Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Fluclon 500 mg Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains flucloxacillin sodium equivalent to 500 mg flucloxacillin.

Excipients with known effect: contains up to 25 mg of sodium per capsule.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsule, hard
Size 0 elongated, hard gelatin capsules with a blue cap and body printed with a twin triangle logo and the identifying code 'FXN 500'.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Fluclon is indicated for the treatment of infections due to penicillinase-producing staphylococci and other gram-positive organisms susceptible to this anti-infective.

Consideration should be given to official guidence on the appropriate use of antibiotic agents.

4.2 Posology and method of administration

Posology
The dosage depends on severity and nature of the infection.
The dosage may be increased if necessary.

Usual Adult (and children over 10 years of age) dosage:	250 – 500 mg three times a day.
Children under 10 years of age:	Not recommended.
Osteomyelitis, endocarditis:	Up to 8 g daily in divided doses six to eight-hourly.

Abnormal renal function:
In common with other penicillins, flucloxacillin usage in patients with renal impairment does not usually require dosage reduction. In patients with severe renal failure (creatinine clearance < 10 ml/min) a reduction in dose or an extension of the dose interval should be considered. In high dose regimens the maximum recommended dose is 1 g every 8 to 12 hours. Since flucloxacillin is not removed by dialysis no supplementary dosages need be administered.

Method of administration: Oral

4.3 Contraindications

Hypersensitivity to beta-lactam antibiotics (e.g. penicillins, cephalosporins) or to any of the excipients listed in section 6.1.

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

4.4 Special warnings and precautions for use

1. Orally administered forms should be given ½ to 1 hour before meals.

2. Prolonged use of an anti-infective agent may result in the development of superinfection due to organisms resistant to that anti-infective.

3. Flucloxacillin appears to be 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 designing therapy.

4. 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 individuals with a history of beta-lactam hypersensitivity.

5. Flucloxacillin should be used with caution in patients with evidence of hepatic dysfunction. (see section 4.8). During prolonged treatments (e.g. osteomyelitis, endocarditis), regular monitoring of hepatic and renal functions is recommended.

   This medicinal product contains up to 25 mg sodium per 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

Cross-resistance and cross sensitisation with other penicillins and cephalosporins may occur.

Probenecid decreases the renal tubular secretion of flucloxacillin. Concurrent administration of probenecid delays the renal excretion of flucloxacillin.

Bacteriostatic drugs may interfere with the bactericidal action of flucloxacillin.

In common with other antibiotics, flucloxacillin may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral contraceptives.

The efficacy of warfarin may be affected by flucloxacillin. Close monitoring of the International Normalised Ratio (INR) is recommended and dose adjustments of warfarin may be necessary.

4.6 Fertility, pregnancy and lactation

Pregnancy
Animal studies with flucloxacillin have shown no teratogenic effects.

Flucloxacillin has been in clinical use since 1970 and in the limited number of cases where it has been used in human pregnancy no evidence of untoward effect has been reported. The product should not be used during pregnancy unless considered essential by the physician.

Breast-feeding
Trace quantities of penicillins can be detected in breast milk.

4.7 Effects on ability to drive and use machines

Flucon capsules have no or negligible influence on the ability to drive and use machines.

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).

Blood and lymphatic system disorders
Very rare: Neutropenia (including agranulocytosis) and thrombocytopenia. These are reversible when treatment is discontinued. Eosinophilia.

Immune system disorders
Very rare: Anaphylactic shock (exceptional with oral administration) (see 4.4 special warnings and precautions for use), angioneurotic oedema.

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

Gastrointestinal disorders
Common: Minor gastrointestinal disturbances.
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 section 4.4 Special warnings and special precautions for use). Changes in liver function 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 of the reaction has been protracted and lasted for several months. Very rarely, deaths have been reported, almost always in patients with serious underlying disease.

There is evidence that the risk of flucloxacillin induced liver injury is increased in subjects carrying the HLA-B*5701 allele. Despite this strong association, only 1 in 500-1000 carriers will develop liver injury. Consequently, the positive predictive value of testing the HLA-B*5701 allele for liver injury is very low (0.12%) and routine screening for this allele is not recommended.

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.

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, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Gastrointestinal effects such as nausea, vomiting and diarrhoea may be evident and should be treated symptomatically. Flucloxacillin is not removed from the circulation by haemodialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: J01CF 05
Pharmacotherapeutic group: Beta-lactamase resistant penicillins

Flucloxacillin, an isoxazolyl penicillin, is a potent inhibitor of the growth of most penicillinase-producing staphylococci. It is markedly resistant to cleavage by penicillinase and is relatively stable in an acidic medium.

There is evidence that the risk of flucloxacillin induced liver injury is increased in subjects carrying the HLA-B*5701 allele. Despite this strong association, only 1 in 500-1000 carriers will develop liver injury. Consequently, the positive predictive value of testing the HLA-B*5701 allele for liver injury is very low (0.12%) and routine screening for this allele is not recommended.

5.2 Pharmacokinetic properties

Absorption
Fluclon is stable in acid media and can therefore be administered by oral route. The peak serum levels of flucloxacillin reached after 1 h are as follows:

- After 250 mg by the oral route (in fasting subjects): approximately 8.8 mg/l.
- After 500 mg by the oral route (in fasting subjects): approximately 14.5 mg/l.

The total quantity absorbed by the oral route represents approximately 79% of the quantity administered.

Distribution
Protein binding: the serum protein binding rate is 95%.
Flucloxacillin diffuses well into most tissues.

Crossing the meningeal barrier: flucloxacillin diffuses in only small proportion into the cerebrospinal fluid of subjects whose meninges are not inflamed.
Crossing into mother’s milk: flucloxacillin is excreted in small quantities in mother’s milk.

Biotransformation
In normal subjects, approximately 10% of the flucloxacillin administered is metabolised to penicilloic acid. The elimination half life of flucloxacillin is in the order of 53 min.

Elimination
Excretion occurs mainly through the kidney. Sixty five percent of the dose administered orally is recovered in unaltered active form in the urine within 8h. A small portion of the dose administered is excreted in the bile. The excretion of flucloxacillin is slowed in cases of renal failure.

5.3 Preclinical safety data

No further information provided.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Magnesium Stearate

Capsule shell components

Gelatin
Patent Blue V (E131)
Erythrosine (E127)
Titanium Dioxide (E171)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C.
Keep the container tightly closed.

6.5 Nature and contents of container

Polypropylene tubes with low density polyethylene caps. High density polypropylene film may be used as packing material.

Pack sizes: 50, 100, 250, 500 and 1,000 capsules.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements

7 MARKETING AUTHORISATION HOLDER

Clonmel Healthcare Ltd.
Waterford Road
Clonmel
Co. Tipperary

8 MARKETING AUTHORISATION NUMBER

PA0126/063/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 14th February 1995

Date of last renewal: 14th February 2010

10 DATE OF REVISION OF THE TEXT

April 2015