1. **NAME OF THE MEDICINAL PRODUCT**

Flucloxacillin 125mg/5ml powder for oral solution

2. **QUALITATIVE AND QUANTITATIVE COMPOSITION**

Flucloxacillin Sodium 136mg equivalent to Flucloxacillin 125mg.

For full list of excipients, see section 6.1.

3. **PHARMACEUTICAL FORM**

- Powder for oral solution
- Pink free flowing powder.

4. **CLINICAL PARTICULARS**

4.1 **Therapeutic indications**

Flucloxacillin Sodium is used for the treatment of infections due to staphylococci resistant to benzylpenicillin. It is also used for mixed streptococcal and staphylococcal infections when the staphylococci are penicillin-resistant.

Typical indications include: skin and soft tissue infections (boils, abscesses, carbuncles, furunculosis, cellulitis, infected wounds, infected burns, protection for skin grafts, otitis media and externa), respiratory tract infections (pneumonia, lung abscess, empyema, sinusitis, pharyngitis, tonsillitis, quinsy). Other infections include: osteomyelitis, enteritis, endocarditis, urinary tract infections, meningitis and septicaemia.

4.2 **Posology and method of administration**

Dose: Take orally an hour before food or on an empty stomach.

Dosage for all indications except osteomyelitis, endocarditis and surgical prophylaxis:

Adults (including the elderly):
Oral – 10ml four times daily.
Osteomyelitis, endocarditis: Up to 320ml (8g) daily in divided doses 6-8 hourly.

Surgical prophylaxis: Following IV administration of the injectable form of flucloxacillin, oral administration of 20ml flucloxacillin elixir (containing 500mg flucloxacillin) should be administered six hourly for up to 72 hours postoperatively.

Children: 2-10 years:
5ml four times daily.

Under 2 years:
2.5ml four times daily.

In serious infections, dosages may be doubled. Treatment for over 2 weeks should be considered with caution, due to the risk of cholestatic jaundice after prolonged treatment.

4.3 Contraindications
It is contraindicated in patients known to be hypersensitive to penicillins or any of the ingredients.

4.4 Special warnings and precautions for use
Flucloxacillin should be given with caution to patients with a history of allergy. Preparations should be made to deal with anaphylactic shock before the first dose is given. Care is necessary where large doses of sodium salts are given to patients with impaired renal function or congestive heart failure.

The use of Flucloxacillin (like other Penicillins) in patients with renal impairment does not usually require dosage reduction. In the presence of severe renal failure (Creatinine clearance less than 10ml/min), however, a reduction in dose or an extension of dose interval should be considered.

Flucloxacillin is not significantly removed by dialysis and so no supplementary dosages need to be administered either during or at the end of the dialysis period.

Hepatitis and Cholestatic jaundice have been reported. These reactions are related neither to the dose nor to the route of administration. The onset of these effects may be delayed for up to two months post-treatment; in several cases, the course of the reactions has been protracted and lasted for some months. In very rare cases, a fatal outcome has been reported.

Contact with penicillins should be avoided since skin sensitisation may occur.
4.5 Interaction with other medicinal products and other forms of interaction
Serum concentrations of Flucloxacillin are enhanced if Probenecid is given concomitantly.

4.6 Pregnancy and lactation
Flucloxacillin diffuses across the placenta into the foetal circulation and is excreted in the milk of nursing mothers. The use of Flucloxacillin in pregnancy should be reserved for cases considered essential by the clinician.

4.7 Effects on ability to drive and use machines
Not applicable.

4.8 Undesirable effects
When Flucloxacillin Sodium is administered to a hypersensitive patient, anaphylactic shock with collapse and sometimes death may occur within minutes. A generalised sensitivity reaction can occur within 1-3 weeks with urticaria, fever, eosinophilia, joint pains, angioneurotic oedema, erythema multiforme, and exfoliative dermatitis, although an accelerated urticarial reaction can develop within hours.

Convulsions and other signs of toxicity to the central nervous system may occur with very high doses of Flucloxacillin particularly when administered to infants and the elderly, and to patients with renal failure. Administration of Flucloxacillin by mouth is liable to produce transient diarrhoea and sometimes nausea, heartburn and pruritis ani. Skin rashes may occur. If a rash occurs, treatment should be discontinued.

4.9 Overdose
Treatment should be symptomatic. Patient should be kept under observation with high doses (mainly parenteral), neurotoxicity may develop.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
ATC Code: J01CF05

Flucloxacillin Sodium, like other isoxazolyl penicillins, is a potent inhibitor of the growth of most penicillinase-producing staphylococci. This agent, in general, is less effective against microorganisms susceptible to penicillin G and are not as useful against gram-negative bacteria.
Flucloxacillin Sodium is bactericidal. It is considered to act by inhibiting transpeptidase, the enzyme responsible for cross-linking of peptidoglycan during the final stages of synthesis of the bacterial cell wall and so exerts its effects against dividing bacteria. It is active against most gram-positive organisms and neisseria spp.

A minimum inhibitory concentration against penicillin-resistant staphylococci of 0.25-0.5g/ml has been reported. It’s activity against both penicillin-resistant and penicillin-sensitive staphylococci is 4 to 8 times that of methicillin sodium, but against penicillin-sensitive staphylococci, its activity is only about one quarter that of benzylpenicillin or phenoxymethyl-penicillin. Its activity against streptococci is less than that of benzylpenicillin but sufficient to be useful when these organisms are present with penicillin-resistant staphylococci.

Resistance to Flucloxacillin has developed in both penicillinase and non-penicillinase producing staphylococci with cross resistance to other penicillins, including the penicillinase-resistant penicillins such as cloxacillin, nafcillin and oxacillin; to the cephalosporins and to other antibiotics including chloramphenicol, erythromycin, tetracycline, kanamycin, streptomycin, and lincomycin. This resistance is intrinsic and unrelated to penicillin production.

5.2 Pharmacokinetic properties
Flucloxacillin Sodium is better absorbed from the gastrointestinal tract than cloxacillin sodium but absorption is also reduced by food in the stomach or small intestine. After an oral dose of 250mg to 500mg, in fasting subjects, peak serum concentrations in about 1 hour may range from 3 to 27μg per ml with mean peak concentrations of about 11 to 15μg per ml. A therapeutic concentration persists for about 4 hours. Doubling the dose can double the plasma concentration. Some 50% of a dose by mouth is excreted in the urine within 6 hours, serum concentrations are enhanced if probenecid is given concomitantly.

About 90-95% of Flucloxacillin in the circulation is bound to plasma albumin to a greater extent, none is removed from the circulation to a significant degree by haemodialysis.

The isoxazolyl penicillins, like Flucloxacillin, are rapidly excreted by the kidney. There is also significant hepatic elimination of these agents in the bile. The plasma half life of Flucloxacillin is 60 minutes in healthy subjects.

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

- Sodium Benzoate (E211)
- Disodium Edetate
- Saccharin Sodium
- Mono-Ammonium-Glycyrrhizante
- Sodium Citrate (dried) (E331)
- Flavour Pineapple
- Flavour Menthol
- Erythrosine (E127)
- Sucrose

6.2 Incompatibilities

As for Penicillin. Incompatible with Colistin Polymixin B Sulphate. Loss of potency after mixing with Streptomycin has also been reported.

6.3 Shelf life

Unopened: 3 years
After reconstitution or when the container is opened for the first time: 7 days.

6.4 Special Precautions for Storage

Unopened bottle: Do not store above 25°C. Store in the original container. Keep the container tightly closed.
Reconstituted solution: Store at 2-8°C.

6.5 Nature and contents of container

Nature: 150ml amber glass Beatson Clark container with polypropylene screw cap or 150ml high density polyethylene bottle with tamper evident cap: 100ml

6.6 Special precautions for disposal

To reconstitute, add 58ml of water, replace the lid and shake the bottle well.

Any unused product or waste material should be disposed of in accordance with local requirements.
7. **Marketing Authorisation Holder**

   Medreich Plc  
   Warwick House  
   Plane Tree Crescent  
   Feltham  
   TW13 7HF

8. **MARKETING AUTHORIZATION NUMBER(S)**

   PL 21880/0063

9. **DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORIZATION**

   26/05/2011

10. **DATE OF REVISION OF THE TEXT**

    07/10/2013