FLUCLOxacillin 250mg Powder for Solution for Injection or Infusion
PL 31745/0018

FLUCLOxacillin 500mg Powder for Solution for Injection or Infusion
PL 31745/0019

FLUCLOxacillin 1g Powder for Solution for Injection or Infusion
PL 31745/0020

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PL 31745/0018

FLUCLOXACILLIN 500MG POWDER FOR SOLUTION FOR INJECTION OR INFUSION
PL 31745/0019

FLUCLOXACILLIN 1G POWDER FOR SOLUTION FOR INJECTION OR INFUSION
PL 31745/0020

LAY SUMMARY

On 15 November 2012, the MHRA granted Ibigen Srl Marketing Authorisations (licences) for the medicinal products Flucloxacillin 250mg, 500mg and 1g Powder for Solution for Injection or Infusion (PL 31745/0018-20).

These are prescription-only medicines (legal status POM) containing the active ingredient flucloxacillin sodium. Flucloxacillin injection is used to treat a wide range of bacterial infections which may include those affecting:

- The chest (pneumonia, emphysema and lung abscess)
- Tonsils (tonsillitis, quinsy)
- Pharynx (pharyngitis)
- Sinuses (sinusitis)
- Ears (otitis media and otitis externa)
- Skin and soft tissue (boils, abscesses, carbuncles, impetigo. Cellulites, furunculosis, ulcers and acne)
- Wounds and burns
- Heart (endocarditis)
- Bones and joints (osteomyelitis)
- Membranes of the brain (meningitis)
- Gut (enteritis)
- Blood (Septicaemia)
- Kidney, bladder or the urethra (the tube which carries urine from the bladder).

Flucloxacillin injection can also be used to prevent infections following skin grafts or during major surgical procedures, particularly in heart or orthopaedic surgery.

Flucloxacillin is one of a group of medicines called “penicillins”. These medicines are also known as “antibiotics” and they work by killing the bacteria that cause infections.

No new or unexpected safety concerns arose from these applications and it was, therefore, judged that the benefits of taking Flucloxacillin 250mg, 500mg and 1g Powder for Solution for Injection or Infusion outweigh the risks, hence Marketing Authorisations have been granted.
FLUCLOXACILLIN 250MG POWDER FOR SOLUTION FOR INJECTION OR INFUSION
PL 31745/0018

FLUCLOXACILLIN 500MG POWDER FOR SOLUTION FOR INJECTION OR INFUSION
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SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted Marketing Authorisations for the medicinal products Flucloxacillin 250mg, 500mg and 1g Powder for Solution for Injection or Infusion (PL 31745/0018-20) on 15 November 2012 to Ibigen Srl.

These are applications for Flucloxacillin 250mg, 500mg and 1g Powder for Solution for Injection or Infusion, submitted as abridged simple applications according to Article 10c of Directive 2001/83/EC, cross-referring to Flucloxacillin 250mg, 500mg and 1g Powder for Solution for Injection or Infusion (PL 24610/0007-9), which were granted to Bowmed Limited on 1 July 2008.

These are prescription-only medicines (legal status POM) that are indicated for the treatment of infections due to sensitive Gram-positive organisms, including β-lactamase-producing staphylococci and streptococci. Typical indications include:

*Skin and soft tissue infections:*
- Boils, Cellulitis, Infected burns
- Abscesses, Infected skin conditions, Protection for skin grafts
- Carbuncles e.g. ulcer, eczema, and acne.
- Impetigo
- Furunculosis, Infected wounds

*Respiratory tract infections:*
- Pneumonia, Lung abscess, Emphysema
- Sinusitis, Pharyngitis, Otitis media and externa
- Tonsillitis, Quinsy

*Other infections caused by flucloxacillin-sensitive organisms:*
- Osteomyelitis, Urinary tract infection
- Enteritis, Meningitis
- Endocarditis, Septicaemia

Flucloxacillin is also indicated for use as a prophylactic agent during major surgical procedures when appropriate; for example cardiothoracic and orthopaedic surgery.

These products contain the active ingredient flucloxacillin sodium, which belongs to group of medicines called isoxazolyl penicillin antibiotics. It is a potent inhibitor of the growth of most penicillinase-producing staphylococci. It is generally less effective against micro-organisms susceptible to penicillin G and is not useful against gram-negative bacteria. Flucloxacillin sodium bactericidal and considered to act by inhibiting transpeptidase, the enzyme responsible for cross-linking of peptidoglycan during the final stage of synthesis of the bacterial cell wall, and so exerts its effect against dividing bacteria. It is active against most gram-positive organisms and *neisseria spp.*
PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 31745/0018-20

PROPRIETARY NAME(S): Flucloxacillin 250mg, 500mg and 1g Powder for Solution for Injection or Infusion

ACTIVE(S): Flucloxacillin sodium

COMPANY NAME: Ibigen Srl


LEGAL STATUS: POM

1. INTRODUCTION

These are simple, piggyback applications for Flucloxacillin 250mg, 500mg and 1g Powder for Solution for Injection or Infusion submitted under Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC. The proposed MA holder is Ibigen Srl, Via Fossignano 2, 04011 – Aprilia (LT), Italy.

The applications cross-refer to Flucloxacillin 250mg, 500mg and 1g Powder for Solution for Injection or Infusion (PL 24610/0007-9), which were granted to Bowmed Limited on 1 July 2008.

The current applications are considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 NAME(S)

The proposed names of the products are Flucloxacillin 250mg, 500mg and 1g Powder for Solution for Injection or Infusion. The products have been named in-line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes

The products contain 250mg, 500mg and 1g flucloxacillin sodium. They are packed in clear Type III glass vials with chlorobutyl rubber closures in cartons of 1, 5, 10, 20 and 50 vials. Not all pack sizes are to be marketed, but the marketing authorisation holder has committed to submitting mock-ups for approval to the regulatory authorities before marketing any pack size.

The proposed shelf-lives (36 months unopened) and storage conditions (Store below 25°C) are consistent with the details registered for the cross-reference products.

After reconstitution, the shelf-life details state “From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C unless reconstitution/ dilution has taken place in controlled and validated aseptic conditions.” This is consistent with the cross-reference products.

2.3 Legal status

On approval, the products will be available as prescription-only medicines (legal status POM).
2.4 Marketing authorisation holder/Contact Persons/Company
Ibigen Srl, Via Fossignano 2, 04011 – Aprilia (LT), Italy.

The 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 products and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

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

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

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

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

2.10 TSE Compliance
No materials of animal or human origin are included in these products. These details are consistent with the cross-reference products.

3. EXPERT REPORTS
The applicant has included detailed expert reports in Module 2 of the application. Signed declarations and copies of the experts’ CVs are enclosed in Module 1.4 for the quality, non-clinical and clinical experts. All are considered to have sufficient experience for their responsibilities.

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

5. SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
The proposed SmPCs are consistent with the details registered for the respective cross-reference products.

6. PATIENT INFORMATION LEAFLET (PIL)/CARTON
The patient information leaflets have been prepared in-line with the details registered for the respective cross-reference products.
Carton and blister
The proposed artwork is comparable to the artwork registered for the cross-reference products 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 and has included sufficient space for a standard UK pharmacy dispensing label.

7. CONCLUSIONS
The data submitted with these applications are acceptable. From a quality perspective, Marketing Authorisations should be granted.

NON-CLINICAL ASSESSMENT
No new non-clinical data have been supplied with these applications and none are required for applications of this type.

CLINICAL ASSESSMENT
No new clinical data have been supplied with these applications and none are required for applications of this type.
OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

QUALITY
The important quality characteristics of Flucloxacillin 250mg, 500mg and 1g Powder for Solution for Injection or Infusion are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit-risk balance.

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

CLINICAL PHARMACOLOGY/EFFICACY
No new clinical pharmacology/efficacy data have been submitted with these applications and none are required for applications of this type.

SAFETY
No new safety data have been submitted with these applications and none are required for applications of this type.

No new or unexpected safety concerns arise from these applications.

The SmPCs, PIL and labelling are satisfactory.

BENEFIT-RISK ASSESSMENT
The quality of the products is acceptable and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with flucloxacillin sodium is considered to have demonstrated the therapeutic value of the compounds. The benefit-risk is, therefore, considered to be positive.
FLUCLOxacillin 250mg, 500mg, 1g Powder for Sol for Injection/Infusion PL 31745/0018

FLUCLOxacillin 500mg Powder for Solution for Injection or Infusion PL 31745/0019

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**STEPS TAKEN FOR ASSESSMENT**

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<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation applications on 15 February 2012</td>
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<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant, the MHRA considered the applications valid on 2 May 2012</td>
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<td>3</td>
<td>Following assessment of the applications, the MHRA requested further information relating to the dossiers on 26 June 2012</td>
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<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information on 6 August 2012</td>
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<td>5</td>
<td>The applications were determined on 15 November 2012</td>
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### STEPS TAKEN AFTER AUTHORISATION - SUMMARY

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<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
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Summary of Product Characteristics and Patient Information Leaflet
The current approved UK versions of the Summaries of Product Characteristics (SmPCs) and Patient Information Leaflets (PILs) for these products are available on the MHRA website.