FLUCLOXACILLIN 250MG/5ML GRANULES FOR ORAL SOLUTION
PL 20416/0210

UKPAR

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The Medicines and Healthcare products Regulatory Agency (MHRA) granted Crescent Pharma Limited a Marketing Authorisation (licence) for the medicinal product Flucloxacillin 250mg/5ml Granules for Oral Solution (PL 20416/0210) on 18 August 2011. This is a prescription-only medicine (POM) used to treat various bacterial infections, which include skin and soft tissue infections, throat and chest infections, and other infections (such as urinary tract infection and prevention of infection during surgery).

Flucloxacillin 250mg/5ml Granules for Oral Solution contains the active ingredient flucloxacillin (as flucloxacillin sodium), which belongs to the penicillin group of antibiotics, which kill bacteria or prevent their growth.

No new or unexpected safety concerns arose from this simple application and it was, therefore, judged that the benefits of taking Flucloxacillin 250mg/5ml Granules for Oral Solution outweigh the risks; hence a Marketing Authorisation has been granted.
FLUCLOXACILLIN 250MG/5ML GRANULES FOR ORAL SOLUTION
PL 20416/0210

Scientific Discussion

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INTRODUCTION

The MHRA granted a Marketing Authorisation for the medicinal product Flucloxacillin 250mg/5ml Granules for Oral Solution (PL 20416/0210) to Crescent Pharma Limited on 18 August 2011. The product is available as a prescription-only medicine indicated for the treatment of infections due to gram-positive organisms, including infections caused by β-lactamase-producing staphylococci associated with:

- skin and soft tissue: boils, abscesses, carbuncles, infected skin conditions (e.g. ulcer, eczema, and acne), furunculosis, cellulitis, infected wounds and burns, protection for skin grafts and impetigo
- respiratory tract: pneumonia, lung abscess, empyema, sinusitis, pharyngitis, tonsillitis and quinsy
- other infections: otitis media and externa, osteomyelitis, enteritis, endocarditis, urinary tract infection, meningitis, septicaemia.

Flucloxacillin 250mg/5ml Granules for Oral Solution is also used as a prophylactic agent during major surgical procedures, where appropriate (e.g. cardiothoracic and orthopaedic surgery).

The application was submitted as an abridged application according to Article 10c of Directive 2001/83/EC, as amended, cross-referring to Flucloxacillin 250mg/5ml Granules for Oral Solution (PL 20416/0077), which was granted a Marketing Authorisation to Crescent Pharma Limited on 02 March 2004.

Flucloxacillin 250mg/5ml Granules for Oral Solution contains the active ingredient flucloxacillin as flucloxacillin sodium. The bactericidal action of flucloxacillin sodium depends on its ability to reach and bind penicillin-binding proteins (PEP-1 and PBP-3) located in bacterial cytoplasmic membranes. Flucloxacillin sodium inhibits bacterial septum and cell wall synthesis probably by acylation of membrane bound transpeptidase enzymes; thus preventing cross linkage of peptidoglycan chains which are necessary for bacterial cell wall strength and rigidity. Cell division and growth are also inhibited and lysis and elongation of susceptible bacteria frequently occur.

No new data were submitted nor were they necessary for this simple application, as the data are identical to those of the previously granted cross-reference product.
PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 20416/0210

PROPRIETARY NAME: Flucloxacillin 250mg/5ml Granules for Oral Solution

ACTIVE(S): Flucloxacillin sodium

COMPANY NAME: Crescent Pharma Limited

E.C. ARTICLE: Article 10c of Directive 2001/83/EC

LEGAL STATUS: POM

1. INTRODUCTION
This is an abridged application for Flucloxacillin 250mg/5ml Granules for Oral Solution, submitted under Article 10c of Directive 2001/83/EC, as amended. The proposed Marketing Authorisation Holder is Crescent Pharma Limited, Units 3 and 4, Quidhampton Business Units, Polhampton Lane, Overton, Hampshire, RG25 3ED.

The application cross-refers to Flucloxacillin 250mg/5ml Granules for Oral Solution (PL 20416/0077) which was granted a Marketing Authorisation to Crescent Pharma Limited on 02 March 2004.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Name(s)
The proposed name of the product is Flucloxacillin 250mg/5ml Granules for Oral Solution. The product has been named in line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes
Each 5 ml of reconstituted product (oral solution) contains 250 mg of flucloxacillin (as flucloxacillin sodium) as the active ingredient. The product is packaged in round, natural high-density polyethylene (HDPE) bottles with tamper evident polypropylene (PP) closures in a pack size of 100 ml.

The proposed shelf-lives (2 years before reconstitution and 1 week after reconstitution) and storage conditions (“Do not store above 25ºC. Keep the bottle tightly closed.” for the dry granules and “Store in a refrigerator. Use within one week of preparation.” for the reconstituted product) are consistent with the details registered for the cross-reference product.

2.3 Legal status
On approval, the product will be available as a prescription-only medicine (POM).

2.4 Marketing Authorisation Holder/Contact Persons/Company
Crescent Pharma Limited, Units 3 and 4, Quidhampton Business Units, Polhampton Lane, Overton, Hampshire, RG25 3ED.

The Qualified Person (QP) responsible for pharmacovigilance is stated and his CV is included.
2.5 Manufacturers
The proposed manufacturing sites are consistent with those registered for the cross-reference product and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

2.6 Qualitative and quantitative composition
The proposed composition is consistent with the details registered for the cross-reference product.

2.7 Manufacturing process
The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size is stated.

2.8 Finished product/shelf-life specification
The proposed finished product specification is in line with the details registered for the cross-reference product.

2.9 Drug substance specification
The proposed drug substance specification is consistent with the details registered for the cross-reference product.

2.10 TSE Compliance
None of the excipients contain materials of animal or human origin. This is consistent with the cross-reference product.

2.11 Bioequivalence
No bioequivalence data are required to support this informed consent application, as the proposed product is manufactured to the same formula and utilising the same process as the reference product.

3. EXPERT REPORTS
The applicant cross-refers to the data for Flucloxacillin 250mg/5ml Granules for Oral Solution (PL 20416/0077), to which it claims to be identical. This is acceptable.

4. PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product name. The appearance of the product is identical to the cross-reference product.

5. SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
The proposed Summary of Product Characteristics is consistent with the details registered for the cross-reference product.

6. PATIENT INFORMATION LEAFLET (PIL) AND LABELLING
PIL
The patient information leaflet has been prepared in-line with the details registered for the cross-reference product.

Crescent Pharma Limited has previously submitted results of consultations with target patient groups (‘user testing’), in accordance with Article 59 of Council Directive 2001/83/EC, for the reference product Flucloxacillin 250mg/5ml Granules for Oral Solution.
Solution (PL 20416/0077). The results indicate that the leaflet is well-structured and organised, easy to understand, and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

As the leaflet for Flucloxacillin 250mg/5ml Granules for Oral Solution (PL 20416/0077) and this product are considered the same, no further user testing of the leaflet for this product is necessary.

Bottle label
The proposed artwork is consistent with the artwork registered for the cross-reference product and complies with statutory requirements. In line with current legislation, the applicant has also included the name of the product in Braille on the outer packaging.

7. CONCLUSION
The data submitted with the application are acceptable. The grant of a Marketing Authorisation is recommended.
NON-CLINICAL ASSESSMENT

As this is an abridged application submitted under Article 10c, no new non-clinical data have been supplied and none are required.

The Marketing Authorisation Holder has provided adequate justification for not submitting an Environment Risk Assessment (ERA). As the product is intended for generic substitution with products that are already marketed, no increase in environmental burden is anticipated. Thus, the justification for non-submission of an Environmental Risk Assessment is accepted.

The grant of a Marketing Authorisation is recommended.
CLINICAL ASSESSMENT

As this is an abridged application submitted under Article 10c, no new clinical data have been supplied and none are required.

The Marketing Authorisation Holder has provided details of a suitable pharmacovigilance system that fulfils the requirements and provides adequate evidence that they have the services of a qualified person responsible for pharmacovigilance, and have the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

The Marketing Authorisation Holder has not submitted a Risk Management Plan (RMP). As the application is for an identical version of already authorised reference product, for which safety concerns requiring additional risk minimisation have not been identified, a risk minimisation system is not considered necessary. The reference product has been in use for many years and the safety profile of the active ingredient is well-established.

The grant of a Marketing Authorisation is recommended.
OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

QUALITY
The data for this application are consistent with those previously assessed for the cross-reference product and as such have been judged to be satisfactory.

NON-CLINICAL
No new non-clinical data were submitted and none are required for this type of application.

EFFICACY
This application is identical to a previously granted application for Flucloxacillin 250mg/5ml Granules for Oral Solution (PL 20416/0077). No new or unexpected safety concerns arise from this application.

PRODUCT LITERATURE
The SmPC, PIL and labelling are satisfactory and consistent with that for the cross-reference product.

BENEFIT/RISK ASSESSMENT
The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant’s product is identical to the cross-reference product. Extensive clinical experience with flucloxacillin sodium is considered to have demonstrated the therapeutic value of the product. The benefit/risk is, therefore, considered to be positive.
FLUCLOXACILLIN 250MG/5ML GRANULES FOR ORAL SOLUTION
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STEPS TAKEN FOR ASSESSMENT

1  The MHRA received the Marketing Authorisation application on 03 June 2011.
2  Following standard checks and communication with the applicant the MHRA considered the application valid on 16 June 2011.
3  Following assessment of the application, no further information relating to the dossier was required.
4  The application was determined on 18 August 2011.
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Flucloxacillin 250mg/5ml Granules for Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Flucloxacillin sodium 272.00 mg equivalent to 250 mg flucloxacillin per 5 ml of reconstituted product.

Excipients: Each 5 ml contains 3g of sucrose, 16mg of sodium, 5mg of aspartame, 0.4g of amaranth, 2mg of E217 & 6mg of E219.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Flucloxacillin granules for oral solution.
Red granules.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Flucloxacillin 250mg/5ml Granules for Oral Solution is indicated for the treatment of infections due to gram-positive organisms including infections caused by β-lactamase-producing staphylococci associated with:-

SKIN AND SOFT TISSUE: boils, abscesses, carbuncles, infected skin conditions e.g. ulcer, eczema, and acne, furunculosis, cellulitis, infected wounds and burns, protection for skin grafts and impetigo.

RESPIRATORY TRACT: pneumonia, lung abscess, empyema, sinusitis, pharyngitis, tonsillitis and quinsy.

OTHER INFECTIONS: otitis media and externa, osteomyelitis, enteritis, endocarditis, urinary tract infection, meningitis, septicaemia.

AS A PROPHYLACTIC: agent during major surgical procedures where appropriate e.g. cardiothoracic and orthopaedic surgery.

4.2 Posology and method of administration
DOSAGE: Doses should be administered ½ - 1 hour before meals.

ADULTS (INCLUDING ELDERLY): 250 mg four times daily. The dose may be doubled where necessary.

Osteomyelitis, endocarditis: Up to 8g daily, in divided doses six to eight hourly.

Surgical prophylaxis: 1 – 2 G IV at induction of anaesthesia followed by 500 mg six hourly orally for up to 72 hours.

CHILDREN: Over 10 years – as for adults
2 – 10 years - ½ adult dose
Under 2 years - ¼ adult dose

ABNORMAL RENAL FUNCTION: Dose reduction is usually not required in patients with renal impairment. However, in the presence of severe renal failure (creatinine clearance < 10 ml/min) a reduction in dose or an extension of dose interval should be considered.

Route of administration: Oral use

For instructions on dilution of the product before administration, see section 6.6.
4.3 **Contraindications**
Patients with a history of hypersensitivity to β-lactam antibiotics, (e.g. penicillins, cephalosporins) or to any of the excipients.

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

4.4 **Special warnings and precautions for use**
Before initiating therapy with flucloxacillin careful enquiry should be made concerning any previous hypersensitivity to β-lactams. Patients receiving β-lactam antibiotics have been reported to experience serious and occasionally fatal hypersensitivity reactions (anaphylaxis). Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients on oral therapy. Patients with a history of β-lactam hypersensitivity are more likely to experience these reactions.

Flucloxacillin should be used with caution in patients with evidence of hepatic dysfunction, patients ≥50 years and those with serious underlying disease. In these patients, hepatic events may be severe, and in very rare circumstances, deaths have been reported (see section 4.8).

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

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.

Overgrowth of non-susceptible organisms may occasionally result after prolonged use.

Sucrose: Each 5ml dose contains 3g sucrose; this should be taken into account in patients with diabetes. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Sodium: Each 5ml dose contains 16mg of sodium. To be taken into consideration by patients on a controlled sodium diet.

Aspartame: Contains a source of phenylalanine. May be harmful for people with phenylketonuria.

Amaranth: May cause allergic reactions.

E217 & E219: May cause allergic reactions (possibly delayed).

4.5 **Interaction with other medicinal products and other forms of interaction**
Probenecid decreases the renal excretion of penicillins and serum concentrations of flucloxacillin are enhanced if probenecid is administered concurrently.

Oral courses of broad-spectrum anti-bacterials may affect the hypothrombinaemic response to oral anticoagulants.

Methotrexate excretion is reduced by penicillins. Patients should be monitored carefully for sign of methotrexate toxicity.

Penicillins may decrease the efficacy of combined oral contraceptives. Patients should be warned of this.

4.6 **Pregnancy and lactation**
Studies conducted with animals have shown no teratogenic effects. The product has been in clinical use since 1970 and the limited number of reported cases of use in human pregnancy has shown no evidence of untoward effect.
Use in pregnancy should be reserved for cases considered essential by the clinician.

Breast feeding is not contraindicated with flucloxacillin. Trace quantities of the drug are excreted in the breast milk. While adverse effects are apparently rare, three potential problems exist for the nursing infant: modification of bowel flora, direct effects on the infant such as allergy/sensitisation and interference with interpretation of culture results when pyrexia of unknown origin occurs.

4.7 Effects on ability to drive and use machines
None

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, <1/1,000); 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 agranulocytosis) and thrombocytopenia. These are reversible when treatment is discontinued. Haemolytic anaemia.

**Immune system disorders:**
Very rare: Anaphylactic shock (exceptional with oral administration) (See section 4.4 Special warnings and special 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 laboratory test results (reversible when treatment is discontinued).

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. Hepatic events may be severe and in very rare circumstances a fatal outcome has been reported. Most reports of deaths have been in patients ≥50 years 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 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 is reported to be derived from clinical studies involving a total of approximately 929 adult and paediatric patients taking flucloxacillin.

4.9 Overdose
Problems of overdosage are unlikely to occur; if encountered they should be treated symptomatically. More specific measures may be necessary in patients with impaired renal function. Flucloxacillin is not significantly removed by dialysis.

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
J01CF05 Beta-lactamase resistant penicillins

Bactericidal action of flucloxacillin depends on its ability to reach and bind. Penicillin binding proteins (PEP-1 and PBP-3) located in bacterial cytoplasmic membranes.

Flucloxacillin inhibits bacterial septum and cell wall synthesis probably by acylation of membrane bound transpeptidase enzymes; thus preventing cross linkage of peptidoglycan chains which are necessary for bacterial cell wall strength and rigidity.

Cell division and growth are also inhibited and lysis and elongation of susceptible bacteria frequently occur.

Rapidly dividing bacteria are the most susceptible to the action of flucloxacillin.

5.2 Pharmacokinetic properties
Flucloxacillin sodium is better absorbed from the gastro-intestinal tract than cloxacillin sodium. The absorption is decreased in the presence of food in the stomach and small intestine.

Flucloxacillin in common with other penicillins is widely distributed throughout the body. Approximately 95% of the drug is bound to plasma proteins. The half-life of flucloxacillin is 30-60 minutes. It is rapidly excreted by the kidneys. Following an oral dose of 250–500 mg in fasting subjects peak serum concentrations are attained in an hour and may range from 3–27 mcg/ml with the mean concentration being 11–15 mcg/ml.

Therapeutic concentration persists for about 4 hours. Doubling the dose can double the plasma concentration. Approximately 50% of the oral dose is eliminated in the urine within 6 hours. Serum concentrations are enhanced if probenecid is administered concomitantly.

5.3 Preclinical safety data
There are no preclinical data of relevance to the prescriber, which are additional to those already included in other sections of the SmPC.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Sodium Propyl Parahydroxybenzoate E217
Sodium Methyl Parahydroxybenzoate E219
Sodium Citrate
Citric Acid Anhydrous
Aspartame E951
Amaranth (E123)
Cherry Flavour
Sucrose

6.2 Incompatibilities
Incompatible with colistin sulphomethate sodium, gentamicin, kanemycin and Polymycin B Sulphate. Loss of potency after mixing with streptomycin has also been reported.
6.3 Shelf life
Before reconstitution: 2 years.
After reconstitution: 1 week

6.4 Special precautions for storage
In the form of dry granules: Do not store above 25°C. Keep the bottle tightly closed.

After reconstitution: Store in a refrigerator. Use within one week of preparation.

6.5 Nature and contents of container
Round, natural HDPE bottles with tamper evident polypropylene closure containing 66 gm of granules. The brimfill capacity of the bottle is 175 ml and the nominal working capacity is 150 ml.

6.6 Special precautions for disposal
To reconstitute the granules to make the solution, add 58 ml of water and shake well until the powder is dissolved. When reconstituted the solution produced is essentially a clear red cherry coloured solution.

7 MARKETING AUTHORISATION HOLDER
Crescent Pharma Limited
Units 3 & 4, Quidhampton Business Units
Polhampton Lane
Overton
Hampshire
RG25 3ED

8 MARKETING AUTHORISATION NUMBER(S)
PL 20416/0210

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
18/08/2011

10 DATE OF REVISION OF THE TEXT
18/08/2011
PATIENT INFORMATION LEAFLET

Flucloxacillin 250mg/5ml Granules for Oral Solution

Please read all of this leaflet carefully before you start taking this medicine.

Keep the leaflet; you may need to read it again. If you have any questions or are not sure about anything, ask your doctor or pharmacist.

This medicine is for you. Only a doctor can prescribe it. Never give this medicine to anyone else. It may harm them even if their symptoms are the same as yours.

IN THIS LEAFLET:
1. What this medicine is and what it is used for
2. Before you take this medicine
3. How to take this medicine
4. Possible side effects
5. How to store this medicine
6. Further information

1. WHAT THIS MEDICINE IS AND WHAT IT IS USED FOR
Each 5ml of oral solution contains 250mg of flucloxacillin (as flucloxacillin sodium) as the active ingredient.

This medicine belongs to the penicillin group of antibiotics. It is used to treat various bacterial infections by killing the bacteria or preventing their growth. These include skin and soft tissue infections, throat and chest infections, other infections such as urinary tract infection and prevention of an infection occurring during surgery.

2. BEFORE YOU TAKE THIS MEDICINE
Do not take this medicine if:
- you are allergic to any penicillin or other kind of antibiotic or to any of the other ingredients listed (see section 6).
- you have ever had any liver problems after taking flucloxacillin

Check with your doctor before taking this medicine if:
- you are pregnant, think you may be pregnant or breastfeeding
- you have a history of allergy
- you have liver or kidney problems
- you have any serious illness
- you are 50 years old or over
- you are giving this medicine to a newborn child

Taking other medicines
Check with your doctor or pharmacist before taking this medicine if you are taking other medicines, including any that you can buy without a prescription. This is important if you are taking other medicines, especially:
- probenecid – used for treatment of gout
- oral anti-coagulants e.g. warfarin – used for thinning blood
- methotrexate – a cancer drug which can also be used to treat psoriasis
- birth control pills

Tests:
Your doctor may want to carry out regular monitoring of your kidney or liver function if you are taking this medicine long term.

If you need to have a liver function test, tell your doctor you are taking this medicine as it may affect the results.

Driving and using machinery:
This medicine should not affect your ability to drive or operate machinery. However, if you think you are affected do not drive or operate machinery.

Important information about some of the ingredients of this medicine:
- Each 5 ml dose contains 0.9g sucrose: this should be taken into account in patients with diabetes mellitus. Also if you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.
- Amaranth may cause allergic reactions.
- Aspartame contains a source of phenylalanine which may be harmful for people with phenylketonuria.
- E217 and E219 may cause allergic reactions (possibly delayed).

- Each 5ml dose contains approx 16mg of sodium. This may need to be taken into consideration in patients on a controlled sodium diet, particularly if you are prescribed more than the usual dose.

3. HOW TO TAKE THIS MEDICINE
For oral use. Shake the bottle well before use. Take the medicine half an hour to an hour before meals.

Follow your doctor's instructions about taking your medicine. The label will also tell you how much to take and how often. The dose for this medicine may be different for different patients.

Adults (including the elderly): 250mg (one 5ml spoonful) 4 times a day; your doctor may prescribe double this dose where necessary.

Children, over 10 years: The usual dose is the same as the adult dose.

Children 2 to 10 years of age: Half the adult dose i.e. 125mg (2.5ml) 4 times a day.
Common effects (that could happen to less than 1 in 10 people):
- minor stomach upsets such as feeling sick or diarrhoea;
- very rare effects (that could happen to less than 1 in 10,000 people):
  - inflammation of the kidney or liver and a type of jaundice (symptoms include swelling of the skin or whites of the eyes, loss of appetite, pale stools, dark urine). Some of these effects may be delayed and may not occur until up to 2 months after you have stopped taking this medicine;
  - reduction in the numbers of blood cells which can cause unexplained bleeding, bruising, pale skin, weakness, tiredness;
  - joint or muscle pain or fever, which may develop 2 days or more from the start of treatment;
  - effects on the skin such as rashes, red patches, peeling, swelling, blistering.

Under 2 years of age: A quarter of the adult dose i.e. 62.5mg (1.25ml) 4 times a day (this 250mg/5ml strength medicine is not suitable for use). The length of time for treatment varies depending on the severity and type of infection. However, it is important to finish your prescribed dose of this medicine. If you stop taking this medicine too soon, your symptoms may return.

If you forget to take a dose: take your dose as soon as you remember. However, if it is almost time for your next dose, skip the missed dose and continue with your normal dosing schedule. DO NOT DOUBLE THE DOSES.

If you have taken too much medicine:
- Contact your doctor straight away or go to the nearest hospital casualty department. Take with you any remaining medicine and the pack so that the medicine can be identified.

4. POSSIBLE SIDE EFFECTS

Flucloxacillin is usually well tolerated; however, like all medicines it may sometimes cause side effects.

If you experience any of the following very rare effects (could happen to less than 1 in 10,000 people) while you are taking this medicine, STOP taking it and contact your doctor IMMEDIATELY:
- sudden wheeziness, difficulty breathing, swelling of the face, eyes, lips, tongue or throat, itching or itchy skin rashes (may be signs of allergy or a severe allergic reaction);
- severe bloody diarrhoea with fever and abdominal pain.

Tell your doctor if you notice any of the following side effects or notice any others not listed:

5. HOW TO STORE THIS MEDICINE

Store in a refrigerator. Use within 7 days of preparation.

KEEP ALL MEDICINES OUT OF THE REACH AND SIGHT OF CHILDREN.

If you have any medicines that are out of date, return them to your pharmacist for safe disposal.

6. FURTHER INFORMATION

Ingredients
Each 5ml of oral solution contains 250mg of flucloxacillin (as flucloxacillin sodium) as the active ingredient.

It also contains the inactive ingredients: amaranth (E123), cherry flavour, sodium methylparahydroxybenzoate (E211), sodium propylparahydroxybenzoate (E217), sodium citrate, aspartame (E951), citric acid anhydrous, sucrose and water (when dispensed by the pharmacist).

Although the bottle of your medicine appears to be only partially full, it contains the correct amount of the solution. The extra space is to allow you to shake the medicine.

What the medicine looks like:
Flucloxacillin Oral Solution is a clear, red solution.

Each bottle contains 100 ml.

Who makes this medicine and holds the product licence:
Crescent Pharma Limited, Units 3 & 4, Quilchampton Business Units, Portham Lane, Overton, Hants, RG25 3ED

Date label prepared: December 2010

If you would like this leaflet in a different format please contact the Licence holder at the above address.
MHRA PAR – Flucloxacillin 250mg/5ml Granules for Oral Solution (PL 20416/0210)