PREVURO. The haemolysis appears to be linked to a glucose-6-phosphate dehydrogenase deficiency in the red blood cells of the affected patients. Any sign of haemolysis is an indication to discontinue the medicine.
- *Pseudomonas* is the organism most commonly implicated in superinfections in patients treated with PREVURO.
- PREVURO 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, PREVURO 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 (paraesthesia).
- PREVURO should be used in caution with patients with anaemia, diabetes mellitus, electrolyte imbalance, debilitating conditions and vitamin B (particularly folate) deficiency, which may predispose to peripheral neuropathy.
- Acute, subacute and chronic pulmonary reactions have been observed in patients treated with PREVURO. If these reactions occur, PREVURO 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 PREVURO. Patients on PREVURO are susceptible to false positive urinary glucose (if tested for reducing substances).
- Discontinue treatment with PREVURO 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 drug should be withdrawn immediately, and appropriate measures should be taken.

Excipient with known effect

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

4.5 Interaction with other medicines and other forms of interaction

Probenecid or sulphinpyrazone may reduce the excretion of PREVURO and should not be given concomitantly.

Magnesium trisilicate may reduce the absorption of PREVURO.

PREVURO may cause false positive reactions in urine tests for glucose using copper reduction methods.

Antagonism between PREVURO and nalidixic acid, and PREVURO and oxolinic acid has been demonstrated *in vitro* and PREVURO should not be given concomitantly with quinolones.

Decreased anti-bacterial activity by carbonic anhydrase inhibitors and urine alkalisation.

Increased absorption with food or medicines delaying gastric emptying.

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

- Typhoid vaccine (oral): Antibacterials inactivate oral typhoid vaccine and certain laboratory tests.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential/ Contraception in males and females

No data available.

Pregnancy

Data in pregnant women indicate no teratogenicity or foetal/ neonatal toxicity. Animal studies do not show reproductive toxicity as clinically relevant doses. Therefore, PREVURO can be used during pregnancy, except in 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).

Breastfeeding

PREVURO is excreted in breast milk. PREVURO can be used during breastfeeding, but it is contraindicated in those patients with a deficiency of glucose 6-phospahte dehydrogenase or nursing mothers of infants under one month of age.

Fertility

No data available.

4.7 Effects on ability to drive and use machines

PREVURO may cause dizziness and drowsiness as dizziness and vertigo can occur if symptoms occur.

4.8 Undesirable effects

Tabulated list of adverse reactions

The undesirable effects are listed according to organ systems and following frequencies: Unknown (cannot be estimated from the available data).

System organ class	Frequency	Undesirable effect
Infections and infestations	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.
	Unknown	Agranulocytosis, leukopenia, granulocytopenia, haemolytic anaemia, thrombocytopenia, glucose-6-phosphate dehydrogenase deficiency anaemia, megaloblastic anaemia, eosinophilia.
Immune system disorders	Unknown	Allergic skin reactions, angioedema, anaphylaxis, cutaneous vasculitis.
Psychiatric disorders	Unknown	Depression, euphoria, confusion, psychotic reactions.
Nervous system disorders	Unknown	Peripheral neuropathy including optic neuritis (sensory as well as motor involvement), nystagmus, vertigo, dizziness, headache, drowsiness, benign intracranial hypertension.
Cardiac disorders	Less frequent	Collapse, cyanosis.

Respiratory, thoracic and mediastinal disorders	Unknown	Acute pulmonary reactions, subacute pulmonary reactions*, chronic pulmonary reactions, cough, dyspnoea, pulmonary fibrosis; possible association with lupus-erythematous-like syndrome.
Gastrointestinal disorders	Unknown	Sialadenitis, pancreatitis, nausea, anorexia, emesis, abdominal pain, diarrhoea.
Hepatobiliary disorders	Unknown	Cholestatic jaundice, chronic active hepatitis**, hepatic necrosis, autoimmune hepatitis.
Skin and subcutaneous tissue disorders	Unknown	Transient alopecia, exfoliative dermatitis, erythema multiforme (including Stevens-Johnson syndrome), maculopapular, erythematous or eczematous eruptions, urticaria, rash, pruritus, lupus-like syndrome associated with pulmonary reaction, drug rash with eosinophilia and systemic symptoms (dress syndrome), cutaneous vasculitis.
Renal and urinary disorders	Unknown	Yellow or brown discolouration of urine, interstitial nephritis.
General disorders and administration site conditions	Unknown	Asthenia, fever, chills, drug fever, arthralgia.
Investigations	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 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 rarely 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.

** Fatal events have been reported.

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 Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

In overdose, side effects can be precipitated and/or be of increased severity (see section 4.8).

Symptoms

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

Treatment

There is no known specific antidote. Treatment is symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 18.5 Urinary tract antiseptics

Pharmacotherapeutic group: Antimicrobials for systemic use, Nitrofurantoin derivative. ATC code: J01XE01.

Mechanism of action

Nitrofurantoin is an antibacterial medicine for specific urinary tract infections. Nitrofurantoin is a broad-spectrum antibacterial medicine, active against the majority of urinary pathogens. The wide range of organisms sensitive to the bactericidal activity include:

- *Escherichia coli.*
- *Enterococcus faecalis.*
- *Klebsiella species.*
- *Enterobacter species.*
- *Staphylococcus species e.g. S. aureus, S. saprophyticus, S. epidermidis citrobacter species.*
- Clinically most common urinary pathogens are sensitive to nitrofurantoin. Most strains of *Proteus* and *Serratia* are resistant.
- All *Pseudomonas* strains are resistant.

5.2 Pharmacokinetic properties

The nitrofurantoin macro crystals 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 rapidly and completely absorbed from the gastrointestinal tract and is rapidly excreted in the urine. Blood concentrations at therapeutic dosages are usually low.

Elimination

Antibacterial 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.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

PREVURO 50:

Lactose monohydrate.

Maize starch.

Talc.

Hard capsule

Body

Gelatine.

Titanium dioxide.

Cap

Gelatine.

Titanium dioxide.

Yellow iron oxide (E172).

PREVURO 100:

Lactose monohydrate.

Maize starch.

Talc.

Hard capsule

Body

Gelatine.

Titanium dioxide.

Yellow iron oxide (E172).

Cap

Gelatine.

Titanium dioxide.

Yellow iron oxide (E172).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at or below 25 °C.

Do not remove the blisters from the outer carton until required for use.

Store in the original package/container.

6.5 Nature and contents of container

PREVURO are packed in a PVC/aluminium blister of 10 capsules.

Not all packs and pack sizes are necessarily marketed.

6.6 Special precautions for disposal of a used medicine or waste materials derived from such medicine and other handling of the product

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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8 REGISTRATION NUMBERS

PREVURO 50: 57/18.5/0295
PREVURO 100: 57/18.5/0296

9 DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

Date of first authorisation: 08 July 2025
Date of latest renewal: -

10 DATE OF REVISION OF TEXT

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