Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Fucidin 500mg Powder and Solvent for Concentrate for Solution for I.V. Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial of powder contains 500 mg of Sodium Fusidate.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Powder and solvent for concentrate for solution for infusion
A white to off-white crystalline powder accompanied by a clear and colourless buffer solution as solvent for reconstitution. The reconstituted product is further diluted with the appropriate infusion fluid prior to administration by intravenous infusion.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In the treatment of systemic infections due to micro-organisms sensitive to this anti-infective.

4.2 Posology and method of administration

Adults only:

(Weighing more than 50kg)

The usual total daily dose is 1,500 - 2,000mg in divided doses, i.e. given three to four times daily. Add the fusidate/buffer solution to 500ml of infusion and infuse slowly over a period of at least 2 to 4 hours into a wide bore vein with good blood flow. If a superficial vein is employed a more prolonged period of at least 6 hours is advisable.

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.

Children

(and adults weighing less than 50kg).

The usual total daily dose is 20mg/kg body weight daily divided into 3 equal doses.

Each dose corresponds to 0.13ml of the fusidate buffer solution per kg bodyweight. This volume should be further diluted at least ten fold with the appropriate infusion fluid.

4.3 Contraindications

Use in patients hypersensitive to the active ingredient.

Use in patients with biliary tract obstruction.

4.4 Special warnings and precautions for use

Regular monitoring of liver function should be carried out in patients on high dosage of fusidate.

Prolonged administration of an anti-infective may result in the development of super infection with organisms resistant to that anti-infective.

Fucidin should be used with caution in patients with impaired liver function or those concurrently on potentially hepatotoxic drugs.

Caution should be exercised with other antibiotics which have similar biliary excretion pathways e.g. lincomycin and rifampicin.

A bilirubin displacing effect of Fucidin has been demonstrated in vitro. Although kernicterus has not been observed in new-borns receiving Fucidin, this effect should be borne in mind when giving Fucidin to infants, especially icteric, prematurely born acidotic or very ill neonates.

When reconstituted 1 vial contains 3.1 mMol sodium. The sodium content should be taken into consideration for patients on a controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

Fucidin administered systemically and concomitantly with oral anticoagulants such as coumarin derivatives or anticoagulants with similar action may increase the plasma concentration of these agents enhancing the anticoagulant effect. Adjustment of the oral anticoagulant dose may be necessary in order to maintain the desired level of anticoagulation. The mechanism of this suspected interaction remains unknown.

Specific pathways of Fucidin metabolism in the liver are not known, however, an interaction between Fucidin and drugs being CYP-3A4 biotransformed can be suspected. The mechanism of this interaction is presumed to be a mutual inhibition of metabolism. The use of Fucidin systemically should be avoided in patients treated with CYP-3A4 biotransformed drugs.

Co-administration of Fucidin systemically and HMG-CoA reductase inhibitors such as statins causes increased plasma concentrations of both agents resulting in an elevation of creatine kinase level (rhabdomyolysis), muscle weakness and pain.

Co-administration of Fucidin systemically and HIV protease inhibitors such as Ritonavir and Saquinavir causes increased plasma concentrations of both agents which may result in hepatotoxicity.

Co-administration of Fucidin 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. However animal studies and many years of clinical experience suggest that Fucidin is devoid of teratogenic effects.

Fucidin crosses the placenta and should be avoided during the third trimester due to the theoretical risk of kernicterus.

Concentrations of Fucidin found in breast milk are negligible and its use is not contraindicated in nursing mothers.

4.7 Effects on ability to drive and use machines

Presumed to be safe or unlikely to produce an effect.

4.8 Undesirable effects

Side effects include rash, reversible jaundice and rarely thrombophlebitis. Rarely haematological disorders have been reported including bone marrow depression, thrombocytopenia and neutropenia. Acute renal failure has been described in patients with jaundice, particularly in the presence of other factors predisposing to renal failure.

4.9 Overdose

There has been no experience of overdosage with Fucidin. Treatment should be restricted to symptomatic and supportive measures. Dialysis is of no benefit, since the drug is not significantly dialysed.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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 1.5g daily for three to four days. Fucidin is excreted mainly in the bile, little or none being excreted in the urine.

5.3 Preclinical safety data

No additional data.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Diluent

Disodium edetate
Disodium Phosphate Dihydrate (E339)
Citric acid Monohydrate
Water for injections

6.2 Incompatibilities

Sodium Fusidate reconstituted at 50 mg/ml in buffer solution is physically incompatible with infusion fluids containing lipid infusions and peritoneal dialysis fluids. High concentrations of dextrose (≥ 20%) are incompatible.

Generally precipitation may occur in dilutions which result in a pH of less than 7.4.

Immediate and persistent precipitation occurred upon mixing of sodium fusidate with vancomycin (25 mg/ml) and gentamicin sulphate (1.5 mg/ml).

6.3 Shelf Life

Dry powder and buffer solution: 3 years

Reconstituted solution: The reconstituted solution should be added to the infusion solution immediately. The infusion solution should then be used within 24 hrs. Unused portions in the vial must be discarded.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and reconstitution/dilution should be carried out under controlled and validated aseptic conditions.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

The dry substance is contained in 12 ml glass (Type 1) vials closed with a butyl rubber stopper, secured with a metal ring.

The buffer solution is contained in 12 ml glass (Type 1) vials closed with an ethylene propylene rubber stopper, secured with a metal ring.

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

For single use only: Discard any unused contents.
Recommended procedure:

Reconstitution: Add the 10ml of sterile buffer provided to the vial containing 500mg sodium fusidate, to dissolve the powder. The powder should be completely dissolved and the reconstituted concentrate will be clear. The reconstituted concentrate must be further diluted before infusion (see below for compatible infusion fluids).

In vitro compatibility studies of Fucidin for Intravenous Infusion with commonly used infusion solutions have been carried out. The results showed that sodium fusidate reconstituted at 50 mg/ml in buffer solution is physically and chemically compatible for 24 hours at room temperature with the following infusion solutions (the figure in parenthesis shows the concentration of sodium fusidate in the final admixture):

Sodium Chloride Intravenous Infusion BP 0.9% (1-2 mg/ml)
Dextrose Intravenous Infusion BP 5% (1-2mg/ml)
Compound Sodium Lactate Intravenous Infusion (“Ringer-Lactate Solution”) (1 mg/ml)
Sodium Lactate Intravenous Infusion BP (1 mg/ml)
Sodium Chloride (0.18%) and Dextrose (4%) Intravenous Infusion BP
(1 mg/ml).
Potassium Chloride (0.3%) and Dextrose (5%) Intravenous Infusion BP
(1 mg/ml).

If additional antibacterial therapy is to be employed, it is generally recommended that for parenteral administrations, separate infusion fluids be used. However Fucidin IV is physically and chemically compatible for 24 hours at room temperature in the following admixtures:

- Cefotaxime (2.5 mg/ml) + sodium fusidate (0.5 mg/ml) in Dextrose-Saline Intravenous Infusion (glass bottles).
- Erythromycin (5 mg/ml) + sodium fusidate (1 mg/ml) in Dextrose-Saline Intravenous Infusion (PVC-bags).
- Flucloxacillin (2.5 mg/ml) + sodium fusidate (0.5 mg/ml) in Dextrose-Saline Intravenous Infusion (glass bottles)
- Gentamicin sulphate (0.16 mg/ml) + sodium fusidate (1 mg/ml) in Dextrose-Saline Intravenous Infusion (PVC-

bags).

Cefotaxime, erythromycin, flucloxacillin and gentamicin sulphate are compatible with sodium fusidate in the listed admixtures, even if minor decreases in potencies take place.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and reconstitution/dilution should be carried out under controlled and validated aseptic conditions.

7 MARKETING AUTHORISATION HOLDER

LEO Laboratories Limited
Cashel Road
Dublin 12

8 MARKETING AUTHORISATION NUMBER

PA 46/4/15

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27 February 1991

Date of last renewal: 13 March 2005

10 DATE OF REVISION OF THE TEXT

March 2005