SHAKE VIGOROUSLY

Each teaspoonful (5 mL) contains 25 mg nitrofurantoin.

USUAL DOSAGE:

ADULT
50 to 100 mg four times a day with food.

CHILDREN
5 to 7 mg/kg of body weight per 24 hours, given in four divided doses. Read package insert for full prescribing information.

Dispense in tight, light-resistant amber bottles. Use within 30 days.

Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [See USP for Controlled Room Temperature]. Avoid exposure to strong light which may darken the drug. Protect from freezing. Keep this and all medication out of the reach of children.

DO NOT USE If Inner Foil Seal Printed “Sealed For Your Protection” is Broken or Missing

NDC 70408-239-32
Nitrofurantoin Oral Suspension, USP
25 mg/5 mL
FOR ORAL USE ONLY
URINARY TRACT ANTIBACTERIAL

Rx Only
240 mL

Shake vigorously

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DESCRIPTION:
Nitrofurantoin, a synthetic chemical, is a stable, yellow, crystals-
tominate compound. Nitrofurantoin Oral Suspension, USP is an antibacterial agent for specific urinary tract infections. Nitrofurantoin Oral Suspension, USP is available in 25 mg/mL liquid suspension for oral administration.

CLINICAL PHARMACOLOGY
Orally administered Nitrofurantoin Oral Suspension, USP is readily absorbed and rapidly excreted in urine. Blood concen-
trations at therapeutic dosage are usually low. It is highly soluble in water, to which it may impart a brown color.
Following a dose regimen of 100 mg q.i.d. for 7 days, average urinary drug recovery (0 to 24 hours) on day 1 and day 7 were 42.7% and 43.6%.
Unlike many drugs, the presence of food or agents delaying gastric emptying can increase the bioavailability of Nitrofurantoin Oral Suspension, USP, presumably by allowing better distribution in gastric juices.

Microbiology:
Model for Action: Nitrofurantoin is reduced by a wide range of enzymes including bacterial flavoproteins to reactive intermediates which are then oxidized to toxic intermediates of the natural product cytochrome pathway.

Interaction with Other Antimicrobials
Antagonism has been demonstrated in vitro between nitrofu-
rantoin and quinolone antimicrobial agents. Nitrofurantoin, in the form of Nitrofurantoin Oral Suspension, USP, has been shown to be active against most strains of the following bacteria both in vitro and in clinical infections: (See INDICA-
TIONS AND USAGE).

Gram-Positive Aerobes
• Staphylococcus aureus
• Streptococcus species

Gram-Negative Aerobes
• Escherichia coli

NOTE: Some strains of Enterobacter species and Klebsiella species are resistant to nitrofurantoin.
The following in vitro data are available, but their clinical significance has not been established. Nitrofurantoin exhibits in vitro activity against the following bacteria; however, the safety and effectiveness of nitrofurantoin in treating clinical infec-
tions due to these bacteria have not been established in adequate and well controlled clinical trials.

Gram-Positive Aerobes
• Coagulase-negative staphylococci (including Staphylo-
coccus epidermidis and Staphylococcus saprophyticus)
• Streptococcus agalactiae
• Viridans group streptococci

Gram-Negative Aerobes
• Citrobacter koseri
• Citrobacter freundii
• Klebsiella oxytoca
Nitrofurantoin is not active against the following species of Proteus species or Seratia species. It has no activity against Pseudomonas species.

Sensitivity Tests Methods
When available, the clinical microbiology laboratory should proced-
ure that results in vitro susceptibility test data for antimicrobial drugs used in local hospitals and practice areas to the physician as periodic reports that describe the suscept-
ibility profile of nosocomial and community-acquired pathogens. These reports should aid the physician in selecting an antibiotic drug product for treatment.

DIffusion Techniques
Quantitative methods that require measurement of zone diameters also provide reproducible estimates of the suscept-
bigility of bacteria to antimicrobial compounds. The zone size provides an estimate of the susceptibility of bacteria to antimicrobial compounds. The zone size should be deter-
mioned using a standardized method.1 This procedure uses paper disks impregnated with 300 mcg of nitrofurantoin to test the susceptibility of bacteria to nitrofurantoin. The disk diffusion interpretive criteria are provided in Table 1.

Table 1: Susceptibility interpretive criteria for Nitrofurantoin

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Minimum Inhibitory Concentrations (mcg/ml)</th>
<th>Disk Diffusion Zone Diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrofurantoin</td>
<td>=2.0 ≤16 ≤4 ≤2 ≤1 ≤0.5</td>
<td>=10 ≤14 ≤18 =20 ≤24 ≤28 ≤32</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>=2.0 ≤16 ≤4 ≤2 ≤1 ≤0.5</td>
<td>=10 ≤14 ≤18 =20 ≤24 ≤28 ≤32</td>
</tr>
<tr>
<td>Staphylococcus epidermidis</td>
<td>=2.0 ≤16 ≤4 ≤2 ≤1 ≤0.5</td>
<td>=10 ≤14 ≤18 =20 ≤24 ≤28 ≤32</td>
</tr>
<tr>
<td>Streptococcus species</td>
<td>=2.0 ≤16 ≤4 ≤2 ≤1 ≤0.5</td>
<td>=10 ≤14 ≤18 =20 ≤24 ≤28 ≤32</td>
</tr>
</tbody>
</table>

In susceptible, Intermediate, Resistant
A report of “Susceptible” indicates that the antimicrobial is likely to inhibit the growth of the pathogen if the antimicrobial compound reaches the concentration in the infection site necessary to inhibit growth of the pathogen. A report of “Intermediate” indicates that the result should be considered equivocal. and, if the microorganism is not fully susceptible to alternative, clini-
cally feasible drugs, the test should be repeated. This category should be used to classify the susceptibility of pathogenic bacteria when the antimicrobial compound if the antimicrobial compound reaches the concentrations usually achievable at the infection site; other therapy should be selected.

Quality Control
Standardized susceptibility test procedures require the use of labo-
atory controls to monitor and ensure the accuracy and precision of assays. Identification methods used in the assay, and the techniques of the individuals performing the test.1,2,3

INDICATIONS & USAGE
Nitrofurantoin Oral Suspension, USP is specifically indicated for the treatment of urinary tract infections when due to susceptible strains of Escherichia coli, enterococci, Staphylococcus aureus, and certain susceptible strains of Klebsiella and Enterobacter species.

Nitrofurantoin is not indicated for the treatment of pyelonephritis or pyonephrosis.

Nitrofurantoin lacks the broad tissue distribution other of other antimicrobial agents approved for urinary tract infections. Consequently, many patients who are treated with Nitrofurantoin Oral Suspension, USP are predisposed to persistence or reoccurrence of bacteriuria. Urine specimens for bacteriuria and susceptibility testing should be obtained before and after completion of therapy. If persistence or reap-
pearance of bacteriuria occurs after treatment with Nitrofurantoin Oral Suspension, USP, other therapeutic agents with broader tissue distribution should be selected. In considering the use of Nitrofurantoin Oral Suspension, USP; lower eradication rates should be balanced against the increased potential for systemic toxicity and for the develop-
ment of antimicrobial resistance when agents with broader tissue distribution are utilized.

CONTRAINDICATIONS:
Anuria, oliguria, or significant impairment of renal function (creatinine clearance under 60 ml per minute or clinically significant elevated serum creatinine) are contraindications. Treatment of this type of patient carries an increased risk of toxicity because of impaired elimination of the drug.
Because of the possibility of hemolytic anemia due to immaturity erythrocyte enzymes (glutathione instanta-
ybility), the drug is contraindicated in pregnant patients at term (38 to 42 weeks gestation), during labor and delivery, or when

the onset of labor is imminent. For the same reason, the drug is contraindicated in neonates under one month of age.
Nitrofurantoin Oral Suspension, USP is contraindicated in patients with a previous history of gastrointestinal dysfunction associated with nitrofurantoin. Nitrofurantoin Oral Suspension, USP is also contraindicated in those patients with known hypersensitivity to nitrofurantoin.

WARNINGS:

Pulmonary reactions:
ACUTE, SUBACUTE, OR CHRONIC PULMONARY REACTIONS HAVE BEEN OBSERVED IN PATIENTS TREATED WITH NITRO-
FURANTOIN ORAL SUSPENSION. IF THESE REACTIONS OCCUR RARELY AND GENERALLY IN PATIENTS RECEIVING THeraPY FOR SIX MONTHS OR LONGER. CLOSE MONI-
TURING OF THE CLINICAL CONDITION OF PATIENTS RECEIVING LONG-TERM THERAPY IS WARRANTED AND REQUIRES THE BENEFITS OF THERAPY BE WEIGHTED AGAINST POTENTIAL RISKS. (SEE RESPIRATORY REACTIONS).

Hepatotoxicity:
Hepatic reactions, including hepatitis, cholestatic jaundice, chronic active hepatitis, and hepatic necrosis, occur rarely. Fatalities have been reported. The onset of chronic active hepatitis may be insidious, and patients should be monitored periodically for changes in biochemical tests that would indicate liver injury. If hepatitis occurs, the drug should be stopped immediately and appropriate measures should be taken.

Neuropathy:
Peripheral neuropathy, which may become severe or irre-
solvable, 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, immunologic 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 postmarketing experience with nitrofurantoin formulations.

Hemolytic anemia:
Cases of hemolytic anemia of the primaquine-sensitivity type have been induced by nitrofurantoin. Hemolysis appears to be linked to a glucose-6-phosphate dehydrogenase defi-
ciency 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. Hemolysis is an indication for discontinuing Nitrofurantoin Oral Suspension, USP; hemolysis ceases when the drug is withdrawn.

Quinolone-difficile-associated diarrhoea:
Clindamycin associated diarrhoea (CDAD) has been reported with use of nearly all antibacterial agents, including Nitrofurantoin Orall Suspension, USP, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin-producing strains of C. difficile cause more morbidity and mortality, as these infections may be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea 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 should be discontinued, and appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated.

PRECAUTIONS:

Information for Patients:
Patients should be advised to take Nitrofurantoin Oral Suspension, USP with food 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 should occur during therapy.

Diarrhea is a common problem caused by antibiotics which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with antibiotics, patients can develop loose (non-bloody) stools (with or without diarrhea 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.

Patients should be advised not to use antacid preparations containing magnesium trisilicate while taking Nitrofurantoin Oral Suspension, USP.
DOSAGE AND ADMINISTRATION

Nitrofurantoin Oral Suspension, USP should be given with food to improve drug absorption and, in some patients, tolerance.

Pediatric Patients:

5 to 7 mg/kg of body weight per 24 hours, given in four divided doses (concomitant under one month of age).

The following table is based on an average weight in each dosage range receiving 5 to 6 mg/kg of body weight per 24 hours, given in four divided doses. It can be used to calculate an average dose of Nitrofurantoin Oral Suspension, USP (25 mg/mL).

<table>
<thead>
<tr>
<th>Weight in Kilograms (kg)</th>
<th>Pediatric Doses (milliliters) and Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 kg to 11 kg</td>
<td>2.5 mL, Four times Daily</td>
</tr>
<tr>
<td>12 kg to 21 kg</td>
<td>5 mL, Four times Daily</td>
</tr>
<tr>
<td>22 kg to 30 kg</td>
<td>7.5 mL, Four times Daily</td>
</tr>
<tr>
<td>31 kg to 41 kg</td>
<td>10 mL, Four times Daily</td>
</tr>
<tr>
<td>42 kg or greater</td>
<td>Adult Dose</td>
</tr>
</tbody>
</table>

Therapy should be continued for one week or for at least 3 days after sterilization of the urinary tract is obtained. Continued infection indicates the need for reevaluation.

For long-term suppressive therapy in adults, a reduction of dosage to 50 to 100 mg at bedtime may be adequate. For long-term suppressive therapy in pediatric patients, doses as low as 1 mg/kg per 24 hours, given in a single dose or in two divided doses, may be adequate. SEE WARNINGS SECTION REGARDING RISKS ASSOCIATED WITH LONG TERM THERAPY.

HOW SUPPLIED:

Nitrofurantoin Oral Suspension, USP is a lemon yellow liquid with a fruity scent available in:

NDC 70408-230-92 240 mL amber PET bottle
NDC 70408-239-34 480 mL amber PET bottle

Avoid exposure to strong light which may darken the drug. Store at 25° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [See USP (For Controlled Room Temperature). Protect from freezing. Shake vigorously. Dispense in a light, tight-resistant container made of either glass or amber plastic. Use within 30 days. Keep this and all medication out of the reach of children.

REFERENCES


Manufactured by:

Rextron Laboratories, Inc.
7040 Tillery, OH 43068

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