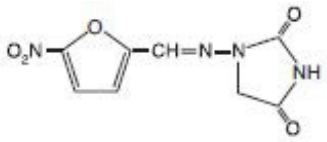
NITROFURANTOIN ORAL SUSPENSION- nitrofurantoin oral suspension suspension
PAI Holdings, LLC dba PAI Pharma

NITROFURANTOIN ORAL SUSPENSION, USP
FOR ORAL USE ONLY
Rx Only

DESCRIPTION

Nitrofurantoin, a synthetic chemical, is a stable, yellow, crystalline compound. Nitrofurantoin Oral Suspension, USP is an antibacterial agent for specific urinary tract infections.

Nitrofurantoin Oral Suspension, USP is available in 25 mg/5 mL liquid suspension for oral administration.



Inactive Ingredients:

Nitrofurantoin Oral Suspension, USP contains carboxymethylcellulose sodium, citric acid, glycerin, magnesium aluminum silicate, methylparaben, N&A fruit gum flavor #960 (MN72), propylparaben, purified water, sodium citrate, sorbitol, and sucralose.

CLINICAL PHARMACOLOGY

Orally administered Nitrofurantoin Oral Suspension, USP is readily absorbed and rapidly excreted in urine. Blood concentrations at therapeutic dosage are usually low. It is highly soluble in urine, to which it may impart a brown color.

Following a dose regimen of 100 mg q.i.d. for 7 days, average urinary drug recoveries (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 dissolution in gastric juices.

Microbiology:

Mode of Action
Nitrofurantoin is reduced by a wide range of enzymes including bacterial flavoproteins to reactive intermediates which are damaging to macromolecules such as DNA and proteins.

Cross-Resistance

Although cross-resistance with other antimicrobials may occur, cross resistance with sulfonamides has not been observed.

Interaction with Other Antimicrobials
Antagonism has been demonstrated *in vitro* between nitrofurantoin 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 **INDICATIONS AND USAGE**).

Gram-Positive Aerobes
- *Staphylococcus aureus*
- *Enterococcus 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 is unknown. Nitrofurantoin exhibits *in vitro* activity against the following bacteria; however, the safety and effectiveness of nitrofurantoin in treating clinical infections due to these bacteria have not been established in adequate and well controlled clinical trials.

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

Gram-Negative Aerobes
- *Citrobacter koseri*
- *Citrobacter freundii*
- *Klebsiella oxytoca*

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

Susceptibility Testing
For specific information regarding susceptibility test interpretive criteria, and associated test methods and quality control standards recognized by FDA for this drug, please see:
http://www.fda.gov/STIC.

INDICATIONS AND 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 perinephric abscesses.

Nitrofurantoins lack the broader tissue distribution of other therapeutic agents approved for urinary tract infections. Consequently, many patients who are treated with Nitrofurantoin Oral Suspension, USP are predisposed to persistence or reappearance of bacteriuria. Urine specimens for culture and susceptibility testing should be obtained before and after completion of therapy. If persistence or reappearance 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 development 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 excretion of the drug.

Because of the possibility of hemolytic anemia due to immature erythrocyte enzyme systems (glutathione instability), 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 cholestatic jaundice/hepatic 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 NITROFURANTOIN. IF THESE REACTIONS OCCUR, NITROFURANTOIN ORAL SUSPENSION, USP SHOULD BE DISCONTINUED AND APPROPRIATE MEASURES TAKEN. REPORTS HAVE CITED PULMONARY REACTIONS AS A CONTRIBUTING CAUSE OF DEATH.

CHRONIC PULMONARY REACTIONS (DIFFUSE INTERSTITIAL PNEUMONITIS OR PULMONARY FIBROSIS, OR BOTH) CAN DEVELOP INSIDIOUSLY. THESE REACTIONS OCCUR RARELY AND GENERALLY IN PATIENTS RECEIVING THERAPY FOR SIX MONTHS OR LONGER. 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 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 withdrawn immediately and appropriate measures should be taken.

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 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 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. Hemolysis is an indication for discontinuing Nitrofurantoin Oral Suspension, USP; hemolysis ceases when the drug is withdrawn.

Clostridium difficile-associated diarrhea:
Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including Nitrofurantoin Oral Suspension, USP, and may range in severity from mild diarrhea 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 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 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.

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

DRUG INTERACTIONS

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.

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 the glucose enzymatic test.

Carcinogenesis, Mutagenesis, Impairment of Fertility

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 utilizing male and female Sprague-Dawley rats and two chronic bioassays in Swiss mice and in BDF^1 mice revealed no evidence of carcinogenicity.

Nitrofurantoin presented evidence of carcinogenic activity in female $B6C3F_1$ 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 were increased incidences 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 on 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 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 drug. 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.

PREGNANCY:

Teratogenic effects:

Pregnancy Category B. 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 fetus 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, fetal 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.

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. The relationship of this finding to potential human carcinogenesis is presently unknown. Because of the uncertainty regarding the human implications of these animal data, this drug should be used during pregnancy only if clearly needed.

LABOR AND DELIVERY:

See **CONTRAINDICATIONS**.

Nursing Mothers

Nitrofurantoin has been detected in human breast milk in trace amounts. Because of the potential for serious adverse reactions from nitrofurantoin in nursing infants under one month of age, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. (See **CONTRAINDICATIONS**.)

Pediatric Use

Safety and effectiveness of Nitrofurantoin Oral Suspension, USP in neonates below the age of one month have not been established. (See **CONTRAINDICATIONS**.)

ADVERSE REACTIONS

Respiratory:

CHRONIC, SUBACUTE, OR ACUTE PULMONARY HYPERSENSITIVITY REACTIONS MAY OCCUR. CHRONIC PULMONARY REACTIONS MAY OCCUR GENERALLY IN PATIENTS WHO HAVE RECEIVED CONTINUOUS TREATMENT FOR SIX MONTHS

OR LONGER. MALAISE, DYSPNEA 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 DEGREES 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, dyspnea, pulmonary infiltration with consolidation of 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 neurosis, occur rarely. (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**.)

Asthenia, vertigo, nystagmus, dizziness, headache, and drowsiness have also been reported with the use of nitrofurantoin.

Benign intracranial hypertension (pseudotumor cerebri), confusion, depression, optic neuritis, and psychotic reactions have been reported rarely. Bulging fontanels, as a sign of benign intracranial hypertension in infants, have been reported rarely.

Dermatologic:

Exfoliative dermatitis and erythema multiforme (including Stevens-Johnson syndrome) have been reported rarely. Transient alopecia also has been reported.

Allergic:

A lupus-like syndrome associated with pulmonary reactions to nitrofurantoin has been

reported. Also, angioedema; maculopapular, erythematous, or eczematous eruptions; pruritus; urticaria; anaphylaxis; arthralgia; myalgia; drug fever; and vasculitis (sometimes associated with pulmonary reactions) have been reported. Hypersensitivity reactions present the most frequent spontaneously-reported adverse events in world-wide postmarketing experience with nitrofurantoin formulations.

Gastrointestinal:

Nausea, emesis, and anorexia occur most often. Abdominal pain and diarrhea are less common gastrointestinal reactions. These dose-related reactions can be minimized by reduction of dosage. Sialadenitis and pancreatitis have been reported. 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**.)

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. There are sporadic reports of Clostridium difficile superinfections, or pseudomembranous colitis, with the use of nitrofurantoin.

Laboratory Adverse Events:

The following laboratory adverse events have been reported with the use of nitrofurantoin; increased AST (SGOT), increased ALT (SGPT), decreased hemoglobin, increased serum phosphorus, eosinophilia, glucose-6-phosphate dehydrogenase deficiency anemia (see **WARNINGS**), agranulocytosis, leukopenia, granulocytopenia, hemolytic anemia, thrombocytopenia, megaloblastic anemia. In most cases, these hematologic abnormalities resolved following cessation of therapy. Aplastic anemia has been reported rarely.

To report SUSPECTED ADVERSE REACTIONS, contact PAI Pharma at 1-800-845-8210 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

OVERDOSAGE

Occasional incidents of acute overdosage of Nitrofurantoin Oral Suspension, USP 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. It is dialyzable.

DOSAGE AND ADMINISTRATION

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

Adults:

50 to 100 mg four times a day — the lower dosage level is recommended for

uncomplicated urinary tract infections.

Pediatric Patients:

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

The following table is based on an average weight in each 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/5 mL) for pediatric patients.

Table 3: Pediatric Dosing Table

Weight in Kilograms (kg)	**Pediatric Doses (milliliters) and Frequency**
7 kg to 11 kg	2.5 mL Four times Daily
12 kg to 21 kg	5 mL Four times Daily
22 kg to 30 kg 7.5 mL	Four times Daily
31 kg to 41 kg 10 mL	Four times Saily
42 kg or greater	See Adult Dose

Therapy should be continued for one week or for at least 3 days after sterility of the urine 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 0121-1996-10: 10 mL unit dose cup. Case contains 10 unit-dose cups of 10 mL (NDC 0121-1996-95), packaged in one tray of 10 unit-dose cups each.

Avoid exposure to strong light which may darken the drug. This package is child-resistant. 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]. Protect from freezing. Shake vigorously. Use within 90 days

Keep this and all medication out of the reach of children.

Distributed by:

PAI Pharma
Greenville, SC 29605

R01/24

PRINCIPAL DISPLAY PANEL

NDC 0121-1996-05

Nitrofurantoin Oral Suspension, USP
50 mg/10 mL
FOR ORAL USE ONLY

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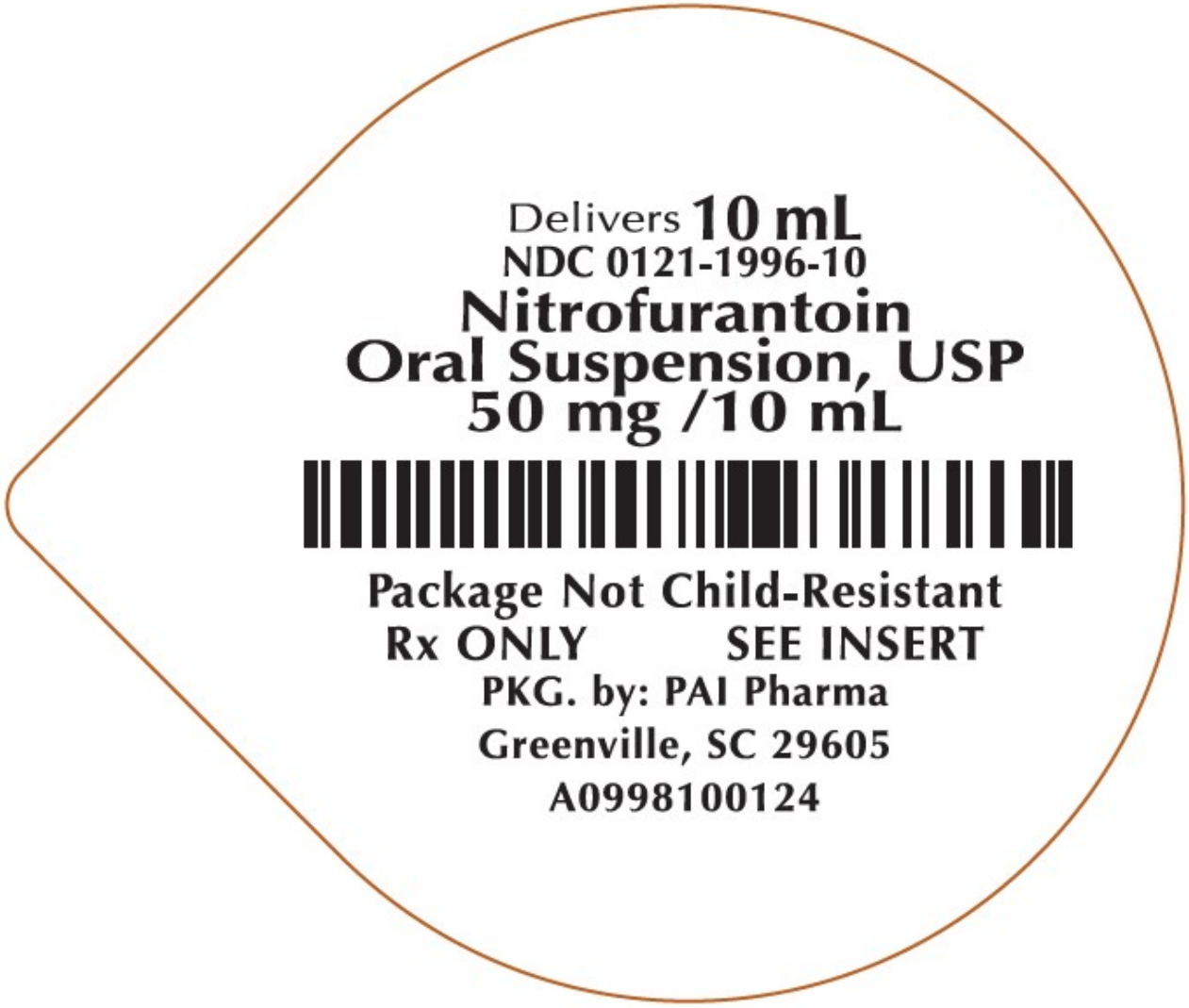

NITROFURANTOIN ORAL SUSPENSION

nitrofurantoin oral suspension suspension

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0121-1996(NDC:70408-239)
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
NITROFURANTOIN (UNII: 927AH8112L) (NITROFURANTOIN - UNII:927AH8112L)	NITROFURANTOIN	25 mg in 5 mL

Inactive Ingredients

Ingredient Name	Strength
CARBOXYMETHYLCELLULOSE SODIUM (UNII: K679OBS311)	
ANHYDROUS CITRIC ACID (UNII: XF417D3PSL)	
GLYCERIN (UNII: PDC6A3C0OX)	
MAGNESIUM ALUMINUM SILICATE (UNII: 6M3P64V0NC)	
METHYLPARABEN (UNII: A2I8C7HI9T)	
PROPYLPARABEN (UNII: Z8IX2SC1OH)	
WATER (UNII: 059QF0KO0R)	
SODIUM CITRATE (UNII: 1Q73Q2JULR)	
SORBITOL (UNII: 506T60A25R)	
SUCRALOSE (UNII: 96K6UQ3ZD4)	

Product Characteristics

Color	yellow	**Score**	
Shape		**Size**	
Flavor	FRUIT	**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0121-1996-95	10 in 1 CASE	06/10/2024	04/30/2026
1	NDC:0121-1996-10	10 mL in 1 CUP, UNIT-DOSE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA201355	06/10/2024	04/30/2026

Labeler - PAI Holdings, LLC dba PAI Pharma (044940096)

Revised: 11/2025 PAI Holdings, LLC dba PAI Pharma