8026186-9093

For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

NFTOR

(Nitrofurantoin SR Tablets)

Composition:

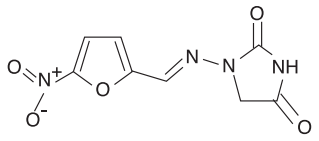
Each uncoated sustained release tablet contains :

Nitrofurantoin I.P. 100 mg

Excipients q.s

Discription:

The chemical name of NFTOR is 1-(5-nitrofurfury lideneamino)imidazolidine-2,4-dione. Its molecular formula is $C_8H_6N_4O_5$ and has a molecular weight of 238.2. The structural formula is :



Pharmacodynamics:

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.

Pharmacokinetics:

Nitrofurantoin is partially metabolized, mainly in the liver. A small fraction of the drug is reduced to form aminofurantoin. About 40% is excreted unchanged into urine.

Dosage and Method of Administration:

The normal adult dose of NFTOR is 100 mg twice daily. NFTOR should be taken with food, as this improves the absorption of the drug by 45%. The tablet should be swallowed and not chewed, cut or crushed from its original form.

Indications:

For the treatment of acute uncomplicated urinary tract infections (acute cystitis) caused by susceptible strains of *Escherichia coli* or *Staphylococcus saprophyticus.*

Contraindications :

Hypersensitivity to any components of this product.

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 the drug is contraindicated in pregnant patients, during labor and delivery, or when the onset of labor is imminent. For the same reason, the drug is contraindicated in neonates.

Nitrofurantoin is contraindicated in patients with a previous history of cholestatic jaundice/hepatic dysfunction associated with nitrofurantoin.

Warnings and Precautions:

Pulmonary reactions:

Acute, subacute, or chronic pulmonary reactions have been observed in patients treated with nitrofurantoin. If these reactions occur, NFTOR 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.

Hepatotoxicity:

Hepatic reactions, including hepatitis, cholestatic jaundice, chronic active hepatitis, and hepatic necrosis, occur rarely. Fatalities have been reported. 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, 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:

Hemolysis is an indication for discontinuing nitrofurantoin; 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, and may range in severity from mild diarrhea to fatal colitis.

Precautions:

NFTOR is contraindicated in patients with glucose-6-phosphate dehydrogenase deficiency because of risk of extravascular hemolysis resulting in anemia.

Information for Patients: Patients should be advised to take nitrofurantoin 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 occur during therapy.

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.

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 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 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 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 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: Pregnancy Category B. In a single published study conducted in mice at 68 times the human dose, 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. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

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

Pediatric Use: Nitrofurantoin in contraindicated in infants below the age of one month.

Geriatric Use: 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. Spontaneous reports also suggest an increased proportion of severe hepatic reactions, including fatalities, in elderly patients. Elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

ADVERSE REACTIONS:

NFTOR cause nausea and vomiting, fever, rash. It can also cause pulmonary fibrosis. All these side effects are much more common in the elderly. Patients should be informed that nitrofurantoin colours urine a dark orange-brown; this is completely harmless. Neonates (babies up to the age of one month) have immature enzyme systems in their red blood cells (glutathione instability) and nitrofurantoin must therefore not be used because it can cause haemolytic anaemia. For the same reason, nitrofurantoin should not be given to pregnant women after 38 weeks of pregnancy, or who are about to give birth. NFTOR is contraindicated in patients with decreased renal function due to systemic accumulation and subtherapeutic levels reached in the urinary tract.

Respiratory:

Chronic, subacute, or acute pulmonary hypersensitivity reactions may occur. Chronic pulmonary reactions 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 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 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 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.

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 necrosis, occur rarely.

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.

Asthenia, vertigo, nystagmus, dizziness, headache, and drowsiness also have 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: Hypersensitivity reactions, 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 chills have been reported

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.

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.

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, 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.

Overdosage:

There is no specific antidote, but a high fluid intake should be maintained to promote urinary excretion of the drug. It is dialyzable.

Expiry Date :

Do not use later than the date of expiry

Legal Status: Rx

Route of administration: Oral

Storage :

Store below 25^{o}C, Protect from light and moisture.

Keep out of the reach of children.

Presentation :

NFTOR is available as blister strip of 10 tablets.

torrent

Marketed by :
TORRENT PHARMACEUTICALS LTD.
Indrad-382 721, Dist. Mehsana, INDIA.

Manufactured by :
CORONET LABS PVT. LTD.
Nanhera Anantpur, Puhana- Iqubalpur Road,
Roorkee, Distt. Haridwar (Uttarakhand)