AGOG Pharma Ltd.
(WHO - GMP CERTIFIED - GOVT RECOGNISED EXPORT HOUSE)
Regd. Office & Factory : Plot No. 33, Sector II, The Vasai Taluka Industrial Co-op. Estate Ltd. Gauraipada, Vasai (E), Dist. Thane - 401 208. INDIA.
Tel. : 95250 - 2455801 / 2452714 / 2453525 • Fax : 95250 - 2452074 (0091 - 250 - 2452074) • Email : agog@vsnl.net & agogpharma@rediffmail.com

Brand Name : **AGOTOIN TABLETS** **Generic Name** : NITROFURANTOIN TABLETS BP 100 MG		2021
Module 1 **1.5**	Administrative Information and Product Information Product Information	**Confidential**

1.5 PRODUCT INFORMATION

1.5.1 Prescribing Information (Summary of Products Characteristics)

1. NAME OF DRUG PRODUCT

1. Name of drug product

NITROFURANTOIN BP 100 MG TABLETS

1.1 (Trade) name of product

AGOTOIN TABLETS

1.2 Strength

Each uncoated tablet contains:
Nitrofurantoin BP 100 mg

1.3 Pharmaceutical Dosage Form

Uncoated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITIONS

2.1 Qualitative Declaration

Each uncoated tablet contains:
Nitrofurantoin BP 100 mg

2.2 Quantitative Declaration

Ingredients	Specification	Label Claim	Qty. / Tab.
ACTIVE			
Nitrofurantoin	BP	100 mg	100.00 mg
INACTIVE			
2. Lactose	BP	-	48.00 mg
3. Microcrystalline Cellulose Powder	BP	-	20.00 mg
4. Poly vinyl pyrrolidone k-30	BP	-	5.000 mg
5. Isopropyl Alcohol	BP	-	60.00 mg
6. Purified talc	BP	-	2.000 mg
7. Magnesium stearate	BP	-	1.000 mg
8. Sodium starch glycolate	BP	-	2.000 mg
9. Cross carmellose sodium	BP	-	2.000 mg
10. Polyplasdone XL-10	USP	-	5.000 mg
11. Polacrillin Potassium	USP	-	5.000 mg

BP = British Pharmacopoeia.
USP = united state pharmacopoeia

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3. PHARMACEUTICAL DOSAGE FORM

Uncoated tablets

Yellow coloured, circular, flat, uncoated tablets having embossed ‘AGOG’ on one side & a breakline on the other side of each tablets.

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4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

A bacteriostatic or bactericidal agent depending on the concentration and susceptibility of the infecting organism. Nitrofurantoin is active against some gram positive organisms such as S. aureus, S. epidermidis, S. saprophyticus, Enterococcus faecalis, S. agalactiae, group D streptococci, viridians streptococci and Corynebacterium. Its spectrum of activity against gram negative organisms includes E. coli, Enterobacter, Neisseria, Salmonella and Shigella. It may be used as an alternative to trimethoprim/sulfamethoxazole for treating urinary tract infections though it may be less effective at eradicating vaginal bacteria. May also be used in females as prophylaxis against recurrent cystitis related to coitus. Nitrofurantoin is highly stable to the development of bacterial resistance, a property thought to be due to its multiplicity of mechanisms of action

4.2 Posology and Method of Administration

Adults

Acute Uncomplicated Urinary Tract Infections: 50mg four times daily for seven days.

Severe Chronic Recurrence: 100mg four times a day for seven days.

Long Term Suppression: 50mg - 100mg once a day.

Prophylaxis: 50mg four times daily for the duration of procedure and 3 days thereafter.

Paediatric population

Children and Infants over three months of age

Acute Urinary Tract Infections 3mg/kg/day in four divided doses for seven days.

Suppressive therapy: 1mg/kg/ once a day.

Elderly

Provided there is no significant renal impairment in which Nitrofurantoin is contraindicated, the dosage should be that for any normal adult. See precautions and risks to elderly patients associated with long term therapy (section 4.8).

Renal impairment

Nitrofurantoin is contraindicated in patients with renal dysfunction and in patients with an eGFR of less than 45 ml/minute (see sections 4.3 & 4.4).

Method of administration

For oral use. This medicine should always be taken with food or milk. Taking Nitrofurantoin with a meal improves absorption and is important for optimal efficacy

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4.3 Contraindications

Patients suffering from renal dysfunction with an eGFR of less than 45 ml/minute.

G6PD deficiency

Acute porphyria.

In infants under three months of age as well as pregnant patients at term (during labour and delivery) because of the theoretical possibility of haemolytic anaemia in the foetus or in the newborn infant due to immature erythrocyte enzyme systems.

4.4 Special Warnings and Precautions for Use

Nitrofurantoin is not effective for the treatment of parenchymal infections of unilaterally non-functioning kidney. A surgical cause for infection should be excluded in recurrent or severe cases.

Nitrofurantoin may be used with caution as short-course therapy only for the treatment of uncomplicated lower urinary tract infection in individual cases with an eGFR between 30-44 ml/min to treat resistant pathogens, when the benefits are expected to outweigh the risks.

Since pre-existing conditions may mask adverse reactions, Nitrofurantoin should be used with caution in patients with pulmonary disease, hepatic dysfunction, neurological disorders, and allergic diathesis.

Peripheral neuropathy and susceptibility to peripheral neuropathy, which may become severe or irreversible, has occurred and may be life threatening. Therefore, treatment should be stopped at the first signs of neural involvement (paraesthesiae).

Nitrofurantoin should be used in caution with patients with anaemia, diabetes mellitus, electrolyte imbalance, debilitating conditions and vitamin B (particularly folate) deficiency.

Acute, subacute and chronic pulmonary reactions have been observed in patients treated with nitrofurantoin. If these reactions occur, nitrofurantoin should be discontinued immediately.

Chronic pulmonary reactions (including pulmonary fibrosis and diffuse interstitial pneumonitis) can develop insidiously, and may occur commonly in elderly patients. Close monitoring of the pulmonary conditions of patients receiving long-term therapy is warranted (especially in the elderly).

Hepatotoxicity

Hepatic reactions, including hepatitis, autoimmune 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.

Patients on Nitrofurantoin are susceptible to false positive urinary glucose (if tested for reducing substances).

Nitrofurantoin should be discontinued at any sign of haemolysis in those with suspected glucose-6-phosphate dehydogenase deficiency.

Discontinue treatment with Nitrofurantoin if otherwise unexplained pulmonary, hepatic, haematological or neurological syndromes occur.

Tablets contain lactose

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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4.5 Interaction with Other Drugs, Other Forms of Interactions

1. Increased absorption with food or agents delaying gastric emptying.

2. Decreased absorption with magnesium trisilicate.

3. Decreased renal excretion of Nitrofurantoin by probenecid and sulfinpyrazone.

4. Decreased anti-bacterial activity by carbonic anhydrase inhibitors and urine alkalisation.

5. Anti-bacterial antagonism by quinolone anti-infectives.

6. Interference with some tests for glucose in urine.

7. As Nitrofurantoin belongs to the group of Antibacterials, it will have the following resulting interactions:

Typhoid Vaccine (oral): Antibacterials inactivate oral typhoid vaccine

4.6 Use in Pregnancy and Lactation

Pregnancy

Animal studies with nitrofurantoin have shown no teratogenic effects. Nitrofurantoin has been in extensive clinical use since 1952 and its suitability in human pregnancy has been well documented. However, as with all other drugs, the maternal side effects may adversely affect the course of pregnancy. The drug should be used at the lowest dose as appropriate for the specific indication, only after careful assessment.

Nitrofurantoin is however contraindicated in infants under three months of age and in pregnant women during labour and delivery, because of the possible risk of haemolysis of the infants' immature red cells.

Breastfeeding

Breastfeeding an infant known or suspected to have an erythrocyte enzyme deficiency (including G6PD deficiency), must be temporarily avoided, since Nitrofurantoin is detected in trace amounts in breast milk

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4.7 Effects on ability to drive and use machines

Nitrofurantoin may cause dizziness and drowsiness and the patient should not drive or operate machinery if affected this way.

4.8 Undesirable effects

A tabulated list of undesirable effects is outlined below:

The undesirable effects are listed according to organ systems and following frequencies:

Rare (≥1/10,000 to <1/1,000)

Not known (cannot be estimated from the available data)

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System organ class	Frequency	Adverse reaction
Infections and infestations	Not known	Superinfections by fungi or resistant organisms such as Pseudomonas. However, these are limited to the genitourinary tract
Blood and lymphatic system disorders	Rare Not known	Aplastic anaemia Agranulocytosis, leucopenia, granulocytopenia, haemolytic anaemia, thrombocytopenia,glucose¬6- phosphate dehydrogenase deficiency anaemia, megaloblastic anaemia and eosinophilia
Immune system disorders	Not known	Allergic skin reactions, angioneurotic oedema and anaphylaxis
Psychiatric disorders	Not known	Depression, euphoria, confusion, psychotic reactions
Nervous system disorders	Not known	Peripheral neuropathy including optic neuritis (sensory as well as motor involvement), nystagmus, vertigo, dizziness, headache and drowsiness. Benign intracranial hypertension
Cardiac disorders	Rare	Collapse and cyanosis
Respiratory, thoracic and mediastinal disorders	Not known	Acute pulmonary reactions, Subacute pulmonary reactions*, Chronic pulmonary reactions, Cough, Dyspnoea, Pulmonary fibrosis; possible association with lupus-erythematous-like syndrome.
Gastrointestinal disorders	Not known	Sialadenitis, Pancreatitis, Nausea, Anorexia, Emesis, Abdominal pain and Diarrhea.
Hepatobiliary disorders	Not known	Cholestatic jaundice, Chronic active hepatitis (fatalities have been reported), Hepatic necrosis, autoimmune hepatitis
Skin and subcutaneous tissue disorders	Not known	Transient alopecia Exfoliative dermatitis and erythema multiforme (including Stevens-Johnson Syndrome), maculopapular, erythematous or eczematous eruptions, urticaria, rash, and pruritus. Lupus-like syndrome associated with pulmonary reaction. Drug Rash With Eosinophilia And Systemic Symptoms (DRESS syndrome), cutaneous vasculitis
Renal and urinary disorders	Not known	Yellow or brown discolouration of urine, interstitial nephritis
General disorders and administration site conditions	Not known	Asthenia, fever, chills, drug fever and arthralgia
Investigations	Not known	False positive urinary glucose

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*Acute pulmonary reactions usually occur within the first week of treatment and are reversible with cessation of therapy. Acute pulmonary reactions are commonly manifested by fever, chills, cough, chest pain, dyspnoea, pulmonary infiltration with consolidation or pleural effusion on chest x-ray, and eosinophilia. In subacute pulmonary reactions, fever and eosinophilia occur less often than in the acute form.Chronic pulmonary reactions occur rarely in patients who have received continuous therapy for six months or longer and are more common in elderly patients. Changes in ECG have occurred, associated with pulmonary reactions.

4.8 Overdoses

Symptoms

Symptoms and signs of overdose include gastric irritation, nausea and vomiting.

Management

There is no known specific antidote. However, Nitrofurantoin can be haemodialysed in cases of recent ingestion. Standard treatment is by induction of emesis or by gastric lavage. Monitoring of full blood count, liver function and pulmonary function tests, are recommended. A high fluid intake should be maintained to promote urinary excretion of the drug

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5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmaco-Kinetic Properties

Absorption

Orally administered Nitrofurantoin is readily absorbed in the upper gastrointestinal tract and is rapidly excreted in the urine. Blood concentrations at therapeutic dosages are usually low.

Elimination

Maximum urinary excretion usually occurs 2-4 hours after administration of Nitrofurantoin. Urinary drug dose recoveries of about 40-45% are obtained. It has an elimination half-life of about 30 minutes.

5.2 Pharmaco-dynamic properties

Pharmacotherapeutic group: Antibacterials for systemic use, nitrofurantoin derivatives

Mechanism of action

Nitrofurantoin is a broad spectrum antibacterial agent, active against the majority of urinary pathogens. The wide range of organisms sensitive to the bactericidal activity include:

Escherichia coli

Enterococcus Faecalis

Klebsiella Species

Enterobacter Species

Staphylococcus Species e.g. S. Aureus, S. Saprophyticus, S. Epidermidis

Citrobacter Species

Clinically most common urinary pathogens are sensitive to Nitrofurantoin. Most strains of Proteus and Serratia are resistant. All Pseudomonas strains are resistant.

5.3 Preclinical safety data

Carcinogenic effect of Nitrofurantoin in animal studies was observed. However, human data and extensive use of Nitrofurantoin over 50 years do not support such suggestion

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6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Lactose	BP	48.00 mg
Microcrystalline Cellulose Powder	BP	20.00 mg
Poly vinyl pyrrolidone k-30	BP	5.000 mg
Isopropyl Alcohol	BP	60.00 mg
Purified talc	BP	2.000 mg
Magnesium stearate	BP	1.000 mg
Sodium starch glycolate	BP	2.000 mg
Cross carmellose sodium	BP	2.000 mg
Polyplasdone XL-10	USP	5.000 mg
Polacrillin Potassium	USP	5.000 mg

6.2 Incompatibilities

None reported

6.3 Shelf-Life

36 months from the date of manufacture.

6.4 Special Precautions for Storage

Store below 30°C in cool, dry and dark place.
Protect from light.

6.5 Nature and Contents of Container

Jar pack of 1000 tablets & Blister pack of 10X10 tablets.
Material of construction of primary packaging material is attached.

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Date: 14/08/2024
Director of the manufacturer
(Signature, Full name, Stamp)

Date: 14/08/2024
Director of applicant company
(Signature, Full name, Stamp)