

1. NAME OF THE MEDICINAL PRODUCT

Fucidin 250 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 250 mg of sodium fusidate.

Excipient with known effect

Lactose monohydrate 71.9 mg per tablet

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

White to off-white greyish marbled film-coated oval tablet without embossing.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

In the treatment of infections due to micro-organisms sensitive to this anti-infective, such as Staphylococci.

4.2 Posology and method of administration

Posology

Adults only: The usual total daily dose is 1500 mg in divided doses.

In severe infections doses may be doubled or appropriate combined therapy may be used.

Since fusidic acid is excreted in the bile, no dosage modifications are needed in renal impairment. The dosage in patients undergoing haemodialysis needs no adjustment as fusidic acid is not significantly dialysed.

Paediatric population

Children: The usual total daily dose is 20 to 50 mg/kg in divided doses.

Method of administration

For oral administration.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

Concomitant treatment with statins (HMG-CoA reductase inhibitors). (See section 4.4, 4.5).

4.4 Special warnings and precautions for use

Statin (HMG-CoA reductase inhibitors) and systemic Fucidin must not be co-administered, (see section 4.3). There have been reports of rhabdomyolysis (including fatalities) in patients receiving this combination. Statin treatment should be discontinued

throughout the duration of treatment with systemic Fucidin. The patient should be advised to seek medical advice immediately if they experience any symptoms of muscle weakness, pain or tenderness. Statin therapy may be re-introduced 7 days after the last dose of systemic Fucidin.

In exceptional circumstances, where prolonged systemic Fucidin is needed, e.g. for the treatment of severe infections, the need for co-administration of HMG-CoA reductase inhibitors and systemic Fucidin should only be considered on a case by case basis and under close medical supervision.

In a few cases, serious cutaneous reactions putting life at risk such as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome, toxic epidermal necrolysis (Lyell's syndrome) and Stevens-Johnson syndrome have been reported with systemic Fucidin. Patients should be advised to monitor cutaneous reactions as well as signs and symptoms suggestive of these reactions which usually appear in the first weeks of therapy. If such reactions are suspected to be due to systemic Fucidin, treatment with systemic Fucidin should be stopped and it is recommended not to reintroduce the therapy.

Fusidic acid is metabolised in the liver and excreted in the bile. Elevated liver enzymes and jaundice have occurred during systemic Fucidin therapy but are usually reversible on discontinuation of the drug.

Systemic Fucidin should be given with caution and liver function should be monitored if used in patients with hepatic dysfunction. Caution is required in patients with biliary disease and biliary tract obstruction. Caution is required in patients treated with HIV-protease inhibitors (see section 4.5). Fusidic acid competitively inhibits binding of bilirubin to albumin. Caution is necessary if systemic Fucidin is administered to patients with impaired transport and metabolism of bilirubin. Particular care is advised in neonates due to the theoretical risk of kernicterus.

Bacterial resistance has been reported to occur with the use of fusidic acid. As with all antibiotics, extended or recurrent use may increase the risk of developing antibiotic resistance.

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

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

4.5 Interaction with other medicinal products and other forms of interaction

Statins (HMG-CoA reductase inhibitors)

Concomitant treatment with statins (HMG-CoA reductase inhibitors) is contraindicated.

Co-administration of systemic Fucidin and statins may cause possibly fatal rhabdomyolysis. Treatment with statins should therefore be discontinued throughout the duration of the treatment with systemic Fucidin. Statin therapy may be reintroduced 7 days after the last dose of systemic Fucidin (See section 4.3 and 4.4).

Oral anticoagulants

Systemic Fucidin administered concomitantly with oral anticoagulants such as coumarin derivatives or anticoagulants with similar actions may alter the anticoagulant effect.

Adjustment of the oral anticoagulant dose may be necessary in order to maintain the desired level of anticoagulation.

HIV protease inhibitors

Co-administration of systemic Fucidin and HIV protease inhibitors such as ritonavir and saquinavir may cause increased plasma concentrations of both agents which may result in hepatotoxicity.

Concomitant use is not recommended. (See section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited data (less than 300 pregnancy outcomes) from the use of fusidic acid in pregnant women. Animal studies do not indicate direct or indirect harmful effect with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of systemic Fucidin during pregnancy.

Breast-feeding

Physico-chemical data suggest excretion of fusidic acid in human milk. A risk to the suckling child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from systemic Fucidin therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility

There are no clinical studies with systemic Fucidin regarding fertility. Pre-clinical studies did not show any effect of sodium fusidate on the fertility in rats.

4.7 Effects on ability to drive and use machines

Fucidin has no or negligible influence on the ability to drive or to use machines.

4.8 Undesirable effects

The estimation of the frequency of undesirable effects is based on a pooled analysis of data from clinical trials and from spontaneous reporting.

The most frequently reported undesirable effects of Fucidin administered orally are gastrointestinal disorders like abdominal discomfort and pain, diarrhoea, dyspepsia, nausea and vomiting. Anaphylactic shock has been reported.

Undesirable effects are listed by MedDRA SOC and the individual undesirable effects are listed starting with the most frequently reported. Within each frequency group, adverse reactions are presented in the order of decreasing seriousness.

Very common ($\geq 1/10$)

Common ($\geq 1/100$ to $< 1/10$)

Uncommon ($\geq 1/1,000$ to $< 1/100$)

Rare ($\geq 1/10,000$ to $< 1/1,000$)

Very rare ($< 1/10,000$)

Not known (cannot be estimated from available data)

Blood and lymphatic system disorders	
Uncommon	Pancytopenia

	Leukopenia ^{a)} Thrombocytopenia Anaemia
Immune system disorders	
Uncommon	Anaphylactic shock/anaphylactic reaction
Rare	Hypersensitivity
Nervous system disorders	
Uncommon	Headache Somnolence
Gastrointestinal disorders	
Common	Vomiting Diarrhoea Abdominal pain Dyspepsia Nausea Abdominal discomfort

Hepatobiliary disorders	
Uncommon	Hepatic failure Cholestasis Hepatitis ^{b)} Jaundice ^{c)} Hyperbilirubinaemia Liver function test abnormal ^{d)}
Rare	Hepatic function abnormal
Skin and subcutaneous tissue disorders	
Uncommon	Acute generalised exanthematous pustulosis Urticaria Rash ^{e)}
Rare	Angioedema Pruritus Erythema
Not known	Toxic epidermal necrolysis (Lyell's syndrome) ^{f)} Stevens-Johnson syndrome ^{f)} Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome ^{f)}
Musculoskeletal and connective tissue disorders	
Uncommon	Rhabdomyolysis ^{g)}
Renal and urinary disorders	
Uncommon	Renal failure ^{h)}
General disorders and administration site conditions	
Common	Lethargy/Fatigue/Asthenia

a) Haematological disorders affecting the white cell line (neutropenia, granulocytopenia and agranulocytosis) have been reported

b) Hepatitis also includes hepatitis cholestatic/cytolytic hepatitis

c) Jaundice also includes jaundice cholestatic

d) Including alanine aminotransferase increased, aspartate aminotransferase increased, blood alkaline phosphatase increased, blood bilirubin increased and gamma-glutamyltransferase increased

e) Rash includes various types of rash reactions such as drug eruption, erythematous and maculo-papular rash

f) These adverse reactions were identified through post-marketing surveillance. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency (see section 4.4).

- g) Rhabdomyolysis may be fatal
- h) Renal failure also includes renal failure acute

Paediatric population

Frequency, type and severity of adverse reactions in children are expected to be the same as in adults, based on limited data.

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 HPRA Pharmacovigilance, website: www.hpra.ie

4.9 Overdose

Acute symptoms of overdose include gastrointestinal disturbances. Management should be directed towards alleviation of symptoms. Dialysis will not increase the clearance of fusidic acid.

An overdose of 4 g/day for a duration of 10 days in an adult has been reported without any adverse events.

An overdose of 1,250 mg/day for a duration of 7 days in a child (3 years old) has been reported without any adverse events.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Steroid antibacterials,
ATC code: J01XC01

Fucidin exerts powerful activity against a number of gram-positive organisms. Staphylococci including the strains resistant to penicillin and other antibiotics are particularly susceptible to Fucidin. Concentrations of 0.03-0.12 mcg/ml inhibit nearly all strains of *Staphylococcus aureus*.

5.2 Pharmacokinetic properties

Fucidin readily penetrates tissue. Bactericidal levels have been assayed in bone and necrotic tissue. Blood levels are cumulative, reaching concentrations of 50-100 mcg/ml after oral administration of 1.5 g daily for 3 to 4 days. Fucidin is excreted mainly in the bile, little or none being excreted in the urine.

5.3 Preclinical safety data

There are no preclinical There are no preclinical data of relevance to the prescriber which are additional to that already included in other areas of the SPC.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core:
Microcrystalline cellulose

Crospovidone
Lactose monohydrate
Magnesium stearate
Colloidal anhydrous silica
Talc
All-rac- α -tocopherol

Film-coating:
Hypromellose
Titanium dioxide

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Aluminium/aluminium blister packs and strip blister packs of 10 x 10 tablets, 10 tablets, 4 tablets (FMS) and 2 tablets (FMS)

Not all pack sizes may be marketed.

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 for disposal.

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

LEO Laboratories Limited
Cashel Road
Dublin 12
Ireland

8. MARKETING AUTHORISATION NUMBER

PA 46/4/14

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 13 March 1990
Date of last renewal: 13 March 2010

10. DATE OF (PARTIAL) REVISION OF THE TEXT

January 2021