New Zealand Data Sheet

1 PRODUCT NAME

Macrobid 100mg Modified-release Capsules.

Nitrofurantoin

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Macrobid is a modified release, hard gelatin capsule containing the equivalent of 100mg of Nitrofurantoin in the form of nitrofurantoin macrocrystals and nitrofurantoin monohydrate. Excipient (s) with known effect: Lactose monohydrate [194.6 mg per capsule].
For the full list of excipients, see section 6.1

Pharmacotherapeutic group: Urinary Anti-infectives

ATC Code: J01XE01

3 PHARMACEUTICAL FORM

Macrobid is available as 100 mg opaque black and yellow modified-release capsules.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Macrobid is indicated for the treatment of acute uncomplicated urinary tract infections (acute cystitis) caused by susceptible strains of Escherichia coli or Staphylococcus saprophyticus. Therapy with Macrobid may be initiated before results of culture and susceptibility tests are known; therapy should be continued or altered, as appropriate, in accordance with results of the tests.

Macrobid is indicated for the prophylaxis of urinary tract infections after surgery or procedures involving genitourinary tract.

Macrobid is not indicated for the treatment of pyelonephritis or perinephric abscesses.

4.2 Dose and method of administration

Acute, Uncomplicated Urinary Tract Infections (acute cystitis)
Adults and Paediatric Patients Over 12 Years:
One 100 mg capsule every 12 hours for seven days.

Prophylactic Therapy
Adults and Paediatric Patients Over 12 Years:
One 100 mg capsule every 12 hours for three days.

First dose is to be given immediately before surgery or procedure.

Special populations

Use in renal impairment

Nitrofurantoin is contraindicated in patients with anuria, oliguria, or significant impairment of renal function (creatinine clearance under 60 mL per minute or clinically significant elevated serum creatinine) (see section 4.3).

Use in renal impairment increases the risk of adverse effects (and toxicity) and efficacy is reduced as antibacterial efficacy relies on adequate glomerular filtration.

Elderly patients may have pre-existing renal impairment and accurate calculation of creatinine clearance is recommended.

Monitor patients closely whose renal function may change acutely.

Use in hepatic impairment

Use caution when prescribing nitrofurantoin in patients with hepatic dysfunction, which may mask the signs and symptoms of adverse reactions.

Use of nitrofurantoin is contraindicated in patients with a previous history of cholestatic jaundice/ hepatic dysfunction with nitrofurantoin.

Paediatric population

Safety and effectiveness in paediatric patients below the age of twelve years have not been established.

Nitrofurantoin is contraindicated in neonates and infants under 3 months of age due to the possibility of haemolytic anaemia due to immature erythrocyte enzyme systems (glutathione instability) (see section 4.3).

Method of administration

Macrobid capsules should be taken with food. The medicine should be swallowed whole.

4.3 Contraindications

Macrobid is contraindicated in:

- Anuria, oliguria, or significant impairment of renal function (creatinine clearance under 60 mL per minute or clinically significant elevated serum creatinine)
- Pregnant patients at term (38-42 weeks gestation), during labour and delivery, or when the onset of labour is imminent.
- Neonates and infants under three months of age.
- Patients with a previous history of cholestatic jaundice/hepatic dysfunction or pulmonary toxicity associated with nitrofurantoin.
- Patients with known hypersensitivity to nitrofurantoin or to any of the excipients.
- Acute porphyria.
- G6PD deficiency.

4.4 Special warnings and precautions for use

Pulmonary reactions

Acute, sub-acute or chronic pulmonary reactions have been observed in patients treated with nitrofurantoin in acute and prophylactic treatment. Pulmonary reactions with nitrofurantoin can be fatal.

Use caution when prescribing nitrofurantoin in patients with pulmonary disease which may mask the signs and symptoms of adverse reactions.

Advise patients and caregivers to be vigilant for new or worsening respiratory symptoms while taking nitrofurantoin and promptly investigate any symptoms that may indicate a pulmonary adverse reaction. Patients and carers should be reminded about the symptoms of pulmonary damage.

If these reactions occur, Macrobid should be discontinued immediately, and appropriate measures take.

Acute pulmonary reactions usually occur within the first week of treatment and are reversible with cessation of therapy. Increased vigilance for respiratory symptoms in patients who have just started therapy is warranted (especially in the elderly). Acute pulmonary reactions are commonly manifested by fever, chills, cough, chest pain, dyspnoea, pulmonary infiltration with consolidation or pleural effusion on chest xray, and eosinophilia. In subacute pulmonary reactions, fever and eosinophilia occur less often than in the acute form (see section 4.8).

Chronic pulmonary reactions (diffuse interstitial pneumonitis or pulmonary fibrosis, or both) can develop insidiously and may occur more commonly in elderly patients. These reactions occur generally in patients receiving therapy for six months or longer. Malaise, dyspnoea on exertion, difficulty breathing, cough, coughing up blood or mucus, and altered pulmonary function are common manifestations which can occur insidiously. Close monitoring of the pulmonary condition of patients receiving long-term therapy is warranted and requires that the benefits of therapy be weighed against potential risks (see section 4.8 Respiratory).

Upon cessation of therapy, recovery may require several months. If the symptoms are not recognised as being drug-related and nitrofurantoin therapy is not stopped, the symptoms may become more severe.

Changes in ECG may occur associated with pulmonary reactions.

Patients who have experienced pulmonary toxicity with nitrofurantoin must not be re-exposed (see section 4.3).

Hepatotoxicity

Hepatic reactions, including hepatitis, cholestatic jaundice, chronic active hepatitis, autoimmune hepatitis and hepatic necrosis, have been reported with nitrofurantoin. Fatalities have been reported. Hepatic reactions have been reported in patients taking both short term and long-term treatment.

Use caution when prescribing nitrofurantoin in patients with hepatic dysfunction, which may mask the signs and symptoms of adverse reactions.

The onset of hepatitis may be gradual and may not have obvious symptoms at first.

Cholestatic jaundice is generally associated with short-term therapy (usually up to 2 weeks). Chronic active hepatitis, occasionally leading to hepatic necrosis is generally associated with long-term therapy (usually after 6 months).

It is important to monitor patients periodically for changes in biochemical tests that could indicate hepatic dysfunction and for clinical signs or symptoms of liver abnormality, especially in patients taking long-term nitrofurantoin.

Advise parents and caregivers of the symptoms of hepatic dysfunction: yellowing of the skin or eyes, upper right abdominal pain, dark urine and pale or grey-coloured stools, itching or joint pain and swelling to seek immediate medical advice if these occur.

If hepatotoxicity occurs, the drug should be withdrawn immediately, and appropriate measures should be taken.

Patients who have experienced hepatic toxicity with nitrofurantoin must not be re-exposed (see section 4.3).

Renal impairment
Renal function should be monitored, especially those who are at risk of renal impairment (such as the elderly) or where renal function may acutely change (such as use of nephrotoxic medicines) (see section 4.2).

Neuropathy
Peripheral neuropathy, which may become severe or irreversible, has occurred. Fatalities have been reported. Conditions such as renal impairment (creatinine clearance under

60 mL per minute or clinically significant elevated serum creatinine), anemia, diabetes mellitus, electrolyte imbalance, vitamin B deficiency, and debilitating disease may enhance the occurrence of peripheral neuropathy. Patients receiving long-term therapy should be monitored periodically for changes in renal function.

Optic neuritis has been reported rarely in post-marketing experience with nitrofurantoin formulations.

Haemolytic anemia
Cases of haemolytic anemia of the primaquine-sensitivity type have been induced by nitrofurantoin. Haemolysis appears to be linked to a glucose-6-phosphate dehydrogenase deficiency in the red blood cells of the affected patients. This deficiency is found in 10 percent of Blacks and a small percentage of ethnic groups of Mediterranean and Near- Eastern origin. Haemolysis is an indication for discontinuing Macrobid; haemolysis ceases when the drug is withdrawn.

Clostridium difficile-associated diarrhoea
Clostridium difficile-associated diarrhoea (CDAD) has been reported with use of nearly all antibacterial agents, including nitrofurantoin, and may range in severity from mild diarrhoea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C. difficile.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhoea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated.

Excipients
Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine. See section 2 and 6.1.

PRECAUTIONS:
Information for Patients
Patients should be advised to take Macrobid with food (ideally breakfast and dinner) to further enhance tolerance and improve drug absorption. Patients should be instructed to complete the full course of therapy; however, they should be advised to contact their physician if any unusual symptoms occur during therapy.

Patients should be advised not to use antacid preparations containing magnesium trisilicate while taking Macrobid.

Patients should be counselled that antibacterial drugs including Macrobid should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When Macrobid are prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by Macrobid or other antibacterial drugs in the future.

Diarrhoea is a common problem caused by antibiotics which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with antibiotics, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months after having taken the last dose of the antibiotic. If this occurs, patients should contact their physician as soon as possible.

Paediatric Use
Macrobid are contraindicated in infants below the age of three months. (See contraindications). Safety and effectiveness in paediatric patients below the age of twelve years have not been established.

Geriatric Use

Clinical studies of Macrobid did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. Spontaneous reports suggest a higher proportion of pulmonary reactions, including fatalities, in elderly patients; these differences appear to be related to the higher proportion of elderly patients receiving long- term nitrofurantoin therapy.

As in younger patients, chronic pulmonary reactions generally are observed in patients receiving therapy for six months or longer (see Warnings). Spontaneous reports also suggest an increased proportion of severe hepatic reactions, including fatalities, in elderly patients (see Warnings).

In general, the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy in elderly patients should be considered when prescribing Macrobid. This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Anuria, oliguria, or significant impairment of renal function (creatinine clearance under 60 mL per minute or clinically significant elevated serum creatinine) are contraindications (see Contraindications). Because elderly patients are more likely to have decreased renal function, it may be useful to monitor renal function.

4.5 Interaction with other medicines and other forms of interaction

Antacids containing magnesium trisilicate, when administered concomitantly with nitrofurantoin, reduce both the rate and extent of absorption. The mechanism for this interaction probably is adsorption of nitrofurantoin onto the surface of magnesium trisilicate.

Uricosuric drugs, such as probenecid and sulfinpyrazone, can inhibit renal tubular secretion of nitrofurantoin. The resulting increase in nitrofurantoin serum levels may increase toxicity, and the decreased urinary levels could lessen its efficacy as a urinary tract antibacterial.

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

Antagonism has been demonstrated in vitro between nitrofurantoin and quinolone antimicrobials. The clinical significance of this finding is unknown.

Pharmacodynamic

Use with other medicines that are known to cause pulmonary or hepatic toxicity such as methotrexate may increase the risk of these adverse effects.

Use with medicines that may impair renal function (see section 4.2, 4.4).

Laboratory Test Interactions

As a result of the presence of nitrofurantoin, a false-positive reaction for glucose in the urine may occur. This has been observed with Benedict’s and Fehling’s solutions but not with the glucose enzymatic test.

4.6 Fertility, pregnancy and lactation

Effects on Fertility
See section 5.3

Use in Pregnancy
Nitrofurantoin is contraindicated in pregnant women at term, during labour and delivery, or when the onset of labour is imminent because of the possibility of haemolytic anaemia in the infant (see section 4.3).

Animal studies with nitrofurantoin have shown no teratogenic effects.

Nitrofurantoin has had widespread clinical use. The limited number of epidemiological studies available have not shown a potential for nitrofurantoin to cause birth defects.

As with all other drugs, the maternal side effects may adversely affect the course of pregnancy. The drug should be used at the lowest dose as appropriate for the specific indication and only after careful assessment of benefits and risks.

Use in Lactation
Nitrofurantoin has been detected in human breast milk in trace amounts.

Infants less than 1 month of age, who are premature, or who have glucose-6-phosphate dehydrogenase deficiency (G6PD) may be at risk of haemolytic anaemia from nitrofurantoin in breast milk. A decision should be made whether to discontinue nursing or to discontinue the medicine, taking into account the importance of the medicine to the mother (see section 4.3 Contraindications.)

4.7 Effects on ability to drive and use machines

Nitrofurantoin does not interfere with the ability to drive or use machines.

4.8 Undesirable effects

In clinical trials of Macrobid, the most frequent clinical adverse events that were reported as possibly or probably drug-related were nausea (8%), headache (6%), and flatulence (1.5%).

Table 1. Tabulated list of adverse reactions

System organ class	**Adverse reaction**
Infections and infestations	As with other antimicrobial agents, superinfections with resistant organisms, e.g., Pseudomonas species or Candida species, can occur. There are sporadic reports of Clostridium difficile superinfections, or pseudomembranous colitis, with the use of nitrofurantoin
Blood and lymphatic system disorders	Glucose-6- phosphate dehydrogenase deficiency anaemia, agranulocytosis, leukopenia, granulocytopenia, haemolytic anaemia, thrombocytopenia, megaloblastic anaemia, aplastic anaemia, eosinophilia.
Immune system disorders	Angioedema, anaphylaxis,
Psychiatric disorders	Psychotic reactions, depression, confusion, euphoria
Nervous system disorders	Peripheral neuropathy (including optic neuritis), asthenia, vertigo, dizziness, drowsiness, amblyopia, nystagmus, benign intracranial hypertension, headache (common)
Cardiac	Cyanosis, collapse
Respiratory, thoracic and mediastinal disorders	Chronic, subacute, or acute pulmonary hypersensitivity reactions, cough, dyspnoea,
Gastrointestinal disorders	Diarrhoea, dyspepsia, abdominal pain, constipation, emesis, sialadenitis, pancreatitis, nausea (common), anorexia, flatulence (common)
Hepatobiliary disorders	Hepatic reactions, including hepatitis, cholestatic jaundice, chronic active hepatitis, hepatic necrosis, autoimmune hepatitis (see section 4.4)
Skin and subcutaneous disorders	Maculopapular, erythematous, or eczematous eruptions, alopecia, exfoliative dermatitis and erythema multiforme (including Stevens-Johnson Syndrome), pruritus, urticaria, rash, drug rash with eosinophilia and systemic symptoms (DRESS), lupus-like syndrome associated with pulmonary reaction, allergic skin reactions, cutaneous vasculitis
Renal and urinary disorders	Yellow or brown discolouration of urine, interstitial nephritis,
General disorders and administration site conditions	Arthralgia, myalgia, drug fever, chills, fever, malaise,
Investigations	increased AST (SGOT), increased ALT (SGPT), decreased haemoglobin, increased serum phosphorus, false positive urinary glucose

Description of selected adverse reactions:

Gastrointestinal:
There have been sporadic reports of pseudomembranous colitis with the use of nitrofurantoin. The onset of pseudomembranous colitis symptoms may occur during or after antimicrobial treatment. (See Warnings).

Neurologic:
Peripheral neuropathy, which may become severe or irreversible, has occurred. Fatalities have been reported. Conditions such as renal impairment (creatinine clearance under 60 mL per minute or clinically significant elevated serum creatinine), anemia, diabetes mellitus, electrolyte imbalance, vitamin B deficiency, and debilitating diseases may increase the possibility of peripheral neuropathy. (See Warnings).

Respiratory:
Chronic, subacute, or acute pulmonary hypersensitivity reactions may occur with the use of Nitrofurantoin.

Chronic pulmonary reactions generally occur in patients who have received continuous treatment for six months or longer. Malaise, Dyspnoea on exertion, cough, and altered pulmonary function are common manifestations which can occur insidiously. Radiologic and histologic findings of diffuse interstitial pneumonitis or fibrosis, or both, are also common manifestations of the chronic pulmonary reaction. Fever is rarely prominent. 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. Pulmonary function may be impaired permanently, even after cessation of therapy. The risk is greater when chronic pulmonary reactions are not recognized early.

In subacute pulmonary reactions, fever and eosinophilia occur less often than in the acute form. Upon cessation of therapy, recovery may require several months. If the symptoms are not recognized as being drug-related and nitrofurantoin therapy is not stopped, the symptoms may become more severe.

Acute pulmonary reactions are commonly manifested by fever, chills, cough, chest pain, dyspnoea, pulmonary infiltration with consolidation or pleural effusion on x-ray, and eosinophilia. Acute reactions usually occur within the first week of treatment and are reversible with cessation of therapy. Resolution often is dramatic. (See Warnings).

Changes in EKG (e.g., non-specific ST/T wave changes, bundle branch block) have been reported in association with pulmonary reactions.

Cyanosis has been reported rarely.

Hepatic:
Hepatic reactions, including hepatitis, cholestatic jaundice, chronic active hepatitis, and hepatic necrosis occur rarely (See Warnings).

Allergic:
Vasculitis (sometimes associated with pulmonary reactions) have been reported. Hypersensitivity reactions represent the most frequent spontaneously-reported adverse events in worldwide post-marketing experience with nitrofurantoin formulations.

Hematologic:
Cyanosis secondary to methemoglobinemia has been reported rarely.

Miscellaneous:
As with other antimicrobial agents, superinfections caused by resistant organisms, e.g., Pseudomonas species or Candida species, can occur.

In clinical trials of Macrobid, the most frequent laboratory adverse events (1-5%), without regard to drug relationship, were as follows: eosinophilia, increased AST (SGOT), increased ALT (SGPT), decreased haemoglobin, increased serum phosphorus. The following laboratory adverse events also have been reported with the use of nitrofurantoin: glucose-6-phosphate dehydrogenase deficiency anemia (see Warnings), agranulocytosis, leukopenia, granulocytopenia, haemolytic anemia, thrombocytopenia, megaloblastic anemia. In most cases, these hematologic abnormalities resolved following cessation of therapy. Aplastic anemia has been reported rarely.

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. Healthcare professionals are asked to report any suspected adverse reactions to https://pophealth.my.site.com/carmreportnz/s/.

4.9 Overdose

Occasional incidents of acute overdosage of nitrofurantoin have not resulted in any specific symptoms other than vomiting. Induction of emesis is recommended. There is no specific antidote, but a high fluid intake should be maintained to promote urinary excretion of the medicine. Nitrofurantoin is dialysable.

For risk assessment and advice on the management of overdose, please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Nitrofurantoin is a nitrofuran antimicrobial agent with activity against certain Gram positive and Gram-negative bacteria.

The mechanism of the antimicrobial action of nitrofurantoin is unusual among antibacterials. Nitrofurantoin is reduced by bacterial flavoproteins to reactive intermediates which inactivate or alter bacterial ribosomal proteins and other macromolecules. As a result of such

inactivations, the vital biochemical processes of protein synthesis, aerobic energy metabolism, DNA synthesis, RNA synthesis, and cell wall synthesis are inhibited. Nitrofurantoin is bactericidal in urine at therapeutic doses. The broad-based nature of this mode of action may explain the lack of acquired bacterial resistance to nitrofurantoin, as the necessary multiple and simultaneous mutations of the target macromolecules would likely be lethal to the bacteria.

Development of resistance to nitrofurantoin has not been a significant problem since its introduction in 1953. Cross-resistance with antibiotics and sulphonamides has not been observed, and transferable resistance is, at most, a very rare phenomenon.

Nitrofurantoin has been shown to be active against most strains of the following bacteria both in vitro and in clinical infections [see Indication):

Aerobic and facultative Gram-positive microorganisms:
Staphylococcus saprophyticus

Aerobic and facultative Gram-negative microorganisms:
Escherichia coli

At least 90 percent of the following microorganisms exhibit an in vitro minimum inhibitory concentration (MIC) less than or equal to the susceptible breakpoint for nitrofurantoin. However, the efficacy of nitrofurantoin in treating clinical infections due to these microorganisms has not been established in adequate and well-controlled trials.

Aerobic and facultative Gram-positive microorganisms:
Coagulase-negative staphylococci (including Staphylococcus epidermidis)
Enterococcus faecalis
Staphylococcus aureus
Streptococcus aga/actiae
Group D streptococci
Viridans group streptococci

Aerobic and facultative Gram-negative microorganisms:
Citrobacter ama/onaticus
Citrobacter diversus
Citrobacter freundii
Klebsiella oxytoca
Klebsiella ozaenae

Nitrofurantoin is not active against most strains of Proteus species or Serratia species. It has no activity against Pseudomonas species.

Susceptibility Test Methods:
When available, the clinical microbiology laboratory should provide cumulative results of the in vitro susceptibility test results for antimicrobial drugs used in resident hospitals to the physician as periodic reports that describe the susceptibility profile of nosocomial and community-acquired pathogens. These reports should aid the physician in selecting the most effective antimicrobial.

Dilution techniques:
Quantitative methods are used to determine antimicrobial minimum inhibitory concentrations (MICs). These MICs provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MICs should be determined using a standardized procedure. Standardized procedures are based on a dilution method (broth or agar) or equivalent with standardized inoculum concentrations and standardized concentrations of nitrofurantoin powder. The MIC values should be interpreted according to the criteria provided in Table 2.

Diffusion technique:
Quantitative methods that require measurement of zone diameters also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. One such standardized procedure requires the use of standardized inoculum concentrations. This procedure uses paper disks impregnated with 300 µg of nitrofurantoin to test the susceptibility of microorganisms to nitrofurantoin. The disk diffusion interpretive criteria are provided in Table 2.

Table 2. Susceptibility Interpretive Criteria for Nitrofurantoin

Pathogen	**Susceptibility Interpretive Criteria**					
	Minimum Inhibitory Concentrations (µg/mL)			Disk Diffusion (zone diameter in mm)		
	S	I	R	S	I	R
Enterobacteriaceae	δ32	64	ε128	ε17	15-16	δ14
Staphylococcus spp.	δ32	64	ε128	ε17	15-16	δ14

A report of Susceptible indicates that the pathogen is likely to be inhibited if the antimicrobial compound in the urine reaches the concentrations usually achievable. A report of Intermediate indicates that the result should be considered equivocal, and, if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where a high dosage of drug can be used. This category also provides a buffer zone, which prevents small, uncontrolled technical factors from causing major discrepancies in interpretation. A report of Resistant indicates that the pathogen is not likely to be inhibited if the antimicrobial compound in the urine reaches the concentrations usually achievable; other therapy should be selected.

Quality Control:
Standardized susceptibility test procedures require the use of quality control microorganisms to control the technical aspects of the test procedures. Standard nitrofurantoin powder should provide the following range of values noted in Table 3.

Table 3. Acceptable Quality Control Ranges for Nitrofurantoin

QC Strain	**Acceptable Quality Control Ranges**	
	Minimum Inhibitory Concentration (µg/mL)	Disk Diffusion (zone diameter in mm)
Escherichia coli	4 – 16	20 -25

ATCC 25922		
Enterococcus faecalis ATCC 29212	4 – 16	NA*
Staphylococcus aureus ATCC 29213	8 – 32	NA*
Staphylococcus aureus ATCC 25923	NA*	18-22

*Not applicable

5.2 Pharmacokinetic properties

Orally administered, all dosage forms of nitrofurantoin are readily absorbed and rapidly excreted in urine. Plasma concentrations at therapeutic dosage are low. The presence of food or agents which delay gastric emptying can increase the bioavailability of nitrofurantoin by up to 40%.

5.3 Preclinical safety data

The administration of high doses of nitrofurantoin to rats causes temporary spermatogenic arrest; this is reversible on discontinuing the drug. Doses of 10 mg/ kg/day or greater in healthy human males may, in certain unpredictable instances, produce slight to moderate spermatogenic arrest with a decrease in sperm count.

Several reproduction studies have been performed in rabbits and rats at doses up to six times the human dose and have revealed no evidence of impaired fertility or harm to the foetus due to nitrofurantoin. In a single published study conducted in mice at 68 times the human dose (based on mg/kg administered to the dam), growth retardation and a low incidence of minor and common malformations were observed.

However, at 25 times the human dose, foetal malformations were not observed; the relevance of these findings to humans is uncertain. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nitrofurantoin has been shown in one published transplacental carcinogenicity study to induce lung papillary adenomas in the F1 generation mice at doses 19 times the human dose on a mg/kg basis. The relationship of this finding to potential human carcinogenesis is presently unknown.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Each capsule contains carbomer 934P, corn starch, compressible sugar, D&C Yellow No. 10, FD&C Blue No. 1, FD&C Red No. 40, gelatin, lactose, magnesium stearate, povidone, talc, and titanium dioxide. CONTAINS LACTOSE.

6.2 Incompatibilities

None

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25ºC.

6.5 Nature and contents of container

Macrobid is available as 100 mg opaque black and yellow modified-release capsules in a bottle of 100.

7 MEDICINE SCHEDULE

Prescription Only Medicine

8 SPONSOR DETAILS

Te Arai BioFarma Limited
PO Box 46205
Herne Bay Auckland 1011

0800 TE ARAI (83 2724)

9 DATE OF FIRST APPROVAL

1 October 2020

10 DATE OF REVISION OF THE TEXT

23 March 2025

Section Changed	Summary of New Information
2	Addition of Excipient(s) with known effect.
4.2	Update to include special populations, including use in renal impairment, use in hepatic impairment, and paediatric population.
4.3	Addition of contraindication for patients who have experienced prior pulmonary toxicity with nitrofurantoin, in acute porphyria and in G6PD deficiency.
4.4	Additional information added to pulmonary and hepatic reactions. New warnings about renal impairment and excipients added.
4.5	Additional information about interactions with carbonic anhydrase inhibitors, urine alkalinising agents, quinolone antimicrobials and methotrexate added.
4.6	Removal of preclinical data.
4.8	ADR table added. ADRs updated to align with UK SmPC for nitrofurantoin. ADR reporting link updated.
5.3	Information moved from section 4.6.