**NAME:IKPEN JOSHUA**

**DEPARTMENT:PHARMACOLOGY**

**MATRIC:17/MHS07/013**

**COURSE CODE:306**

**COURSE:ORGAN SYSTEMS CVS,RENA,RESPIRATORY AND GIT**

**DRUG NAME**

**Nitrofurantoin**, sold under the trade name **Macrobid** among others.[[1]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-AHFS2015-1) It is an [antibiotic](https://en.m.wikipedia.org/wiki/Antibiotic) used to treat [bladder infections](https://en.m.wikipedia.org/wiki/Bladder_infection), but is not as effective for [kidney infections](https://en.m.wikipedia.org/wiki/Pyelonephritis).[[1]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-AHFS2015-1) It is taken by mouth.[[1]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-AHFS2015-1)

Common side effects include nausea, loss of appetite, diarrhea, and headaches.[[1]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-AHFS2015-1) Rarely [numbness](https://en.m.wikipedia.org/wiki/Peripheral_neuropathy), lung problems, or liver problems may occur.[[1]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-AHFS2015-1) It should not be used in people with kidney problems.[[1]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-AHFS2015-1) While it appears to be generally safe during pregnancy it should not be used near delivery.[[1]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-AHFS2015-1)[[2]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-TGA2014-2) While it usually works by slowing bacterial growth, it may result in bacterial death at the high concentrations found in urine.[[1]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-AHFS2015-1)

Nitrofurantoin was first sold in 1953.[[3]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-Ben2015-3) It is on the [World Health Organization's List of Essential Medicines](https://en.m.wikipedia.org/wiki/WHO_Model_List_of_Essential_Medicines), the safest and most effective medicines needed in a [health system](https://en.m.wikipedia.org/wiki/Health_system).[[4]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-WHO21st-4) It is available as a [generic medication](https://en.m.wikipedia.org/wiki/Generic_medication).[[1]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-AHFS2015-1) The wholesale cost in the [developing world](https://en.m.wikipedia.org/wiki/Developing_world) is between 0.10 and 9.20 USD for a course of treatment.[[5]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-ERC2015-5) In the United States, the wholesale cost is about 8 USD for this amount as of 2018.[[6]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-NADAC2018-6) In 2016 it was the 186th most prescribed medication in the United States with more than three million prescriptions.[[7]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-7)

## PHARMACOLOGY

Organisms are said to be susceptible to nitrofurantoin if their [minimum inhibitory concentration](https://en.m.wikipedia.org/wiki/Minimum_inhibitory_concentration) is 32 [μg](https://en.wiktionary.org/wiki/microgram%22%20%5Co%20%22wiktionary%3Amicrogram)/ml or less. The peak blood concentration of nitrofurantoin following an oral dose of nitrofurantoin 100 mg, is less than 1 μg/ml and may be undetectable. Its bioavailability is about 90% and the urinary excretion is 40%[[28]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-28)[[*full citation needed*](https://en.m.wikipedia.org/wiki/Wikipedia%3ACiting_sources#What_information_to_include)] tissue penetration is negligible; the drug is well concentrated in the urine: 75% of the dose is rapidly metabolised by the liver, but 25% of the dose is excreted in the urine unchanged, reliably achieving levels of 200 μg/ml or more. In studies of dogs, the majority of urinary excretion is through glomerular filtration with some tubular secretion.[[29]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-:1-29) There is also tubular absorption which is increased with urine acidification.[[29]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-:1-29) However the activity of nitrofurantoin is also pH dependent and mean inhibitory concentration rises sharply with increased pH above 6.[[29]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-:1-29) Nitrofurantoin cannot be used to treat infections other than simple [cystitis](https://en.m.wikipedia.org/wiki/Cystitis).

At the concentrations achieved in urine (>100 μg/ml), nitrofurantoin is a [bactericide](https://en.m.wikipedia.org/wiki/Bactericide). It is [bacteriostatic](https://en.m.wikipedia.org/wiki/Bacteriostatic) against most susceptible organisms at concentrations less than 32 μg/ml.[[8]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-Macrobid_Drug_Label1-8)

Nitrofurantoin and the [quinolone antibiotics](https://en.m.wikipedia.org/wiki/Quinolone_antibiotic) are mutually antagonistic *in vitro*. It is not known whether this is of clinical significance, but the combination should be avoided.[[8]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-Macrobid_Drug_Label1-8)

Resistance to nitrofurantoin may be chromosomal or plasmid-mediated and involves inhibition of nitrofuran reductase.[[30]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-30) Acquired resistance in *E. coli* continues to be rare.

Nitrofurantoin and its metabolites are excreted mainly by the kidneys. In renal impairment, the concentration achieved in urine may be subtherapeutic. Nitrofurantoin should not be used in patients with a [creatinine clearance](https://en.m.wikipedia.org/wiki/Creatinine_clearance) of 60 ml/min or less. However, a retrospective chart review may suggest nitrofurantoin is not contraindicated in this population

MECHANISM OF ACTION

Nitrofurantoin is concentrated in the urine, leading to higher and more effective levels in the [urinary tract](https://en.m.wikipedia.org/wiki/Urinary_system) than in other tissues or [compartments](https://en.m.wikipedia.org/wiki/Compartment_%28pharmacokinetics%29).[[21]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-:0-21) With a 100 mg oral dose, [plasma](https://en.m.wikipedia.org/wiki/Blood_plasma) levels are typically less than 1 [µg](https://en.m.wikipedia.org/wiki/Microgram)/ml while in the urine it reaches 200 µg/ml.[[34]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-34)

The mechanism of action is unique and complex. The drug works by damaging bacterial [DNA](https://en.m.wikipedia.org/wiki/DNA), since its reduced form is highly reactive.[[8]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-Macrobid_Drug_Label1-8) This is made possible by the rapid reduction of nitrofurantoin inside the bacterial cell by [flavoproteins](https://en.m.wikipedia.org/wiki/Flavoprotein) (nitrofuran reductase) to multiple reactive intermediates that attack [ribosomal](https://en.m.wikipedia.org/wiki/Ribosome) proteins, DNA,[[35]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-35) respiration, [pyruvate](https://en.m.wikipedia.org/wiki/Pyruvate) metabolism and other macromolecules within the cell. Nitrofurantoin exerts greater effects on bacterial cells than mammalian cells because bacterial cells activate the drug more rapidly. It is not known which of the actions of nitrofurantoin is primarily responsible for its bactericidal activity. The broad mechanism of action for this drug likely is responsible for the low development of resistance to its effects, as the drug affects many different processes important to the bacterial cell.[[8]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-Macrobid_Drug_Label1-8)

## History

### **PHARMACOKINETICS, ROUTE OF ADMINISTRATION AND DOSAGE**

Nitrofurantoin is administered orally as a microcrystalline or macrocrystalline formulation, of which the latter has a slower absorption rate. Absorption is almost complete, with 2–4% of the dose being recovered from the feces.18 Serum concentrations are not measurable, except in patients who have [severe renal failure](https://www.sciencedirect.com/topics/medicine-and-dentistry/severe-renal-impairment). This is because of destruction of nitrofurantoin in the tissues and, in particular, a very rapid [renal elimination](https://www.sciencedirect.com/topics/medicine-and-dentistry/urinary-excretion) by [glomerular filtration](https://www.sciencedirect.com/topics/medicine-and-dentistry/glomerulus-filtration) (20%) and tubular secretion, resulting in a [serum half-life](https://www.sciencedirect.com/topics/medicine-and-dentistry/plasma-half-life) of only 20 minutes in patients who have normal renal function.18 Excretion is complete within 6 hours after intake and [urine concentrations](https://www.sciencedirect.com/topics/medicine-and-dentistry/kidney-concentrating-capacity) of 200–400 mg/l are achieved after a dose of 100 mg q8h. In patients who have renal failure – who should not be given nitrofurantoin – there are measurable but still very low serum and urine concentrations.19

Therapeutic doses of nitrofurantoin are 50–100 mg q8h or q6h for adults and 3 mg/kg/day q12h or q8h for children. Prophylactically, the adult dose is 50–100 mg and the pediatric dose 1–2 mg/kg at bedtime. The duration of treatment when nitrofurantoin is used therapeutically should be 5–7 days. Dosages are not affected by liver function.

## ADVERSE EFFECTS

## The most common side effects with nitrofurantoin are nausea, headache, and flatulence. Less common adverse events (occurring in less than 1% of those taking the drug) include:[[8]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-Macrobid_Drug_Label1-8)

* Gastrointestinal: diarrhea, [dyspepsia](https://en.m.wikipedia.org/wiki/Dyspepsia), abdominal pain, constipation, [emesis](https://en.m.wikipedia.org/wiki/Emesis)
* Neurologic: dizziness, drowsiness, [amblyopia](https://en.m.wikipedia.org/wiki/Amblyopia)
* Respiratory: acute pulmonary hypersensitivity reaction
* Allergic: [pruritus](https://en.m.wikipedia.org/wiki/Pruritus), [urticaria](https://en.m.wikipedia.org/wiki/Urticaria%22%20%5Co%20%22Urticaria)
* Dermatologic: [hair loss](https://en.m.wikipedia.org/wiki/Hair_loss)
* Miscellaneous: fever, chills, malaise

Patients should be informed that nitrofurantoin colours urine brown; this is completely harmless.[[8]](https://en.m.wikipedia.org/wiki/Nitrofurantoin#cite_note-Macrobid_Drug_Label1-8)

Some of the more serious but rare side effects of nitrofurantoin have been a cause of concern. These include pulmonary reactions, hepatotoxicity, and neuropathy.