Fucidin Tablets

Summary of Product Characteristics Updated 04-Feb-2014 | Leo Laboratories Limited

1. Name of the medicinal product

Fucidin® Tablets

2. Qualitative and quantitative composition

Each tablet contains Sodium Fusidate Ph.Eur. 250 mg.

3. Pharmaceutical form

Tablet

4. Clinical particulars

4.1 Therapeutic indications

Fucidin® is indicated in the treatment of all staphylococcal infections due to susceptible organisms such as: cutaneous infections, osteomyelitis, pneumonia, septicaemia, wound infections, endocarditis, superinfected cystic fibrosis.

Fucidin® should be administered intravenously whenever oral therapy is inappropriate, which includes cases where absorption from the gastro-intestinal tract is unpredictable.

4.2 Posology and method of administration

For staphylococcal cutaneous infections:

Adults: Standard Dose: 250mg (one tablet) sodium fusidate (equivalent to 240mg fusidic acid) twice daily for 5-10 days.

For staphylococcal infections such as osteomyelitis, pneumonia, septicaemia, wound infections, endocarditis, superinfected cystic fibrosis.

Adults: Standard dose: 500mg (two tablets) sodium fusidate (equivalent to 480mg fusidic acid) three times daily.

In severe cases of fulminating infections, the dosage may be doubled or appropriate combined therapy may be used.

Elderly: No dosage alterations are necessary in the elderly.

Since Fucidin® is excreted in the bile, no dosage modifications are needed in renal impairment.

The dosage in patients undergoing haemodialysis needs no adjustment as Fucidin® is not significantly dialysed.

4.3 Contraindications

Hypersensitivity to fusidic acid and its salts, or to any of the excipients.

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

4.4 Special warnings and precautions for use

Fucidin® must not be co-administered with statins. There have been reports of rhabdomyolysis (including some fatalities) in patients receiving this combination (see section 4.5). In patients where the use of systemic Fucidin® is considered essential, statin treatment should be discontinued throughout the duration of Fucidin® treatment. 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 seven days after the last dose of Fucidin®. In exceptional circumstances, where prolonged systemic Fucidin® is needed e.g for the treatment of severe infections, the need for co-administration of statin and Fucidin® should only be considered on a case by case basis and under close medical supervision.

Fusidic acid is metabolised in the liver and excreted in the bile. Caution should be exercised with other antibiotics which have similar biliary excretion pathways e.g. lincomycin and rifampicin. Elevated liver enzymes and jaundice have occurred during systemic therapy but are usually reversible on discontinuation of the drug (see section 4.8).

Periodic liver function tests should be carried out when the product is given:

• in high oral doses
• for prolonged periods
• to patients with liver dysfunction
• to patients taking potentially hepatotoxic medication
• to patients with biliary tract obstruction
• to patients taking concurrent medication with a similar excretion pathway.

Fusidic acid displaces bilirubin from its albumin binding site in vitro. Caution is necessary if this product is administered to patients with impaired transport and metabolism of bilirubin.

The use of Fusidin® in combination with drugs that are CYP-3A4 biotransformed should be avoided. See Section 4.5.

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.

This medicinal product contains 0.45 mmol (11 mg) sodium per tablet. This should be taken into consideration by patients on a controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

The risk of myopathy including rhabdomyolysis may be increased by the concomitant administration of systemic Fusidin® with statins. Co-administration of this combination may cause increased plasma concentrations of both agents. The mechanism of this interaction (whether it is pharmacodynamics or pharmacokinetic, or both) is yet unknown. There have been reports of rhabdomyolysis (including some fatalities) in patients receiving this combination. If treatment with Fusidin® is necessary, statin treatment should be discontinued throughout the duration of the Fusidin® treatment. Also see section 4.4.

Specific pathways of Fusidin® metabolism in the liver are not known, however, an interaction between Fusidin® and drugs being CYP-3A4 biotransformed can be suspected. The mechanism of this interaction is presumed to be a mutual inhibition of metabolism. There is insufficient data to characterise the effect of fusidic acid on CYPs in-vitro. The use of Fusidin® systemically should be avoided in patients treated with CYP-3A4 biotransformed drugs.

Fusidin® administered systemically and concomitantly with oral anticoagulants such as coumarin derivatives or anticoagulants with similar actions may increase the plasma concentration of these agents enhancing the anticoagulant effect. Anticoagulation should be closely monitored and a decrease of the oral anticoagulant dose may be necessary in order to maintain the desired level of anticoagulation. Similarly, discontinuation of Fusidin® may require the maintenance dose of anticoagulant to be re-assessed. The mechanism of this suspected interaction remains unknown.

Co-administration of Fusidin® Tablets and HIV protease inhibitors such as ritonavir and saquinavir causes increased plasma concentrations of both agents which may result in hepatotoxicity.

Co-administration of Fusidin® systemically and ciclosporin has been reported to cause increased plasma concentration of ciclosporin.

4.6 Pregnancy and lactation

There is inadequate evidence of safety in human pregnancy. Animal studies and many years of clinical experience suggest that fusidic acid is devoid of teratogenic effects. There is evidence to suggest that when given systemically, fusidic acid can cross the placental barrier. If the administration of Fusidin® to pregnant patients is considered essential, its use requires that the potential benefits be weighed against the possible hazards to the foetus.

Safety in nursing mothers has not been established. When fusidic acid (as the sodium salt) has been given systemically, levels have been detected in the breast milk. Caution is therefore required when Fusidin® is used in mothers who wish to breast feed.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Based on clinical trial data, undesirable effects occurred in approximately 15% of patients receiving Fusidin® orally. The most frequently reported undesirable effects to Fusidin® administered orally are dose dependent gastrointestinal disorders. Various skin reactions, reversible jaundice, haematological disorders and generalised hypersensitivity reactions have been reported.

Undesirable effects are listed below, by MedDRA System Organ Class, in decreasing order of frequency within each class. Where frequencies are given, these are based on the clinical trial data, using the stated frequency classification. Where the term 'Not known' is given, these effects are derived from spontaneous reports.

Frequency classification:

Very common >1/10
Common  >1/100 and <1/10
Uncommon  >1/1,000 and <1/100
Rare  >1/10,000 and <1/1,000
Very rare  <1/10,000

• Blood and lymphatic system disorders
Not known: Pancytopenia
Leukopenia*
Thrombocytopenia
Anaemia

*Haematological disorders affecting the white cell line (neutropenia, granulocytopenia, agranulocytosis) and, more rarely, disorders affecting the other two cell lines have been reported, either as isolated events or associated. These abnormalities have been observed especially with treatment of more than 15 days and are reversible upon drug withdrawal.

• Immune system disorders
Rare: Allergic reaction
Not known: Anaphylactic reaction

• Metabolism and nutrition disorders
Uncommon: Anorexia

• Nervous system disorders
Common: Drowsiness
Dizziness
Uncommon: Headache

• Gastrointestinal system disorders
Common: Diarrhoea
Vomiting
Abdominal Pain
Dyspepsia
Nausea

• Hepatobiliary disorders
Not known: Hyperbilirubinaemia
Jaundice (see section 4.4)
Hepatic enzymes increased (see section 4.4)
Hepatorenal syndrome
Liver function abnormalities like hyperbilirubinaemia with or without jaundice and increase in hepatic enzymes such as alkaline phosphatase and transaminases should lead to withdrawal of treatment. Return of laboratory parameters to normal is usual and generally rapid.

Cholestasis

• Skin and subcutaneous tissue disorders
Uncommon: Rash*
Urticaria
Pruritus

*Rash includes various types of reactions such as erythematous, maculo-papular and pustular.

• Musculoskeletal and connective tissue disorders
Not known: Rhabdomyolysis (see Section 4.4 and 4.5)

Rhabdomyolysis may be fatal. Examples of signs and symptoms are: muscle weakness, muscle swelling and muscle pain, dark urine, myoglobinuria, elevated serum creatine kinase, acute renal failure, cardiac arrhythmia.

• Renal and urinary disorders
Not known: Renal failure

Acute renal failure has been described in patients with jaundice, in particular in the presence of other factors predisposing to renal failure.

- General disorders and administration site conditions

Uncommon: Asthenia
Fatigue
Malaise

4.9 Overdose

Acute symptoms of overdose include gastrointestinal disturbances and possible effects on liver function. Treatment should be restricted to symptomatic and supportive measures. Dialysis will not increase the clearance of fusidic acid.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Fusidic acid and its salts are potent anti-staphylococcal agents with unusual ability to penetrate tissue. Bactericidal levels have been assayed in bone and necrotic tissue. Concentrations of 0.03 - 0.12 micrograms/ml inhibit nearly all strains of *Staphylococcus aureus*. Fusidic acid is active against *Staphylococcus epidermidis* and methicillin resistant staphylococci.

5.2 Pharmacokinetic properties

Blood levels are cumulative, reaching concentrations of 20-35 micrograms/ml after oral administration of 250mg twice daily for seven days and 50-100 micrograms/ml after oral administration of 500mg three times daily for three to four days.

Fucidin® is excreted mainly in the bile, little or none being excreted in the urine.

In severe or deep-seated infections and when prolonged therapy may be required, Fucidin® should generally be given concurrently with other anti-staphylococcal antibiotic therapy.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6. Pharmaceutical particulars

6.1 List of excipients

Cellulose microcrystalline, crospovidone, hypromellose, lactose monohydrate, magnesium stearate, silica, all-rac-α-tocopherol, talc, titanium dioxide.

6.2 Incompatibilities

None.

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 and strip blister packs of 2, 4 and 10 and 10 x 10 tablets.

6.6 Special precautions for disposal and other handling

None.

7. Marketing authorisation holder

LEO Laboratories Limited,
Horizon
Honey Lane
8. Marketing authorisation number(s)

PL 00043/5000R

9. Date of first authorisation/renewal of the authorisation

4.6.87 (after review).

10. Date of revision of the text

October 2013

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