1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S4

PROPRIETARY NAME AND DOSAGE FORM

MACRODANTIN CAPSULES 50 mg (hard-gelatin capsule)

MACRODANTIN CAPSULES 100 mg (hard-gelatin capsule)

COMPOSITION

MACRODANTIN CAPSULES 50 mg:

Each hard-gelatin capsule contains 50 mg of nitrofurantoin macrocrystals.

Excipients:

Black iron oxide (C.I. 77499), erythrosine (C.I. 45430), gelatin, lactose, maize starch, purified talc, quinolene yellow (C.I. 47005), titanium dioxide (C.I. 77891)

Contains sugar: Lactose 160,57 mg

MACRODANTIN CAPSULES 100 mg:

Each hard-gelatin capsule contains 100 mg of nitrofurantoin macrocrystals.

Excipients:

Black iron oxide (C.I. 77499), erythrosine (C.I. 45430), gelatin, lactose, maize starch, purified talc, quinolene yellow (C.I. 47005), titanium dioxide (C.I. 77891)

Contains sugar: Lactose 192,04 mg

CATEGORY AND CLASS

A 18.5 Urinary tract antiseptics

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

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.

Pharmacokinetic properties

Nitrofurantoin is rapidly and completely absorbed from the gastrointestinal tract. Anti-bacterial concentrations are not achieved in plasma following ingestion of recommended doses because of rapid elimination.

INDICATIONS

MACRODANTIN 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.

CONTRAINDICATIONS

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.

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.

Contraindicated in those patients with known sensitivity to MACRODANTIN (nitrofurantoin macrocrystals) and in those patients with a deficiency of glucose-6-phosphate dehydrogenase or nursing mothers of infants with this deficiency.

WARNINGS AND SPECIAL PRECAUTIONS

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.

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 MACRODANTIN. 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 MACRODANTIN.

Precautions

Patients should 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.

Elderly patients are especially susceptible to the pulmonary intoxication of MACRODANTIN.

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 If these reactions occur, the medicine should be withdrawn and appropriate measures should be taken.

Excipients

Contains lactose which may have an effect on the glycaemic control of patients with diabetes mellitus. Patients with the rare hereditary conditions of galactose intolerance e.g. galactosaemia, Lapp lactase deficiency, glucose-galactose malabsorption or fructose intolerance should not take MACRODANTIN.

INTERACTIONS

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

Magnesium trisilicate may reduce the absorption of MACRODANTIN.

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

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

HUMAN REPRODUCTION

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

DOSAGE AND DIRECTIONS FOR USE

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.

MACRODANTIN 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.

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

SIDE EFFECTS

Gastrointestinal reactions

Anorexia, nausea, and vomiting are the most frequent reactions; less frequently abdominal pain and diarrhoea.

Hypersensitivity reactions

Skin rashes and fever may occur.

Anaphylaxis, erythema multiforme, exfoliative dermatitis, pancreatitis, a lupus-like syndrome, myalgia and arthralgia have been reported.

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 treatment and resolve with discontinuation of the medicine.

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

the medicine therapy.

Dermatological reactions

Maculopapular, erythematous, or eczematous eruption, pruritus, urticaria and angioedema.

Other sensitivity reactions

Hepatotoxicity including cholestatic jaundice and hepatitis may develop. Chronic active hepatitis and hepatocellular damage have been reported.

Haematological reactions

Haemolytic anaemia, granulocytopenia or agranulocytosis, eosinophilia and megaloblastic anaemia, leucopenia, thrombocytopenia in persons with a genetic deficiency of glucose-6-phosphate dehydrogenase.

Neurological reactions

Peripheral neuropathy, reversible headache, dizziness, nystagmus and drowsiness. Severe polyneuropathies with demyelination and degeneration of both sensory and motor nerves have been reported.

Patients should be warned to report early signs or peripheral neuropathy such as paraesthesia.

Miscellaneous reactions

Transient alopecia. As with other antimicrobial medicines, superinfection by resistant organisms may occur. With MACRODANTIN, however, these are limited to the genito-urinary tract because suppression of normal bacterial flora elsewhere in the body does not occur.

MACRODANTIN colours the urine brown.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENTS

See SIDE EFFECTS.

Treatment is symptomatic and supportive.

IDENTIFICATION

MACRODANTIN CAPSULES 50 mg:

A size “3” hard gelatin capsule with an opaque yellow cap and white body printed “50” in black on the cap and body. Within each hard-gelatin capsule is an odourless yellow crystalline powder.

MACRODANTIN CAPSULES 100 mg:

A size “2” hard gelatin capsule with an opaque yellow cap and body printed “100” in black on the cap and body. Within each hard-gelatin capsule is an odourless yellow crystalline powder.

PRESENTATION

MACRODANTIN CAPSULES 50 mg:

50 hard-gelatin capsules are packed in a white polypropylene container and sealed with a white low density polyethylene snap-on cap with a tear tab, together with or without a white polyurethane foam plug.

250 hard-gelatin capsules are packed in a white polypropylene container and sealed with a white low density polyethylene snap-on cap with a tear tab, together with a white

polyurethane foam plug.

MACRODANTIN CAPSULES 100 mg:

50 hard-gelatin capsules are packed in a white polypropylene container and sealed with a white low density polyethylene snap-on cap with a tear tab, together with or without a white polyurethane foam plug.

8 or 250 hard-gelatin capsules are packed in a white polypropylene container and sealed with a white low density polyethylene snap-on cap with a tear tab, together with a white polyurethane foam plug.

Not all packs and pack sizes are necessarily marketed.

STORAGE INSTRUCTIONS

Store at or below 25 °C.

Protect from light and moisture.

Keep in original packaging until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

MACRODANTIN CAPSULES 50 mg: G/18.5/160

MACRODANTIN CAPSULES 100 mg: G/18.5/161

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

DATE OF PUBLICATION OF THE PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

Dates of registration:

MACRODANTIN CAPSULES 50 mg: 11 June 1975

MACRODANTIN CAPSULES 100 mg: 11 June 1975

Date of the most recent amendment to the professional information as approved by the Authority: 26 September 1996

Botswana:	S2
50 mg	BOT0901535
100 mg	BOT0901536

Namibia:	NS2
50 mg	90/18.5/001597
100 mg	90/18.5/001596

ZA_MACRCAP_9609_00