Public Assessment Report

UK PAR

Flucloxacillin 250 mg Capsules
Flucloxacillin 500 mg Capsules

(Flucloxacillin sodium)

UK Licence No: PL 44041/0017-0018

Noumed Life Sciences Limited
LAY SUMMARY

Flucloxacillin 250 mg Capsules
Flucloxacillin 500 mg Capsules
(FLUCLOXACILLIN SODIUM)

This is a summary of the Public Assessment Report (PAR) for Flucloxacillin 250 mg and 500 mg Capsules (PL 44041/0017-0018). It explains how the applications for Flucloxacillin 250 mg and 500 mg Capsules were assessed and their authorisation recommended, as well as the conditions of use. It is not intended to provide practical advice on how to use Flucloxacillin 250 mg and 500 mg Capsules.

For practical information about using Flucloxacillin 250 mg and 500 mg Capsules, patients should read the package leaflet or contact their doctor or pharmacist.

Flucloxacillin 250 mg and 500 mg Capsules may be referred to as ‘Flucloxacillin Capsules’ in this Lay summary.

What are Flucloxacillin Capsules’ and what are they used for?

These medicines are the same as Flucloxacillin 250 mg and 500 mg Capsules (PL 21880/0017-0018; Medreich plc), which are already authorised in the UK. The licence holder (Medreich plc, UK) for Flucloxacillin 250 mg and 500 mg Capsules (PL21880/0017-0018) has agreed that its own scientific data can be used as a basis for the grant of identical licences for Flucloxacillin 250 mg and 500 mg Capsules (PL 44041/0017-0018) (informed consent).

Flucloxacillin Capsules belong to a group of antibiotics called “penicillins” and are used to treat the following:

• chest infections
• throat or nose infections
• ear infections
• skin and soft tissue infections
• heart infections
• bone and joint infections
• meningitis
• digestive system infections
• blood infections
• kidney, bladder or urethra (the tube which carries urine from the bladder) infections.

Flucloxacillin Capsules may also be used to prevent infections during major surgery, particularly heart or orthopaedic surgery.

How do Flucloxacillin Capsules work?

Flucloxacillin Capsules contain the active substance flucloxacillin (as flucloxacillin sodium), which is used to treat infection by killing bacteria that cause them. Flucloxacillin belongs to a group of antibiotics called “penicillins”.

How are Flucloxacillin Capsules used?

Flucloxacillin Capsules are available as hard capsules and are taken by mouth.
Flucloxacillin Capsules can only be obtained with a prescription. The capsules should be taken exactly as instructed by the prescribing doctor. The doctor’s directions may differ from the information contained in the package leaflet. The pharmacist’s label should tell the patient how much to take and how often. The patient should check with the doctor or pharmacist if not sure.

The capsules should be taken when the stomach is empty. This means, an hour before food or two hours after food. It is important that the capsules are taken at the right times. The capsules should be swallowed whole with water. The dose will depend on the patient and will be decided by the patient’s doctor.

Please read section 3 of the package leaflet for detailed information on dosing recommendations and the duration of treatment.

What benefits of Flucloxacillin Capsules have been shown in studies?
The applications for Flucloxacillin Capsules (PL 44041/0017-0018) are considered to be identical to the previously authorised licences for Flucloxacillin Capsules (PL 21880/0017-0018; Medreich plc), with the same benefits and risks. So, no new studies have been provided for Flucloxacillin Capsules (PL 44041/0017-0018). However, reference is made to the studies for Flucloxacillin Capsules (PL 21880/0017-0018; Medreich plc).

What are the possible side effects of Flucloxacillin Capsules?
Like all medicines, Flucloxacillin Capsules can cause side effects, although not everybody gets them.

For the full list of all side effects reported with Flucloxacillin Capsules, see section 4 of the package leaflet.

For the full list of restrictions, see the package leaflet.

Why are Flucloxacillin Capsules approved?
No new or unexpected safety concerns arose from these applications. The MHRA, therefore, considered that the benefits of Flucloxacillin Capsules outweigh their risks; and the grant of Marketing Authorisations was recommended.

What measures are being taken to ensure the safe and effective use of Flucloxacillin Capsules?
A Risk Management Plan has been developed to ensure that Flucloxacillin Capsules are used as safely as possible. Based on this plan, safety information has been included in the Summaries of Product Characteristics and the package leaflet for Flucloxacillin Capsules, including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore, new safety signals reported by patients/healthcare professionals will be monitored/reviewed continuously.

Other information about Flucloxacillin Capsules
Marketing Authorisations were granted in the UK to Noumed Life Sciences Limited on 18 October 2016.

The full PAR for Flucloxacillin Capsules follows this summary.
For more information about treatment with Flucloxacillin Capsules read the package leaflet, or contact your doctor or pharmacist.

This summary was last updated in December 2016.
Flucloxacillin 250 mg Capsules
Flucloxacillin 500 mg Capsules
(Flucloxacillin sodium)

PL 440441/0017-0018

SCIENTIFIC DISCUSSION

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I. INTRODUCTION
The Medicines and Healthcare products Regulatory Agency (MHRA) granted Noumed Life Sciences Limited Marketing Authorisations for the medicinal products Flucloxacillin 250 mg and 500 mg Capsules (PL 44041/0017-0018) on 18 October 2016. The products are Prescription Only Medicines (POM) indicated for treatment of infections due to sensitive Gram-positive organisms, including infections caused by β-lactamase-producing Staphylococci and Streptococci. Typical indications include:

- **Skin and soft tissue infections:**
  - boils
  - abscesses
  - carbuncles
  - furunculosis
  - cellulitis
  - infected skin conditions e.g. ulcers, eczema and acne
  - infected wounds
  - infected burns
  - protection for skin grafts
  - impetigo

- **Respiratory tract infections:**
  - pneumonia
  - pharyngitis
  - tonsillitis
  - quinsy
  - empyema
  - lung abscess
  - sinusitis
  - otitis media and externa

- **Other infections caused by Flucloxacillin-sensitive organisms:**
  - osteomyelitis
  - enteritis
  - meningitis
  - septicaemia
  - urinary tract infections
  - endocarditis

Flucloxacillin is also indicated for use as a prophylactic agent during major surgical procedures when appropriate; for example cardiothoracic and orthopaedic surgery. Parenteral usage is indicated where oral dosage is inappropriate.

Consideration should be given to official local guidance (e.g. national recommendations) on the appropriate use of antibacterial agents.

Susceptibility of the causative organism to the treatment should be tested (if possible), although therapy may be initiated before the results are available.

The applications were submitted as simple abridged (informed consent) applications according to Article 10c of Directive 2001/83/EC, as amended. The applications for Flucloxacillin 250 mg and 500 mg Capsules (PL 44041/0017-0018) cross-refer to Flucloxacillin 250 mg and 500 mg Capsules (PL 21880/0017-0018; Medreich plc), which were authorised in the UK on 24 March 2010 through Decentralised procedures (UK/H/1101/001-002/DC). Flucloxacillin 250 mg and 500 mg Capsules
The active ingredient, flucloxacillin (as flucloxacillin sodium), is a well-established antibiotic with bactericidal activity against Gram-positive bacteria.

No new data were submitted nor were they required for these applications, as the products are identical to those of the previously granted cross-reference products.

II. QUALITY ASPECTS

II.1 INTRODUCTION
These are informed consent applications for Flucloxacillin 250 mg and 500 mg Capsules (PL 44041/0017-0018) submitted under Article 10c of Directive 2001/83/EC, as amended.

The applications for Flucloxacillin 250 mg and 500 mg Capsules (PL 44041/0017-0018) cross-refer to Flucloxacillin 250 mg and 500 mg Capsules (PL 21880/0017-0018; Medreich plc), which were authorised in the UK on 24 March 2010 following Decentralised procedures (UK/H/1101/001-002/DC. Flucloxacillin 250 mg and 500 mg Capsules (PL 21880/0017-0018; Medreich plc) cross-refer to Floxapen Capsules 250 mg and 500 mg (Beecham Group plc), which were granted in the UK on 17 July 1987. The applications are considered valid.

II.2 Drug substance
The proposed drug substance specification is consistent with the details registered for the cross reference products.

II.3 Medicinal Product
Name
The proposed names of the products are Flucloxacillin 250 mg and 500 mg Capsules. The products have been named in line with current requirements.

Strength, pharmaceutical form, route of administration, container and pack sizes
Each hard capsule contains 250 mg or 500 mg of flucloxacillin (as flucloxacillin sodium), as the active substance. The capsules are taken orally (by mouth).

The products are packaged in polyvinylchloride/aluminium blisters, in a pack size of 28 hard capsules.

The proposed shelf life for the products is 24 months, with the special storage conditions “Do not store above 25°C. Store in the original pack.”

The packaging, proposed shelf-life and storage conditions are consistent with the details registered for the respective cross-reference products.

Legal status
The products are available as Prescription Only Medicines (POM).

Marketing Authorisation Holder/Contact Persons/Company
Noumed Life Sciences, 5 Cattle Market, Hexham, Northumberland, NE46 1NJ, United Kingdom.

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

Qualitative and quantitative composition
The proposed compositions are consistent with the details registered for the respective cross-reference products.

Manufacturing process
The proposed manufacturing process is consistent with the details registered for the cross-reference products and the maximum batch sizes are stated.

Finished product/shelf-life specification
The proposed finished product specifications are consistent with the details registered for the cross-reference products.

TSE Compliance
With the exception of gelatin, none of the excipients contains materials of animal or human origin. The suppliers of gelatin have provided Certificates of Suitability from the European Directorate for the Quality of Medicines and Healthcare (EDQM) to show that it is manufactured in line with current European guidelines concerning the minimising of risk of transmission of Bovine Spongiform Encephalopathy/Transmissible Spongiform Encephalopathies (BSE/TSE).

This is consistent with the cross-reference products.

Bioequivalence
No bioequivalence data are required to support these simple abridged applications because the proposed products are manufactured to the same formula and utilises the same processes as the reference products Flucloxacillin 250 mg and 500 mg Capsules (PL 21880/0017-0018; Medreich plc).

Product Name and Appearance
See Section II.3 ‘Medicinal Product, Name’ for details of the proposed product names. The appearance of each product is identical to the respective cross-reference product.

Summaries of Product Characteristics (SmPCs)
The proposed SmPCs are consistent with the details registered for the respective cross-reference products.

Patient Information Leaflet (PIL) and Labelling
PIL
The PIL has been prepared in line with the details registered for the cross-reference products.

Carton and label
The proposed artwork is consistent with the artwork registered for the respective cross-reference products and complies with statutory requirements. In line with current legislation, the applicant has also included the name of the each product in Braille on the outer packaging and has included sufficient space for a standard UK pharmacy dispensing label.
II.4  Discussion on chemical, pharmaceutical and biological aspects
The data submitted with the applications are acceptable. The grant of Marketing Authorisations is recommended.

III. NON-ClinICAL ASPECTS
Introduction
As these are informed consent applications submitted under Article 10c of Directive 2001/83/EC, as amended, no new non-clinical data have been supplied and none are required.

Ecotoxicity/Environmental Risk Assessment (ERA)
Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As the applications are identical versions of already authorised products, it is not expected that environmental exposure will increase following approval of the Marketing Authorisations for the proposed products.

Discussion on the non-clinical aspects
The grant of Marketing Authorisations is recommended.

IV. CLINICAL ASPECTS
Introduction
As these informed consent applications submitted under Article 10c of Directive 2001/83/EC, as amended, no new clinical data have been supplied and none are required.

Pharmacovigilance and Risk Management Plan (RMP)
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.

An acceptable Risk Management Plan (RMP) has been submitted. A summary of safety concerns is listed in the following table.

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<th>Summary of safety concerns</th>
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<td><strong>Important identified risks</strong></td>
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<td><strong>Important potential risks</strong></td>
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<td><strong>Missing information</strong></td>
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Routine pharmacovigilance and routine risk minimisation are proposed for all safety concerns.
Discussion on the clinical aspects
The grant of Marketing Authorisations is recommended.

V. USER CONSULTATION
A user consultation with target patient groups on the Patient Information Leaflet (PIL) has been performed on the basis of a bridging report making reference to the PIL for Flucloxacillin 250 mg and 500 mg Capsules (PL 21880/0017-0018; Medreich plc). The bridging report has been found to be acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

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

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

Efficacy
No new efficacy data were supplied or required for these applications. Flucloxacillin has a well-established efficacy profile. These products are identical to the previously granted licences for Flucloxacillin 250 mg and 500 mg Capsules (PL 21880/0017-0018; Medreich plc).

SAFETY
No new safety data were supplied or required for these applications. Flucloxacillin has a well-established safety profile. These products are identical to the previously authorised Flucloxacillin 250 mg and 500 mg Capsules (PL 21880/0017-0018; Medreich plc).

PRODUCT LITERATURE
The SmPCs and PILs are satisfactory, and consistent with those for the respective cross-reference products. The labelling text complies with statutory requirements and is satisfactory.

BENEFIT/RISK ASSESSMENT
The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant’s products are identical to the cross-reference products. Extensive clinical experience with flucloxacillin is considered to have demonstrated the therapeutic value of the compound. The benefit/risk assessment is, therefore, considered to be positive.
In accordance with Directive 2010/84/EU, the current version of the SmPCs and PILs is available on the MHRA website. The current labelling is presented below:

**Flucloxacillin 250 mg Capsules:**
Flucloxacillin 500 mg Capsules:

Flucloxacillin 500 mg Capsules
Read the package leaflet before use

**INGREDIENTS**
Each Capsule contains: Flucloxacillin sodium equivalent to Flucloxacillin 500 mg

**DOSAGE**
For oral administration,
Use as directed by the physician

**WARNING**
KEEP OUT OF SIGHT AND REACH OF CHILDREN

**STORAGE**
Do not store above 25°C.
Store in the original package

**Contains Penicillin**

28 Capsules
Flucloxacillin 250 mg Capsules
Flucloxacillin 500 mg Capsules

(Flucloxacillin sodium)

PL 44041/0017-0018

**STEPS TAKEN AFTER AUTHORISATION - SUMMARY**

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<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
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