Macrodil®
(nitrofurantoin monohydrate/macrocrys|ts)
Capsules
To reduce the development of drug-resistant bacteria and maintain the effectiveness of
Macrodil® and other antibacterial drugs, Macrodil® should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.
DESCRIPTION: Nitrofurantoin is an antibacterial agent specific for urinary tract infections. The Macrodil® brand of nitrofurantoin is a fast disintegrating capsule containing the equivalent of 100 mg of nitrofurantoin in the form of 25 mg of nitrofurantoin macrocrystals and 75 mg of nitrofurantoin monohydrate.
The chemical name of nitrofurantoin macrocrystals is 1-[5-nitro-2-furanyl|methylene] aryl-2-imidazolidinedione. The chemical structure is the following:

Molecular Weight: 238.16

The chemical name of nitrofurantoin monohydrate is 1-[5-nitro-2-furanyl|methylene] aryl-2-imidazolidinedione. The chemical structure is the following:

Molecular Weight: 258.17


CLINICAL PHARMACOLOGY: Each Macrodil® capsule contains two forms of nitrofurantoin. Twenty-five percent is macrocrystalline nitrofurantoin, which has slow dissolution and absorption than nitrofurantoin monohydrate. The remaining 75% is nitrofurantoin monohydrate contained in a powder blend which, upon exposure to gastric and intestinal fluids, forms a gel matrix that releases nitrofurantoin over time. Based on urinary pharmacodynamic data, the extent and rate of urinary excretion of nitrofurantoin from the 100 mg Macrodil® capsule are similar to those of the 50 or 100 mg Nitrofurantoin® (nitrofurantoin macrol提现s) capsule. Approximately 20% to 25% of a single dose of nitrofurantoin is recovered from the urine unchanged.

Nitrofurantoin concentrations after a single oral dose of the 100 mg Macrodil® capsule are low, with peak levels usually less than 1 mcg/mL. Nitrofurantoin is highly soluble in water and may impart a brown color. When Macrodil® is administered with food, the bioavailability of nitrofurantoin is increased by approximately 40%

Mechanism of Action: Nitrofurantoin is a ribonucleic acid antimicrobial agent with activity against Gram-positive and Gram-negative bacteria.

Acute, subacute, or chronic pulmonary reactions have been observed in patients treated with nitrofurantoin. If these reactions occur, Macrodil® should be discontinued and appropriate measures taken. Reports have cited pulmonary reactions as a contributing cause of death.

Coagulase-negative staphylococci (including Staphylococcus epidermidis), Enterococcus faecalis, Streptococcus faecalis, Streptococcus agalactiae, Streptococcus haemolyticus, Klebsiella oxytoca, and Citrobacter freundii have been shown to be resistant to nitrofurantoin.

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

Infections caused by Pseudomonas aeruginosa, enteric gram-negative bacilli, and other aerobic and anaerobic gram-negative bacilli are generally resistant to nitrofurantoin.

Nitrofurantoin is bactericidal in concentrations less than or equal to the susceptible breakpoint for nitrofurantoin.

Nitrofurantoin is active against most strains of Escherichia coli when grown in triplet-selective media containing trimethoprim and nitrofurantoin.

Nitrofurantoin has been shown to be active against most strains of Proteus species or Serratia species. It has no activity against Pseudomonas species.

Auriculoauriculotemporal syndrome: Nitrofurantoin is bactericidal in concentrations less than or equal to the susceptible breakpoint for nitrofurantoin.

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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 male rats have caused an increase in the frequency of atypical spermatocytes and spermatids. The drug-related increase in the percentage of atypical spermatocytes is reversible on discontinuing the drug. Resolution often is dramatic. (See WARNINGS.)

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, dyspnea, 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 is often 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.

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

Hepatitis: Hepatic dysfunction, including hepatitis and cholestasis, has been reported rarely.

Hepatic: Hepatic adverse events, including hepatitis and jaundice, may occur rarely. (See WARNINGS.)

Hypersensitivity: Hypersensitivity reactions represent the most frequent spontaneously-reported adverse events in worldwide postmarketing experience with nitrofurantoin formulations. Hypersensitivity reactions include anaphylaxis, angioedema, urticaria, erythematous rash, pruritus, and pruritic or stingy erythematous eruptions. These adverse reactions have been reported rarely.

Skin: Controlled clinical trials of nitrofurantoin have not included sufficient numbers of subjects aged 65 or 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. In post-marketing surveillance, asymptomatic sterile pyuria and/or a disappeared or decreased nitrite reaction may be signs of lower urinary tract infection in patients over 65 years of age. In a study of nitrofurantoin in elderly patients with a mean age of 87 years, 27% of patients were reported to have had a false positive urine nitrite test in the absence of infection. This finding was not clearly related to the use of nitrofurantoin. Elderly patients, those with impaired renal function, and those with impaired hepatic function are more likely to have drug-related renal impairment. Elderly patients and impaired renal function are more likely to have decreased renal function. (See WARNINGS.)

ADVERSE EFFECTS: In clinical trials of nitrofurantoin, the most frequent clinical adverse effects reported were diarrhea, vomiting, nausea, and constipation. Other adverse effects included rash and urticaria, headache, dizziness, and weakness.

In general, the incidence of drug-related adverse effects may occur during or after antimicrobial therapy. (See WARNINGS.)

Neurologic: Peripheral neuropathy, which may become severe or irreversible, has occurred. Conditions such as renal impairment (creatinine clearance under 60 ml/min or clinically significant elevated serum creatinine) are contraindications (see CONTRAINDICATIONS). Because conditions that may be more likely to have decreased renal function, it may be useful to monitor renal function.

Anemia, neutropenia, and agranulocytosis have been reported rarely. Also, angioedema; maculopapular, erythematous, or eczematous eruptions; pruritus, urticaria, and angioedema have been reported rarely. Cyanosis secondary to methemoglobinemia has been reported rarely.

Miscellaneous: Cyanosis, which may occur rarely, has been reported rarely. Aplastic anemia, leukopenia, agranulocytosis, aplastic crisis, cytopenias, megaloblastic anemia, megaloblastic anemia, and megaloblastic anemia have been reported rarely. Also, angioedema; maculopapular, erythematous, or eczematous eruptions; pruritus, urticaria, and angioedema have been reported rarely. Cyanosis has been reported rarely. Allergic: Lipoatrophy syndrome associated with pulmonary reaction to nitrofurantoin has been reported rarely. Also, aplastic anemia; lymphoproliferative disorders; occupational dermatitis; angioedema; cyanosis; anaphylactic shock; urticaria; angioneurotic edema; hemolytic anemia; agranulocytosis; aplastic anemia; thrombocytopenia; megaloblastic anemia; and pancytopenia have been reported rarely. Also, angioedema; urticaria; maculopapular, erythematous, or eczematous eruptions; pruritus, urticaria, and angioedema have been reported rarely. Cyanosis has been reported rarely.

The use of nitrofurantoin may increase the risk of developing serious skin reactions. (See WARNINGS.)

The presence of a pustular rash on the skin and oral mucosa may be a sign of life-threatening Stevens-Johnson syndrome, toxic epidermal necrolysis, or hemolytic uremic syndrome. These conditions may be associated with life-threatening systemic complications. Stevens-Johnson syndrome, toxic epidermal necrolysis, and hemolytic uremic syndrome have been reported rarely. Also, angioedema; urticaria; maculopapular, erythematous, or eczematous eruptions; pruritus, urticaria, and angioedema have been reported rarely. Cyanosis has been reported rarely.

To report medical information to or to report SUSPECTED ADVERSE REACTIONS, contact Almatica Pharma at 1-877-447-7979 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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 drug. Nitrofurantoin is dialyzable.

DOSEAGE AND ADMINISTRATION: Macrodil capsules should be taken with food.

Adults and Pediatric Patients Over 12 Years: One 100 mg capsule every 12 hours for seven days.

HOW SUPPLIED: Macrodil is available as 100 mg opaque black and yellow capsules imprinted “band Macrodil (band)” on one half and “52427-285” on the other.

NDC 52427-383-01 bottle of 100

Store at controlled room temperature (68°F to 77°F or 15°C to 25°C). Rx Only

CLINICAL STUDIES: Controlled clinical trials comparing Macrodil 100 mg p.o. (12h) and Macrobid 50 mg p.o. q12h in the treatment of acute uncomplicated urinary tract infections demonstrated approximately 75% microorganism eradication of susceptible pathogens in each treatment group.

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