NITROVARD TABLETS
(Vardhman Exports),

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

NITROVARD 100 TABLETS

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each uncoated tablet contains:

Nitrofurantoin BP 100 mg

Excipients with known effects:

Each tablet contains 160 mg of Lactose, 5 mg of Cross Carmellose Sodium & 2 mg of Magnesium Stearate.

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Yellow coloured, circular, uncoated tablets with "NITROVARD 100" embossed on one side and breakline on other side of each tablet.

The scoreline is only to facilitate breaking for ease of swallowing and not to divide into equal doses

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Nitrofurantoin is indicated in the treatment of and prophylaxis against acute of recurrent, uncomplicated lower urinary tract infections or pyelitis either spontaneous or following surgical procedures.
Nitrofurantoin is specifically indicated for the treatment of infections due to susceptible strains of Escherichia coli, Enterococci, Staphylococci, Citrobacter, Klebsiella and Enterobacter.

4.2 Posology and method of administration

Posology:

Adults Acute Uncomplicated Urinary Tract Infections: 50mg four times daily for seven days. Severe Chronic Recurrence: 100mg four times daily for seven days. Long Term Suppression: 50-100mg once a day. Prophylaxis: 50mg four times daily for the duration of the procedure and for the 3 days thereafter.

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/day 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).

Method of Administration

Tablets should be swallowed whole with adequate fluids (at least 100ml of water) and should be taken in an upright sitting or standing position

4.3 Contraindications

Patients with known hypersensitivity to nitrofurantoin or other nitrofurans. Patients suffering from renal dysfunction with creatinine clearance of less than 60ml/minute or elevated serum creatinine. G6PD deficiency (see also Section 4.6)

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.
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 pulmonary conditions of patients receiving long-term therapy is warranted (especially in the elderly).
Patients should be monitored closely for signs of hepatitis (particularly in long-term use). Urine may be coloured yellow or brown after taking Nitrofurantoin. 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.
Gastrointestinal reactions may be minimised by taking the drug with food or milk, or by adjustment of dosage.
For long-term treatment, monitor patients closely for evidence of hepatitis or pulmonary symptoms or other evidence of toxicity.
Discontinue treatment with Nitrofurantoin if otherwise unexplained pulmonary, hepatic, haematological or neurological syndromes occur.

4.5 Interaction with other medicinal products and other forms of interaction

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 sulphinpyrazene.
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: • Oestrogens: In common with other antibiotics, nitrofurantoin may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of oestrogen-containing contraceptive products. Therefore, patients should be warned appropriately and extra contraceptive precautions taken. • Typhoid Vaccine (oral): Antibacterials inactivate oral typhoid vaccine.

4.6. Fertility, Pregnancy and lactation

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 drugs, the maternal side effects may adversely affect the course of pregnancy. The drug should be used at the lowest does 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. Breast feeding 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.

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

Respiratory :
If any of the following respiratory reactions occur the drug should be discontinued.
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. Minor symptoms such as fever, chills, cough and dyspnoea may be significant. Collapse and cyanosis have been reported rarely. 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. It is important to recognise symptoms as early as possible. Pulmonary function may be impaired permanently, even after cessation of therapy.
Hepatic
Hepatic reactions including cholestatic jaundice and chronic active hepatitis, occur rarely. Fatalities have been reported. Cholestatic jaundice is generally associated with short-term therapy (usually up to two weeks). Chronic active hepatitis, occasionally leading to hepatic necrosis is generally associated with long-term therapy (usually after six months). The onset may be insidious. Treatment should be stopped at the first sign of hepatotoxicity.
Neurological
Peripheral neuropathy (including optical neuritis) with symptoms of sensory as well as motor involvement, which may become severe or irreversible, has been reported infrequently. Less frequent reactions of unknown causal relationship are depression, euphoria, confusion, psychotic reactions, nystagmus, vertigo, dizziness, asthenia, headache and drowsiness. Treatment should be stopped at the first sign of neurological involvement.
Gastrointestinal
Nausea and anorexia have been reported. Emesis, abdominal pain and diarrhoea are less common gastrointestinal reactions.
Haematological
Agranulocytosis, leucopenia, granulocytopenia, haemolytic anaemia, thrombocytopenia, megaloblastic anaemia, glucose-6-phosphate dehydrogenase deficiency anaemia, and eosinophilia have been reported. Aplastic anaemia has been reported rarely. Cessation of therapy has generally returned the blood picture to normal.

Hypersensitivity
Allergic skin reactions manifesting as angioneurotic oedema, maculopapular, erythematous or eczematous eruptions, urticaria, rash, and pruritus have occurred.
Lupus-like syndrome associated with pulmonary reaction to nitrofurantoin has been reported.
Exfoliative dermatitis and erythema multiforme (including Stevens-Johnson Syndrome) have been reported rarely.
Other hypersensitivity reactions include anaphylaxis, sialadenitis, pancreatitis, drug fever, and arthralgia.

Miscellaneous
Transient alopecia and benign intracranial hypertension. As with other antimicrobial agents, superinfections by fungi or resistant organisms such as Pseudomonas may occur. However, these are limited to the genito-urinary tract because suppression of normal bacterial flora does not occur elsewhere in the body.
Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

4.9 Overdose

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Used as Antibacterial,

ATC CODE: J01XE01

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 Nitrfurantoin. Most strains of Proteus and Serratia are resistant. All Pseudomonas strains are resistant.

5.2 Pharmacokinetic properties

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

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize Starch,
Lactose,
P.V.P.K-30,
Tween-80,
Purified Talc,
Cross Carmellose Sodium,
Magnesium Stearate,
Sodium Starch Glycolate,
Colloidal Silicon Dioxide,
Sodium Lauryl Sulphate.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years

6.4 Special precautions for storage

Store in a cool and dry place protected from light. Keep all medicines out of reach of children.

6.5 Nature and contents of container

1000 tablets are sealed in PP bag printed with VARDHMAN packed in a 750ml white plastic pet bottle sealed with white cap having two silica bags and a literature.

6.6 Special precautions for disposal and other handling

No special requirements.

7. APPLICANT/MANUFACTURER

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