PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

TURANTO 50 (Capsules)

TURANTO 100 (Capsules)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

TURANTO 50 Capsules

Each capsule contains 50 mg nitrofurantoin macrocrystals.

Contains sugar (77,50 mg lactose monohydrate).

TURANTO 100 Capsules

Each capsule contains 100 mg nitrofurantoin macrocrystals.

Contains sugar (155 mg lactose monohydrate).

Excipients:

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Capsule.

TURANTO 50 Capsules:

Yellow opaque cap and white opaque body, size 3 hard gelatin capsule, imprinted with “C 69” on cap, “50 mg” and two lines encircling the capsules on body with black ink, filled with yellowish powder.

TURANTO 100 Capsules:

Yellow opaque cap and body, size 2 hard gelatin capsule, imprinted with “C 70” on cap, “100 mg” and three lines encircling the capsules on body with black ink, filled with yellowish powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

TURANTO 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 - 100 mg four times a day, with meals and at bedtime.
To prevent recurrences:	50 - 100 mg per day.

Children

Acute urinary tract infections:	Should be calculated on the basis of 5 - 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*:**

Oral

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

TURANTO may be given with meals (food or milk) to minimise gastric upset.

4.3 Contraindications

- Hypersensitivity to nitrofurantoin or other nitrofurans or to any of the excipients listed in section 6.1.
- Patients with a deficiency of glucose-6-phosphate dehydrogenase or breastfeeding mothers of infants with this deficiency.

- Anuria, oliguria and renal impairment are contraindications to therapy with **TURANTO**.
- Treatment of this type of patient carries an increased risk of toxicity because of impaired excretion of **TURANTO**.
- 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.
- 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.

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

Acute, subacute or chronic pulmonary reaction has been observed in patients treated with **TURANTO.** If these reactions occur, **TURANTO** should be withdrawn and appropriate measures should be taken.

Elderly patients are especially susceptible to the pulmonary intoxication of **TURANTO**. Elderly patients and patients undergoing prolonged therapy should be monitored for changes in pulmonary function.

Cases of haemolytic anaemia of the primaquine sensitivity type have been induced by **TURANTO**. 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 **TURANTO**.

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

Pseudomonas is the organism most commonly implicated in superinfections in patients treated with **TURANTO**.

Peripheral neuropathy and susceptibility to peripheral neuropathy which may become severe or irreversible, has occurred and may be life-threatening. Patients should therefore be warned to report early signs of peripheral neuropathy. If peripheral neuropathy occurs the treatment should be discontinued. Care is required in patients with predisposing pulmonary, hepatic, neurological or allergic disorders and in those with conditions such as anaemia, diabetes mellitus, electrolyte imbalance, debility or vitamin B deficiency, which may predispose to peripheral neuropathy.

Although hepatic reactions such as hepatitis, cholestatic jaundice, and hepatic necrosis occur less frequently, fatalities have been reported. Patients should be monitored and **TURANTO** stopped immediately if hepatitis occurs.

Lactose: **TURANTO** contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the Lapp-lactase deficiency or glucose-galactose malabsorption should not take **TURANTO.**

Contains lactose which may have an effect on the glycaemic control of patients with diabetes mellitus.

4.5 Interaction with other medicines and other forms of interaction

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

Magnesium trisilicate may reduce the absorption of **TURANTO**.

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

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

Oestrogens: **TURANTO** may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of oestrogen-containing contraceptive medicines. Therefore, patients should be warned appropriately and extra contraceptive precautions taken.

Typhoid vaccine (oral): **TURANTO** inactivates oral typhoid vaccine.

Increased absorption with food or agents delaying gastric emptying.

Decreased antibacterial activity by carbonic anhydrous inhibitors and urine alkalisation.

4.6 Fertility, pregnancy and lactation

Pregnancy

TURANTO is contraindicated in pregnant women during labour and delivery because of the possible risk of haemolysis of the infant's immature red cells. Safe use in earlier pregnancy has not been established (see section 4.3).

Breastfeeding

Breastfeeding an infant known or suspected to have an erythrocyte enzyme deficiency (including G6PD deficiency), must be temporarily avoided, since nitrofurantoin is detected in trace amounts in breast milk.

4.7 Effects on ability to drive and use machines

TURANTO may cause dizziness or drowsiness.

Patients should be aware of how they react to **TURANTO** before driving or operating machinery.

4.8 Undesirable effects

The following adverse reactions have been reported in association with **TURANTO Capsules**:

System Organ Class	Frequency	Undesirable effects
Infections and infestations:	Less frequent	*S*uperinfection by resistant organisms may occur, however, these are limited to the genitourinary tract because suppression of normal bacterial flora elsewhere in the body does not occur.
Blood and lymphatic system disorders:	Less frequent	Haemolytic anaemia, granulocytopenia or agranulocytosis, eosinophilia and megaloblastic anaemia, leucopenia, thrombocytopenia in persons with a genetic deficiency of glucose-6-phosphate dehydrogenase.
Immune system disorders:	Less frequent	Anaphylaxis, sialadenitis, drug fever, a lupus-like syndrome and angioedema
Psychiatric disorders:	Less frequent	Depression, euphoria, confusion, psychotic reactions.
Nervous system disorders:	Less frequent	Peripheral neuropathy (including optical neuritis), reversible headache, dizziness, nystagmus, drowsiness, vertigo and asthenia. Severe polyneuropathies with demyelination and degeneration of both sensory and motor nerves have been reported. Patients should be warned to report early signs of peripheral neuropathy such as paraesthesia.
Respiratory, thoracic and mediastinal disorders	Less frequent	Pulmonary sensitivity reactions may occur, which can be acute, subacute or chronic. Acute pulmonary sensitivity reaction is commonly manifested by sudden onset of fever, chills, eosinophilia, cough, chest pain, dyspnoea, pulmonary infiltration or consolidation and pleural effusion. The acute reactions usually occur within the first week of

System Organ Class	Frequency	Undesirable effects
		treatment and resolve with discontinuation of **TURANTO**. More insidious subacute reactions have also been reported. Interstitial pulmonary fibrosis can occur in patients on chronic medication. Subacute or chronic pulmonary reaction is associated with prolonged therapy. Insidious onset of malaise, dyspnoea on exertion, cough, altered pulmonary function, and roentgenographic and histologic findings of diffuse interstitial pneumonitis or fibrosis or both are common manifestations. Impaired pulmonary function may result even after cessation of **TURANTO** therapy.
Gastrointestinal disorders	Frequent	Anorexia, nausea, vomiting.
	Less frequent	Abdominal pain, diarrhoea, pancreatitis.
Hepatobiliary disorders	Less frequent	Hepatotoxicity including cholestatic jaundice and hepatitis, chronic active hepatitis and hepatocellular damage.
Skin and subcutaneous tissue disorders	Less frequent	Skin rashes, erythema multiforme, exfoliative dermatitis, maculopapular, erythematous, or eczematous eruption, pruritus, urticaria, transient alopecia.
Musculoskeletal and connective tissue disorders	Less frequent	Myalgia, arthralgia
Renal and urinary disorders	Frequent	Brown discolouration of urine
General disorders and administration site conditions	Less frequent	Fever, benign intracranial hypertension

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 "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

Symptoms and signs of overdose include gastric irritation, nausea and vomiting. There is no specific antidote. Nitrofurantoin can be haemodialysed. Standard treatment is symptomatic and supportive. Induction of emesis can be considered in cases of recent ingestion. 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 the medicine.

5. PHARMACOLOGICAL PROPERTIES

Pharmaceutical groups: A 18.5 Urinary tract antiseptics

ATC code: J01XE01

5.1 Pharmacodynamic properties

Nitrofurantoin is an antibacterial medicine for specific urinary tract infections.

Nitrofurantoin exerts bacteriostatic activity against certain sensitive bacteria.

Anti-bacterial activity is higher in acidic urine.

Resistance

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

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

5.2 Pharmacokinetic properties

Nitrofurantoin is completely absorbed from the GI tract. The macrocrystalline form of nitrofurantoin is absorbed and excreted more slowly. Antibacterial concentrations are not achieved in plasma following ingestion of recommended doses because of rapid elimination. The plasma $t_{½}$ is 0,3 – 1 hour; ~40 % is

excreted unchanged into the urine. The average dose of nitrofurantoin yields a concentration in urine of ~200 µg/ml. This concentration is soluble at pH > 5, but the urine should not be alkalinized, because this reduces antimicrobial activity. The rate of excretion is linearly related to the creatinine clearance, so in patients with impaired glomerular function, the efficacy of nitrofurantoin may be decreased and the systemic toxicity increased. Nitrofurantoin colours the urine brown.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate (Supertab 11SD), pregelatinised starch (Starch 1500), talc and hard gelatin capsules (for 50 mg and 100 mg containing FD&C Yellow 6 (C.I. No.15985), D&C Yellow 10 (C.I. No. 47005), titanium dioxide (C.I. No. 77891), gelatin, sodium lauryl sulfate and black edible printing ink).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months from the manufacturing date

6.4 Special precautions for storage

Store at or below 25 °C.

Protect from light and moisture.

Keep the HDPE container tightly closed.

KEEP OUT OF REACH OF CHILDREN

6.5 Nature and contents of container

HDPE Container Pack:

TURANTO 50 Capsules:

40 ml round, white HDPE container with screw neck with white polypropylene closure with pulp and heat seal liner containing 50 capsules packed in an outer pre-printed carton.

TURANTO 100 Capsules:

40 ml round, white HDPE container with screw neck with white polypropylene closure with pulp and heat seal liner containing 50 capsules packed in an outer pre-printed carton.

6.6 Special precautions for disposal and other handling

No special requirements.

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

7. HOLDER OF CERTIFICATE OF REGISTRATION

Macleods Pharmaceuticals SA (Pty) Ltd

Office block 1, Bassonia Estate Office Park (East),

1 Cussonia Drive, Bassonia Rock, Ext. 12,

Alberton, South Africa.

8. REGISTRATION NUMBER(S)

TURANTO 50: 52/18.5/0758.754

TURANTO 100: 52/18.5/0759.755

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

22 February 2022

10. DATE OF REVISION OF THE TEXT

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