SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Genfura 100mg Tablets

Nitrofurantoin 100mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Nitrofurantoin 100mg

Excipients with known effect:

Each tablet also contains 160.000 mg of lactose.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet
Flat yellow bevelled tablets scored on one side and marked MP24 on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of and prophylaxis against acute or recurrent uncomplicated pyelitis or lower urinary tract infection - 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: 50 mg four times daily, for 7 days.
- Severe chronic recurrence: 100 mg four times a day, for 7 days.
- Long term suppression: 50 mg – 100 mg once a day.

- Prophylaxis: 50 mg 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; 3 mg/kg/day in four divided doses for 7 days.
- Suppressive: 1 mg/kg, once a day.

For children under 25kg body weight, consideration should be given to the use of nitrofurantoin oral suspension.

Elderly:

Provided there is no significant renal impairment, in which Nitrofurantoin is contraindicated; the dosage should be that for any normal adult. See precaution 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 l/minute (see sections 4.3 & 4.4).

Method of administration:

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

4.3 Contraindications

- Hypersensitivity to the active substance, other nitrofurans or to any of the excipients listed in section 6.1.
- Patients suffering from renal dysfunction with an eGFR of less than 45 ml/min.
- G6PD deficiency (see also Section 4.6).
- Acute porphyria.
- In infants under 3 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

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 maybe 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.

Pulmonary adverse reactions

Acute, subacute and chronic pulmonary reactions have been observed in patients treated with Nitrofurantoin. If these reactions occur, Nitrofurantoin should be discontinued immediately. Signs of pulmonary damage include difficulty and or pain when breathing, shortness of breath and coughing up blood or mucus.

Chronic pulmonary reactions

Chronic pulmonary reactions (including pulmonary fibrosis and diffuse interstitial pneumonitis) can develop insidiously and can often occur in elderly patients. Close monitoring of the lung disease of patients receiving long-term therapy is indicated (especially in the elderly).

Acute pulmonary reactions

Pulmonary reactions may be acute and usually occur within the first week of treatment. Increased vigilance for respiratory symptoms in patients who have just started 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 dehydrogenase deficiency.

Discontinue treatment with Nitrofurantoin if otherwise unexplained pulmonary, hepatic, haematological or neurologic symptoms occur.

Nitrofurantoin is not effective for the treatment of parenchymal infections of unilaterally non-functioning kidney. A surgical cause for infections 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 dysfunctions, 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 (paraesthesia).

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

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

medicine. This medicine contains less than 1 mmol sodium (23 mg) per 100 mg tablet, that is to say essentially 'sodium-free'.

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 sulfinpyraz
4. Decreased antibacterial activity by carbonic anhydrase inhibitors and urine alkalinisation.
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 Anti-bacterials, it will have the following resulting interactions:

- Typhoid Vaccine (oral): Anti-bacterials inactivate oral typhoid vaccine.

4.6 Fertility, 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, the maternal side- effects may adversely affect the course of the pregnancy. The drug should be

used at the lowest dose as appropriate for a 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

Breast feeding an infant known or suspected to have any 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

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 form the available data)

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, cutaneous vasculitis
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, diarrhoea
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-John 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

* 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.

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. Healthcare professionals are asked to report any suspected adverse reactions via Yellow Card Scheme: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store .

4.9 Overdose

Symptoms

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

Management

There is no known specific antidote. However, Nitrofurantoin can be haemodialysed. Standard treatment is by induction of emesis or by gastric lavage in 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: Anti-bacterials for systemic use, Nitrofuran derivatives

ATC code: J01XE01

Mechanism of action

Nitrofurantoin is a broad spectrum antibacterial agent, active against the majority of urinary pathogens. The wide range of organism 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.

5.2 Pharmacokinetic properties

Absorption

Orally administered Nitrofurantoin is readily absorbed in the upper gastro-intestinal tract and rapidly excreted in 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.

5.3 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 observation.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose
Maize starch
Pregelatinised maize starch
Sodium starch glycollate
Magnesium stearate
Purified water

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Containers: 48 months

Blister packs: 48 months

6.4 Special precautions for storage

Containers: Do not store above 25°C. Keep the container tightly closed.
Blister packs: Do not store above 25°C. Store in the original package.

6.5 Nature and contents of container

High density polystyrene containers with polythene lids and/or polypropylene containers with polypropylene or polythene lids or
High-density polyethylene containers with high-density polyethylene lids.
Pack sizes: 28, 30, 50, 56, 60, 84, 100, 250, 500 and 1000.

250 micron white opaque rigid PVC pharmaceutical grade 20 micron hard-tempered aluminium foil, coated on the dull side with 6-7 gsm heat-seal lacquer and printed on the bright side.
Pack sizes: 12, 28, 30, 50, 56, 60, 84, 100, 250, 500 and 1000.

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

PL 42976/0018

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

03/02/2009

10 DATE OF REVISION OF THE TEXT

01/02/2024