Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Flucillin 125mg/5ml Powder for Oral Solution.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml contains flucloxacillin 125 mg as flucloxacillin sodium.

Excipients: also includes sucrose 3.1g per 5ml, sodium 0.534mmol per 5ml and trace amounts of sulphur dioxide (E220).
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder for oral solution.
A pink, pineapple-flavoured granular powder for oral solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Flucloxacillin is recommended for the treatment of infections due to pencillinase-producing Staphylococci and other gram-positive organisms susceptible to Flucloxacillin.

4.2 Posology and method of administration

Adults:
750 mg to 1500 mg daily in divided doses. The dosage may be increased if necessary.

Children:
Aged over 12 years: 750 mg to 1500 mg daily in divided doses. The dosage may be increased if necessary.

Aged 2 – 12 years:
The usual daily dose is 50 mg/kg bodyweight in divided doses.

Special Groups:
In the presence of severe renal failure (creatinine clearance < 10 ml/min) a reduction in dose or extension of dose interval should be considered.

Administration:
Oral doses should be administered one hour before meals or on an empty stomach.

4.3 Contraindications

Flucloxacillin should not be given to patients with a history of hypersensitivity to β-lactam antibiotics (e.g. penicillins, cephalosporins) or any of the excipients.

Flucloxacillin is contraindicated in patients with a previous history of flucloxacillin-associated janudice/hepatic dysfunction.

4.4 Special warnings and precautions for use

Before initiating therapy with flucloxacillin, careful inquiry should be made concerning previous hypersensitivity reactions to beta-lactams.Cross-sensitivity between penicillins and cephalosporins is well documented.

Serious and occasionally fatal hypersensitivity reactions (anaphylaxis) have been reported in patients receiving beta-lactam antibiotics. Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients on oral therapy. These reactions are more likely to occur in indivduals with a history of beta-lactam hypersensitivity. If an allergic reaction occurs, flucloxacillin should be discontinued and the appropriate therapy instituted. Serious anaphylactoid reactions may require immediate emergency treatment with adrenaline. Oxygen, i.v. steroids, and airway management, including intubation, may also be required.

Flucloxacillin has been associated with cholestatic jaundice which may occur several weeks after stopping therapy (risk increased in those treated for longer than 2 weeks or who are over 55 years of age).

Flucloxacillin is excreted in a manner similar to that for benzyl penicillin i.e. by glomerular filtration and tubular secretion. This should be borne in mind when prescribing therapy.

Flucloxacillin should be used with caution in patients with evidence of hepatic dysfunction, those with serious underlying disease, and the elderly. In these patients, hepatic events may be severe, and in extremely rare circumstances, deaths have been reported (*See section 4.8, Undesirable effects*).

Dosage should be adjusted in renal impairment (*see section 4.2**,** Posology and method of administration*).

Special caution is essential in the newborn because of the risk of hyperbilirubinemia. Studies have shown that, at high dose following parenteral administration, flucloxacillin can displace bilirubin from plasma protein binding sites, and may therefore predispose to kernicterus in a jaundiced baby. In addition, special caution is essential in the newborn because of the potential for high serum levels of flucloxacillin due to a reduced rate of renal excretion.

During prolonged treatments (e.g. osteomyelitis, endocarditis), regular monitoring of hepatic and renal functions is recommended.

Prolonged use may occasionally result in overgrowth of non-susceptible organisms.

Contains sucrose: Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine.

Sodium content: This medicinal product contains approximately 38.5 mg sodium per 10ml (250mg) dose. To be taken into consideration by patients on a controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

Probenecid reduces the excretion of flucloxacillin.

4.6 Pregnancy and lactation

Flucloxacillin should not be used during pregnancy unless the physician considers the expected benefits to the patient outweigh the potential risks to the foetus.

Flucloxacillin is excreted in breast milk, presenting the risk of candidiasis and also of central nervous system toxicity due to immaturity of the blood brain barrier. There is a theoretical possibility of later sensitisation.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

The following convention has been utilised for the classification of undesirable effects: Very common >1/10), common >1/100, <1/10), uncommon >1/1000, <1/100), rare >1/10,000, <1/1000), very rare (<1/10,000).

Unless otherwise stated, the frequency of the adverse events has been derived from more than 30 years of post-marketing reports.

Blood and lymphatic system disorders

Very rare: Neutropenia (including agranulcytosis) and thrombocytopenia. These are reversible when treatment is discontinued. Eospinphilia, haemolytic anaemia.

Immune system disorders

Very rare: Anaphylactic shock (exceptional with oral administration) (see Item 4.4 Warnings), angioneurotic oedema.

If any hypersensitivity reaction occurs, the treatment should be discontinued. (see also Skin and subcutaneous tissue disorders).

Nervous system disorders

Very rare: In patients suffering from renal failure, neurological disorders with convulsions are possible with the I.V. injection of high doses.

Gastrointestinal disorders

*Common: Minor gastrointestinal disturbances (such as nausea and diarrhoea).

Very rare: Pseudomembranous colitis.

If pseudomembranous colitis develops, flucloxacillin treatment should be discontinued and appropriate therapy, e.g. oral vancomycin should be initiated.

Hepato-biliary disorders

Very rare: Hepatitis and cholestatic jaundice (see Warnings and Precautions). Changes in liver function laboratory test results (reversible when treatment is discontinued).

Hepatitis and cholestatic jaundice may be delayed for up to two months post-treatment. In some cases the course has been protracted and lasted for several months. Hepatic events may be severe, and in very rare circumstances, deaths have been reported. Most reports of deaths have been in patients >50 years of age and in patients with serious underlying disease.

Skin and subcutaneous tissue disorders

*Uncommon: Rash, urticaria and purpura.

Very rare: Erythema multiforme, Stevens-johnson syndrome, and toxic epidermal necrolysis.

(See also Immune system disorders).

Musculoskeletal and connective tissue disorders

Very rare: Arthralgia and myalgia sometimes develop more than 48 hours after the start of the treatment.

Renal and urinary disorders

Very rare: Interstitial nephritis.

This is reversible when treatment is discontinued.

General disorders and administration site conditions

Very rare: Fever sometimes develops more than 48 hours after the start of the treatment.

*The incidence of these AEs was derived from clinical studies involving a total of approximately 929 adult and paediatric patients talking flucloxacillin.

4.9 Overdose

Symptomatic treatment if appropriate. Flucloxacillin is not significantly removed by dialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Flucloxacillin is a penicillinase-resistant semi-synthetic penicillin resistant to gastric acid.

Flucloxacillin has the same spectrum of activity as the earlier antistaphylococcal penicillins methicillin and cloxacillin against gram-positive organisms, including penicillinase-producing strains.

5.2 Pharmacokinetic properties

Peak serum concentrations are reached after one hour, following an oral dose of 250 mg to 500 mg in fasting subjects. Peak serum concentrations range from 3 to 27 µg/ml with a mean peak of 11 to 15 µg/ml. Therapeutic concentrations persist for about 4 hours.

5.3 Preclinical safety data

None known.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium benzoate (E 211)
Disodium edetate
Saccharin sodium
Monoammonium glycyrrhizinate
Sodium citrate
Flavour menthol (contains sulphur dioxide E220)
Flavour pineapple (contains sulphur dioxide E220)
Sucrose
Erythrosine (E 127)

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

Powder: 18 months.
Reconstituted solution: 7 days.

6.4 Special precautions for storage

Powder: Do not store above 25°C.
Reconstituted oral solution: Store in a refrigerator between 2°C - 8°C.

6.5 Nature and contents of container

150 ml amber glass bottle with polypropylene screw caps
Or 150 ml high density polyethylene bottle with tamper evident screw cap.

150ml high density polyethylene bottles with tamper evident and child resistant closures- Polypropylene cap with Uni-Foam wad/liner- Expanded polyethylene liner (Extruded closed cell foam produced from Low Density Polyethylene) (LDPE) not faced with aluminium.

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

To prepare solution, add 58 ml of water and shake until all powder is dissolved. On reconstitution the product is a clear red solution with a pineapple odour and flavour.

7 MARKETING AUTHORISATION HOLDER

Pinewood Laboratories Limited, Trading as Pinewood Healthcare
Ballymacarbry
Clonmel
County Tipperary

8 MARKETING AUTHORISATION NUMBER

PA 0281/031/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 19 March 1987

Date of last renewal: 19 May 2007

10 DATE OF REVISION OF THE TEXT

November 2007.