

MACROFURAN

Capsules

Composition

Each capsule contains Nitrofurantoin 100 mg.

Action

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 that inactivate or alter bacterial ribosomal proteins and other macromolecules. Because of such inactivation, 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. 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.

Pharmacokinetics

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 that delay gastric emptying can increase the bioavailability of Nitrofurantoin by up to 40%.

Indications

Treatment of urinary tract infections such as pyelonephritis, pyelitis and cystitis, when due to susceptible organisms: *Escherichia coli*, enterococci, *Streptococcus pyogenes*, *Staphylococcus aureus* and certain strains of *Klebsiella*, *Aerobacter* and *Proteus*.

Contraindications

- Known hypersensitivity to Nitrofurantoin.
- Nitrofurantoin is contraindicated in patients with glucose-6-phosphate dehydrogenase deficiency, since the drug may cause blood-cell hemolysis.
- Contraindicated in the presence of anuria, oliguria and significantly impaired renal function (creatinine clearance less than 40 ml/min).

- Nitrofurantoin is contraindicated in pregnant women at term and in infants less than 1 month of age, because of the possibility of hemolytic anemia due to immature enzyme systems.

Warnings

If acute, subacute or chronic pulmonary reactions occur, the drug should be withdrawn and appropriate measures taken.

Any sign of hemolysis is an indication to discontinue the drug. The hemolysis appears to be linked to glucose-6-phosphate dehydrogenase deficiency in the red blood cells of affected patients and is reversible upon withdrawal of the drug.

The drug should be withdrawn immediately if paresthesia is reported.

Chronic active hepatitis has been observed rarely and is considered a hypersensitivity reaction. The onset is insidious and therapy with Nitrofurantoin thus requires periodic monitoring of liver function.

Pregnancy

Category B

Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women.

Nursing Mothers

Minimal concentrations of Nitrofurantoin found in breast milk. Safety of use of this drug in nursing mothers has not been established, and its use is absolutely contraindicated when the nursing infant is less than 1 month old.

Paediatric Use

Safety of use in children less than 12 years of age has not been established. Nitrofurantoin contraindicated in infants less than 1 month of age.

Adverse Reactions

Respiratory

Pulmonary hypersensitivity reactions may occur. Chronic pulmonary reactions usually occur only in patients who have received continuous treatment for six months or longer. Malaise, dyspnea on exertion, cough and altered pulmonary function are common manifestations that can occur insidiously. Radiological and histological 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.

Subacute pulmonary reactions may also appear. If therapy is not stopped, the symptoms may become more severe. Recovery may require several months.

Acute pulmonary reactions, characterized by fever, chills, dyspnea and pulmonary infiltration usually occur within the first week of therapy and are reversible on cessation of treatment.

Gastrointestinal

Anorexia, nausea, vomiting, abdominal pain, diarrhea and, rarely, hepatitis. Reduction of dosage may minimize these effects.

Dermatological

Eruption, pruritus, urticaria and angioedema.

Other Sensitivity Reactions

Hepatitis, anaphylaxis, asthmatic attacks, cholestatic jaundice, drug fever and arthralgia.

Hematological

Hemolytic anemia, granulocytopenia, eosinophilia and megaloblastic anemia. The blood system usually returns to normal following cessation of therapy.

Neurological

Peripheral neuropathy, headache, dizziness, nystagmus and drowsiness.

Other

Transient alopecia.

Super infections caused by resistant organisms may occur in the genitourinary tract.

The urine of patients taking Macrofan may be colored dark yellow or brown. This results from the presence of metabolites and is quite harmless.

Precautions

As with other antimicrobial agents, prolonged use may lead to superinfection. If this occurs, appropriate measures should be taken.

Nitrofurantoin may induce severe or irreversible peripheral neuropathy. This may be enhanced in the presence of such predisposing conditions as renal impairment, anemia, diabetes, electrolyte imbalance and vitamin B deficiency.

Drug Interactions*Nitrofurantoin / Anticholinergics*

Anticholinergics increase Nitrofurantoin bioavailability by slowing gastrointestinal motility.

Nitrofurantoin / Probenecid/ Sulfinpyrazone

Probenecid or sulfinpyrazone should not be used concurrently with Nitrofurantoin, since they may inhibit renal excretion of Nitrofurantoin and thus raise serum levels. This may reduce the efficacy of Nitrofurantoin and increase its toxic potential.

Nitrofurantoin / Magnesium Trisilicate

The rate of absorption of oral Nitrofurantoin may be decreased. A lapse of 2 hours is recommended if magnesium Trisilicate is to be administered.

Diagnostic Interference

Serum glucose, bilirubin, alkaline phosphatase, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT) and lactate dehydrogenase (LDH) levels may be increased.

Nitrofurantoin derivatives produce metabolites that may reduce urine glucose determination values (Benedict's reagent).

Dosage and Administration

Specimens for culture and susceptibility testing should be obtained prior to and during drug administration.

Macrofan may be given with food and milk in order to minimize gastric upset.

Macrofan therapy should be continued for at least 1 week and for at least 3 days after the urine is tested and found to be sterile.

Continued infection indicates the need for re-evaluation. The recommended adult dosage is 50-100 mg, 4 times daily.

In children over 1 month in age, the dosage should be calculated based on 5-7 mg/ kg body weight/ 24 hours, given in 4 divided doses.

Over Dosage

Excessive intake will probably cause vomiting. Should over dosage occur, gastric lavage is recommended.

There is no known specific antidote to Nitrofurantoin. A high fluid intake should be maintained to promote urinary excretion.

Presentation

Box of 24 capsules.