

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Macrochantin 100mg Capsules, hard

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Macrochantin 100 mg capsules contain 100 mg Nitrofurantoin in macrocrystalline form.

Excipient : Contains lactose

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsule, hard

Product imported from the UK:

Hard gelatin capsule with an opaque yellow cap and body, containing a pale yellow odourless powder. The capsules are printed with the logo 'Eaton 009' in edible black ink on both the body and cap.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the treatment of and prophylaxis against acute or recurrent, uncomplicated lower urinary tract infections or pyelitis either spontaneous or following surgical procedures.

Nitrofurantoin is specifically indicated for the treatment of infections when due to susceptible strains of *Escherichia coli*, enterococci, staphylococci, *Citrobacter*, *Klebsiella* and *Enterobacter*.

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

Macrochantin is not indicated for the treatment of associated renal cortical or perinephric abscesses.

4.2 Posology and method of administration

See precautions and warnings section for risks associated with long-term therapy

Adults and children over ten years of age

The dose should be taken with food or milk (e.g. at meal times).

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

Severe chronic recurrent infections: 100 mg four times daily for seven days. In the event of severe nausea the dose may be reduced, but not below the adult equivalent of 200 mg/day. Should nausea persist the drug should be withdrawn.

Long term suppressive therapy: 50-100 mg once a day at bedtime is suggested.

Surgical prophylaxis: 50 mg four times daily on the day of the procedure and for the three days after.

Elderly

Provided there is no significant renal impairment, the dosage should be that for any normal adult.

Children over the age of three months

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

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

4.3 Contraindications

Patients suffering from renal dysfunction with a creatinine clearance of less than 60 ml/minute or elevated serum creatinine.

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.

Patients with known hypersensitivity to nitrofurantoin or other nitrofurans.

4.4 Special warnings and precautions for use

Gastrointestinal reactions may be minimised by taking the drug with food or milk or by adjustment of dosage.

Nitrofurantoin is not effective for the treatment of parenchymal infections of unilaterally non-functioning kidney.

Nitrofurantoin should be used with caution in patients with pulmonary disease, hepatic dysfunction, neurological disorders, allergic diathesis, anaemia, diabetes mellitus, electrolyte imbalance, and vitamin B (particularly folate) deficiency.

Nitrofurantoin may cause haemolysis in patients with glucose-6-phosphate dehydrogenase deficiency (Ten percent of black patients and a variable percentage of ethnic groups of Mediterranean, Near Eastern and Asian origin). Haemolysis ceases when the drug is discontinued.

Discontinue treatment with nitrofurantoin if otherwise unexplained pulmonary, hepatotoxic, haematological or neurologic syndromes occur. For long term treatment monitor patient closely for appearance of hepatic, pulmonary or neurological symptoms and other evidence of toxicity.

There has been limited evidence of carcinogenic effects of nitrofurantoin in experimental animals, but the drug has not been shown to be carcinogenic in humans.

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

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant administration of magnesium trisilicate with nitrofurantoin reduces absorption.

Uricosuric drugs such as probenecid and sulphinpyrazone may inhibit renal tubular secretion of nitrofurantoin. The resulting increase in serum levels may increase toxicity. Decreased urinary levels could reduce efficacy as a urinary tract antibacterial.

Concurrent use with quinolones is not recommended.

There may be decreased antibacterial activity for nitrofurantoin in the presence of carbonic anhydrase inhibitors and urine alkalinising agents.

4.6 Fertility, pregnancy and lactation

Based on animal reproduction studies and clinical experience in humans over many years, there is no evidence of any teratogenic effects of nitrofurantoin on the foetus. Caution should be exercised while breast feeding an infant known or suspected to have any erythrocyte enzyme deficiency as nitrofurantoin is detected in trace amounts in breast milk. Nitrofurantoin is contraindicated in pregnant patients at term (during labour and delivery).

As with all drugs, maternal side-effects, should they occur, may adversely affect the course of the pregnancy. The drug should be used at the lowest effective dose only after careful assessment of benefits against potential risks.

4.7 Effects on ability to drive and use machines

Macrochantin does not interfere with the ability to drive or use machines.

4.8 Undesirable effects

Respiratory

If the following 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.

Subacute reactions may take several months to resolve once the drug has been stopped.

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 seldom been reported. 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.

Hypersensitivity

Exfoliative dermatitis and erythema multiforme (including Stevens-Johnson syndrome) have been reported rarely. 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.

Other hypersensitivity reactions include anaphylaxis, sialadenitis, pancreatitis, drug fever and arthralgia.

Haematological

Agranulocytosis, leucopenia, granulocytopenia, haemolytic anaemia, thrombocytopenia, glucose-6-phosphate dehydrogenase deficiency anaemia, megaloblastic anaemia and eosinophilia have occurred. Cessation of therapy has

generally returned the blood picture to normal. Aplastic anaemia has been reported rarely.

Other

Transient alopecia and benign intracranial hypertension.

Superinfections by fungi or resistant organisms such as *Pseudomonas* may occur. However, these are limited to the genito-urinary tract.

4.9 Overdose

Symptoms and signs of overdose 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

The urine of patients receiving Macrochantin may be coloured a dark yellow or brown. This results from the presence of drug and/or metabolite(s) and is quite harmless. Macrochantin can interfere with certain laboratory tests. False positive or spuriously high readings may be produced with urine glucose tests utilising the copper sulphate reduction method, eg Benedict's reagent, Clinitest (Ames). However, there is no interference with the Clinistix test.

5.2 Pharmacokinetic properties

The nitrofurantoin macrocrystals of Macrochantin are specially formulated. The crystal size controls the rate of absorption and thus reduce the incidence of nausea. Clinical and animal studies indicate that Macrochantin therapy decreases the likelihood of nausea in patients who might experience these symptoms on nitrofurantoin therapy.

5.3 Preclinical safety data

Non-clinical data reveal no special hazards for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, and toxicity to reproduction.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule fill contents

Lactose Monohydrate
Maize Starch
Talc

Capsule shell

Quinoline Yellow (E104)
Titanium Dioxide (E171)
Gelatin
Sodium Laurilsulfate

Printing ink

Shellac

Black Iron Oxide (E172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

The shelf-life expiry date of this product is the date shown on the blister and outer package of the product on the market in the country of origin.

6.4 Special precautions for storage

Store in the original package in order to protect from light and moisture.

Do not store above 30°C

6.5 Nature and contents of container

Macrochantin 100 mg capsules are supplied in PVC/aluminium foil blisters in packs of 30. Each pack comprises 3 blister cards containing 10 capsules on each card.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 PARALLEL PRODUCT AUTHORISATION HOLDER

PCO Manufacturing

Unit 10, Ashbourne Business Park

Rath

Ashbourne

Co. Meath

8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA 465/242/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 28th August 2009

10 DATE OF REVISION OF THE TEXT

April 2011