NEW ZEALAND DATA SHEET

1 NIFURAN TABLETS

NIFURAN 50mg tablet

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50 mg nitrofurantoin.

Excipient with known effect:
Gluten: NIFURAN 50mg tablets are gluten free.

Sugars as lactose: Each NIFURAN 50mg tablet contains 85.6mg of lactose monohydrate. If you have been told by your doctor that you may have intolerance to some sugars, please contact your doctor before taking this medicinal product.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

NITROFURANTOIN 50 mg tablets are yellow, round, scored tablets.
The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

NIFURAN is indicated for the prophylaxis and treatment of urinary tract infections due to susceptible bacteria.

Therapy with NIFURAN 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.

4.2 Dose and method of administration

Acute, Uncomplicated Urinary Tract Infections (acute cystitis)

Adults: Usual dose 50-100 mg four times daily for 7 days.

Children 3 months to under 12 years: 5-7 mg/kg body weight per 24 hours, given in four divided doses.

NIFURAN is available as a 50mg tablet only (refer Section 3)

Prophylactic Therapy (up to 6 months)

Adults: Usual dose 50-100 mg at bedtime.

Children 3 months to under 12 years: 1 mg/kg body weight per 24 hours, given in a single dose at night or in two divided doses

The duration of prophylactic therapy is for up to 6 months See section 4.4 Special warnings and precautions for use regarding risks associated with long-term therapy.

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.

If on prophylactic treatment, monitor renal function periodically throughout treatment and monitor for adverse effects.

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
See dosage information above.

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
Nitrofurantoin should be taken with food or milk.

4.3 Contraindications

NIFURAN 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 women at term, during labour and delivery, or when the onset of labour is imminent
- In neonates less than three months of age
- Patients with known hypersensitivity to the medicine or to any of the excipients (refer section 6.1).
- Acute porphyria
- G6PD deficiency
- Patients with a previous history of cholestatic jaundice/hepatic dysfunction or pulmonary toxicity associated with nitrofurantoin

4.4 Special warnings and precautions for use

Warnings

Pulmonary reactions
Acute, subacute, 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, the medicine should be discontinued immediately and appropriate measures taken.

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 x-ray, 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, dyspenoea or exertion, difficulty breathing, cough, coughing up blood or mucus, and altered pulmonary functions 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 Undesirable effects – 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 medicine 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 in those on long term therapy and 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).

Long term prophylactic treatment
Patients who are using nitrofurantoin for prophylaxis of urinary tract infections should be closely monitored throughout treatment, and the continued need for treatment regularly assessed.
Patients on prophylactic treatment are at greater risk of nitrofurantoin adverse reactions, including pulmonary and hepatic reactions. Appropriate monitoring is needed for early detection, and if suspected, nitrofurantoin should be discontinued.
See section 4.2 and 4.4.

Neuropathy
Peripheral neuropathy (including optic neuritis), 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.

Haemolytic anaemia
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. Haemolysis is an indication for discontinuing nitrofurantoin; haemolysis ceases when the medicine 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.

Use in the elderly
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 nitrofurantoin. 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.

Precautions

Patients should be advised to take nitrofurantoin with food to further enhance tolerance and improve its 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 at the same time as nitrofurantoin because of the possibility of impaired absorption.

The tendency of nitrofurantoin to impart a brown colour to the urine is of no clinical significance.

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 medicines, such as probenecid and sulphinpyrazone, 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.

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).

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

4.6 Fertility, pregnancy and lactation

Fertility

See section 5.3

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.

Breast-feeding

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

The most common clinical adverse events reported with use of nitrofurantoin are nausea, headache, and flatulence.

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	Increases AST (SGOT), increased ALT (SGPT), decreased haemoglobin, increased serum phosphorus, false positive urinary glucose

Description of selected adverse events

Neurologic
Peripheral neuropathy (including optic neuritis), 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), anaemia, diabetes mellitus, electrolyte imbalance, vitamin B deficiency, and debilitating diseases may increase the possibility of peripheral neuropathy (see section 4.4 Special warnings and precautions for use).

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 recognised early.

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 section 4.4 Special warnings and precautions for use.)

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 recognised as being drug-related and nitrofurantoin therapy is not stopped, the symptoms may become more severe.

Changes in EKG may occur associated with pulmonary reactions. Cyanosis has been reported rarely.

Hepatic
Hepatic reactions, including hepatitis, cholestatic jaundice, chronic active hepatitis, and hepatic necrosis, occur rarely (see section 4.4. Special warnings and precautions for use.)

Miscellaneous
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.

The most frequent laboratory test abnormalities reported with use of nitrofurantoin are 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 anaemia (see section 4.4 Special warnings and precautions for use), agranulocytosis, leukopenia, granulocytopenia, hemolytic anaemia, thrombocytopenia, megaloblastic anaemia. In most cases, these haematologic abnormalities resolved following cessation of therapy. Aplastic anaemia has been reported rarely.

Paediatric population
No information available.

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 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

Pharmacotherapeutic group: Nitrofuran derivatives – ATC code: J01XE01.

Microbiology

Nitrofurantoin is bactericidal in urine at therapeutic doses. 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. 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 sulfonamides 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:

Gram-Positive Aerobes:

- Coagulase-negative *staphylococci* (including *Staphylococcus epidermidis*)
- *Enterococcus faecalis*
- *Staphylococcus saprophyticus*
- *Staphylococcus aureus*
- *Streptococcus agalactiae*
- Group D *streptococci*
- Viridans group *streptococci*

Gram-Negative Aerobes:

- *Escherichia coli*
- *Citrobacter amalonaticus*
- *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 Tests

Diffusion Techniques

Quantitative methods that require measurement of zone diameters give the most precise estimate of the susceptibility of bacteria to antimicrobial agents. One such standard procedure, which has been recommended for use with disks to test susceptibility of organisms to nitrofurantoin, uses the 300 mcg nitrofurantoin disk. Interpretation involves the correlation of the diameter obtained in the disk test with the minimum inhibitory concentration (MIC) for nitrofurantoin.

Reports from the laboratory giving results of the standard single-disk susceptibility test with a 300 mcg nitrofurantoin disk should be interpreted according to the following criteria:

Zone Diameter (mm)	Interpretation
≥ 17	Susceptible
15-16	Intermediate
≤14	Resistant

A report of "susceptible" indicates that the pathogen is likely to be inhibited by generally achievable urinary levels. A report of "intermediate" indicates that the result be considered equivocal and, if the organism is not fully susceptible to alternative clinically feasible medicines, the test should be repeated. This category provides a buffer zone, which prevents small, uncontrolled technical factors from causing major discrepancies in interpretations. A report of "resistant" indicates that achievable concentrations are unlikely to be inhibitory, and other therapy should be selected.

Standardised procedures require the use of laboratory control organisms. The 300 mcg nitrofurantoin disk should give the following zone diameters:

Organism	Zone Diameter (mm)
E. coli ATCC 25922	20-25
S. aureus ATCC 25923	18-22

Dilution Techniques

Use a standardised dilution method (broth, agar, microdilution) or equivalent with nitrofurantoin powder. The MIC values obtained should be interpreted according to the following criteria:

MIC (mcg/mL)	Interpretation
≤32	Susceptible
64	Intermediate
≥128	Resistant

As with standard diffusion techniques, dilution methods require the use of laboratory control organisms. Standard nitrofurantoin powder should provide the following MIC values:

Organism	MIC (mcg/mL)
E. coli ATCC 25922	4-16
S. aureus ATCC 29213	8-32
E. faecalis ATCC 29212	4-16

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

Nitrofurantoin was not carcinogenic when fed to female Holtzman rats for 44.5 weeks or to female Sprague-Dawley rats for 75 weeks. Two chronic rodent bioassays utilising male and female Sprague-Dawley rats and two chronic bioassays in Swiss mice and in BDF1 mice revealed no evidence of carcinogenicity.

Nitrofurantoin presented evidence of carcinogenic activity in female B6C3F1 mice as shown by increased incidences of tubular adenomas, benign mixed tumors, and granulosa cell tumors of the ovary. In male F344/N rats, there was an increased incidence of uncommon kidney tubular cell neoplasms, osteosarcomas of the bone, and neoplasms of the subcutaneous tissue. In one study involving subcutaneous administration of 75 mg/kg nitrofurantoin to pregnant female mice, lung papillary adenomas of unknown significance were observed in the F1 generation.

Nitrofurantoin has been shown to induce point mutations in certain strains of *Salmonella typhimurium* and forward mutations in L5178Y mouse lymphoma cells. Nitrofurantoin induced increased numbers of sister chromatid exchanges and chromosomal aberrations in Chinese hamster ovary cells but not in human cells in culture. Results of the sex-linked recessive lethal assay in Drosophila were negative after administration of nitrofurantoin by feeding or by injection. Nitrofurantoin did not induce heritable mutation in the rodent models examined.

The significance of the carcinogenicity and mutagenicity findings relative to the therapeutic use of nitrofurantoin in humans is unknown.
The administration of high doses of nitrofurantoin to rats causes temporary spermatogenic arrest; this is reversible on discontinuing the medicine. Doses of 10 mg/kg/day or greater in healthy human males may, in certain unpredictable instances, produce a slight to moderate spermatogenic arrest with a decrease in sperm count.

Teratogenic effects
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.

Non-teratogenic effects
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.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

NIFURAN tablets contain the following excipients:

- Acacia
- Alginic acid
- Lactose monohydrate
- Maize starch
- Sodium laurilsulfate
- Sucrose

NIFURAN tablets are gluten free.

NIFURAN tablets contain lactose.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

60 months from date of manufacture

6.4 Special Precautions

Store at or below 25°C

6.5 Nature and contents of container

Bottles packs of 100 tablets.

6.6 Special precautions for disposal

No special requirements for disposal.

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

7 MEDICINE SCHEDULE

Prescription Only Medicine

8 SPONSOR

Clinect NZ Pty Limited
C/- Ebos Group Limited
108 Wrights Road
Christchurch 8024
New Zealand
Telephone: 0800 138 803

9 DATE OF FIRST APPROVAL

31 December 1969

10 DATE OF REVISION OF THE TEXT

13 August 2025

Summary Table of Changes

Section changed	Summary of new information
2	Excipients with known effect added
3	Information regarding scoreline added
4.1	Rewording of indications section (no change to the actual indications)
4.2	Removing use in neonates under 3 months Special Populations added • Use in Renal Impairment • Use in Hepatic Impairment • Paediatric population
4.3	Rewording on Contraindications. New contraindications added
4.4	Updated Warnings and Precautions
4.5	Additional interactions added
4.6	Teratogenic and non-teratogenic effects moved to 5.3 Pregnancy and Breastfeeding sections updated with additional information
4.8	Undesirable effects tabulated. Additional adverse reactions added to the table. New heading added 'Description of selected adverse reactions' Neurological and Miscellaneous sections updated. Allergic and Dermatologic removed.
5.3	Teratogenic and non-teratogenic effects from 4.6 moved here