FLUCLOXACILLIN ELIXIR BP 125MG/5ML
PL 08215/0086

FLUCLOXACILLIN 250MG/5ML ORAL SOLUTION BP
PL 08215/0087-88

UKPAR

TABLE OF CONTENTS

FLUCLOXACILLIN ELIXIR BP 125MG/5ML
PL 08215/0086

FLUCLOXACILLIN 250MG/5ML ORAL SOLUTION BP
PL 08215/0087-88

LAY SUMMARY

The MHRA granted Kent Pharmaceuticals Limited Marketing Authorisations (licences) for the medicinal products Flucloxacillin Elixir BP 125mg/5ml (PL 08215/0086) and Flucloxacillin 250mg/5ml Oral Solution BP (PL 08215/0087-88) on 16th November 2007. These prescription-only medicines (POM) are used treat bacterial infections of the skin and soft tissue, respiratory tract infections and other generalised infections.

The active ingredient, flucloxacillin sodium is a narrow-spectrum beta-lactam antibiotic that belongs to the penicillin class of antibiotics and acts by inhibiting the synthesis of bacterial cell walls.

These applications are identical to previously granted applications for Flucloxacillin Elixir BP 125mg/5ml (PL 08215/0008) and Flucloxacillin 250mg/5ml Oral Solution BP (PL 08215/0033)granted to Kent Pharmaceuticals Limited on 14th September 1995 and 28th August 2002 respectively.

No new or unexpected safety concerns arose from these simple applications and it was, therefore, judged that the benefits of taking Flucloxacillin Elixir BP 125mg/5ml and Flucloxacillin 250mg/5ml Oral Solution BP outweigh the risks; hence Marketing Authorisations have been granted.

FLUCLOXACILLIN ELIXIR BP 125MG/5ML
PL 08215/0086

FLUCLOXACILLIN 250MG/5ML ORAL SOLUTION BP
PL 08215/0087-88

SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

INTRODUCTION

The UK granted marketing authorisations for the medicinal products Flucloxacillin Elixir BP 125mg/5ml (PL 08215/0086) and Flucloxacillin 250mg/5ml Oral Solution BP (PL 08215/0087-88) to Kent Pharmaceuticals Limited on 16th November 2007. These products are prescription-only medicines.

These applications was submitted as simple abridged applications according to Article 10c of Directive 2001/83/EC, as amended, cross-referring to Flucloxacillin Elixir BP 125mg/5ml (PL 08215/0008) and Flucloxacillin 250mg/5ml Oral Solution BP (PL 08215/0033) granted to the same Marketing Authorisation Holder on the 14th September 1995 and 28th August 2002 respectively.

No new data were submitted nor was it necessary for these simple applications, as the data are identical to that of the previously granted cross-reference product. As the cross-reference products were granted prior to the introduction of current legislation, no Public Assessment Report (PAR) has been generated for it.

The product contains the active ingredient flucloxacillin sodium which is a beta-lactam penicillin antibiotic that is used to treat streptococci and staphylococci bacterial infections. It is not active against methicillin-resistant staphylococci.

PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 08215/0086-88
PROPRIETARY NAME: Flucloxacillin Elixir BP 125mg/5ml and
Flucloxacillin 250mg/5ml Oral Solution BP
ACTIVE(S): Flucloxacillin sodium
COMPANY NAME: Kent Pharmaceuticals Limited
E.C. ARTICLE: Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC
LEGAL STATUS: POM

1. INTRODUCTION

These are simple, informed consent applications for Flucloxacillin Elixir BP 125mg/5ml and Flucloxacillin 250mg/5ml Oral Solution submitted under Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC. The proposed MA holder is Kent Pharmaceuticals Limited, Wotton Road, Ashford, Kent, TN23 6LL, UK.

The application cross-refers to Flucloxacillin Elixir BP 125mg/5ml (PL 08215/0008) and Flucloxacillin 250mg/5ml Oral Solution (PL 08215/0033), approved on 30th January 2000 to the same marketing authorisation holder Kent Pharmaceuticals Limited. The current application is considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Name(s)

The proposed names of the products are Flucloxacillin Elixir BP 125mg/5ml and Flucloxacillin 250mg/5ml Oral Solution BP. The products have been named in line with current requirements.

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

Flucloxacillin Elixir BP 125mg/5ml contains 136mg of flucloxacillin sodium, equivalent to 125mg/5ml when reconstituted in water. Flucloxacillin 250mg/5ml Oral Solution BP contains 272mg flucloxacillin sodium, equivalent to 250mg/5ml when reconstituted in water. It is to be stored in either amber glass bottles or high density polyethylene bottles (HDPE). The proposed shelf-life (36 months) once reconstituted should be used within 7 days. The storage conditions for the dry powder ("Do not store above 25°C) and the storage conditions for the reconstituted solution ("Store at 2°C-8°C in a refrigerator") are consistent with the details registered for the cross-reference product.

2.3 Legal status

On approval, the products will be available as prescription-only medicines (POM).

2.4 Marketing authorisation holder/Contact Persons/Company

Kent Pharmaceuticals Limited, Wotton Road, Ashford, Kent, TN23 6LL, UK.

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 product and evidence of 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 used contain materials of animal or human origin and this is consistent with the cross-reference product.

3. EXPERT REPORTS
The applicant has included abridged 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 name. The appearance of the product is identical to the cross-reference product.

5. SUMMARY OF PRODUCT CHARACTERISTICS
The proposed summary is consistent with the details registered for the cross-reference product.

6. PATIENT INFORMATION LEAFLET/CARTON
PIL
The patient information leaflet/carton has been prepared in-line with the details registered for the cross-reference product.
A package leaflet has been submitted to the MHRA along with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC. The results indicate that the package 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.

7. CONCLUSIONS
The data submitted with these applications are acceptable. Marketing Authorisations should be granted.

PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with this application and none are required for an application of this type.

CLINICAL ASSESSMENT

No new clinical data have been supplied with this application and none are required for an application of this type.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

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

PRECLINICAL
No new preclinical data were submitted and none are required for an application of this type.

EFFICACY
Flucloxacillin sodium is a well known drug and has been used as an antibiotic for many years. These applications are identical to the previously granted applications for Flucloxacillin Elixir BP 125mg/5ml and Flucloxacillin 250mg/5ml Oral Solution BP (PL 08215/0008 and PL 08215/0033).

No new or unexpected safety concerns arise from this application.

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

RISK BENEFIT ASSESSMENT
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant's product is identical to the cross-reference product which, in turn, has been shown to be interchangeable with the innovator product. Extensive clinical experience with flucloxacillin sodium is considered to have demonstrated the therapeutic value of the compound. The risk benefit is therefore considered to be positive.

FLUCLOXACILLIN ELIXIR BP 125MG/5ML
PL 08215/0086

FLUCLOXACILLIN 250MG/5ML ORAL SOLUTION BP
PL 08215/0087-88

STEPS TAKEN FOR ASSESMENT

1	The MHRA received the marketing authorisation applications on 14th December 2005.
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 4th January 2006.
3	Following assessment of the application the MHRA requested further information relating to the quality dossier on 16th March 2006 and 16th August 2006.
4	The applicant responded to the MHRA's requests, providing further information on 23rd March 2006 and 17th July 2007.
5	The applications were determined on 16th November 2007

FLUCLOXACILLIN ELIXIR BP 125MG/5ML
PL 08215/0086

FLUCLOXACILLIN 250MG/5ML ORAL SOLUTION BP
PL 08215/0087-88

STEPS TAKEN AFTER ASSESSMENT

Date submitted	Application type	Scope	Outcome

FLUCLOXACILLIN ELIXIR BP 125MG/5ML
PL 08215/0086

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Flucloxacillin Elixir B.P. 125mg/5ml

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Qualitative composition

Flucloxacillin as Flucloxacillin Sodium Ph Eur

Quantitative composition

125.0mg/5ml of Flucloxacillin when reconstituted (136.0 mg/5ml of Flucloxacillin Sodium)

3 PHARMACEUTICAL FORM
Free flowing pink coloured powder for reconstitution.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Treatment of infections due to penicillinase-producing Staphylococci: as in skin and soft tissue infections, respiratory tract infections and other generalised infections.

4.2 Posology and method of administration
Adults (including the elderly)

Oral: - 250mg every 6 hours, to be administered ½ to 1 hour before meals. In serious infections, the dosage may be doubled.

Children

2 - 10 years: 125mg every 6 hours, to be administered ½ to 1 hour before meals.

Under 2 years: 62.5mg every 6 hours, to be administered ½ to 1 hour before meals.

Route of administration

Oral administration

4.3 Contraindications
Hypersensitivity to β-lactam antibiotics (e.g. penicillins, cephalosporins)and hypersensitivity to the other constituents of the product.

Use in patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency.

4.4 Special warnings and precautions for use
*Abnormal Renal Function***:** In cases of severe renal failure (as classified in the table below), a reduction in dosage of Flucloxacillin is recommended.

Grade	GFR	Serum creatinine (approx)
Severe	<10ml/minute	>700 mol/litre

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 – CSM has advised that cholestatic jaundice may occur up to several weeks after treatment with flucloxacillin has been stopped. Administration for more than 2 weeks and increasing age are risk factors.

History of Allergy

Porphyria

When taken according to the dosage recommendations, this product contains 6.188g of sucrose per 10ml adult dose. This should be taken into account in patients with diabetes mellitus.

4.5 Interaction with other medicinal products and other forms of interaction

Probenecid slows down the excretion of flucloxacillin

Anticoagulants:

Phenindione - although studies have failed to demonstrate interaction, common experience in anticoagulant clinics is that INR can be altered by course of oral broad-spectrum antibiotics.

Warfarin - common experience in anticoagulant clinics is that INR can be altered following a course of oral broad-spectrum antibacterials.

Cytotoxics – reduced excretion of methotrexate (increased risk of toxicity).

Oestrogens and Progestogens – additional contraceptive precautions should be taken while taking a short course of a broad-spectrum antibiotic and for 7 days after stopping the treatment. If these 7 days run beyond the end of a packet, the next packet should be started immediately without a break. (In the case of everyday tablets the inactive ones should be omitted). If the antibiotic course given exceeds 3 weeks, the bacterial flora develops antibiotic resistance and additional contraceptive precautions are unnecessary; if a woman who has been on a course of antibiotics for 3 weeks or more, starts a *combined* oral contraceptive, additional contraceptive measures are also unnecessary.

4.6 Pregnancy and lactation

Use in pregnancy is not contraindicated. Flucloxacillin is secreted into mother's milk and may occasionally cause sensitisation of the infant.

4.7 Effects on ability to drive and use machines

None.

4.8 Undesirable effects

Typical allergic reactions have been observed such as urticarial and erythematous rashes. Anaphylaxishas occasionally resulted from the oral use of penicillin compounds. Gastrointestinal symptoms may occur including diarrhoea and antibiotic associated colitis.

Other hypersensitivity reactions include fever, joint pains, angioedema, serum sickness-like reactions, haemolytic anaemia, neutropenia, thrombocytopenia, coagulation disorders and nterstitial nephritis. Central nervous system toxicity including convulsions have been reported (especially with high doses or in severe renal impairment); paraesthesia with

prolonged use.Hepatitis and cholestatic jaundice may occur for up to several weeks after treatment has been stopped. It is usually related to increased age and administration for longer than two weeks.

4.9 Overdose

With high doses (mainly parenteral), neurotoxicity may develop.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Flucloxacillin is an isoxazolyl penicillin which is a potent inhibitor of the growth of most penicillinase-producing staphylococci. The drug is stable in an acid medium. Flucloxacillin is markedly resistant to cleavage by penicillinase. It is less effective than benzylpenicillin or phenoxymethylpenicillin against non-penicillinase - producing staphylococci or other gram positive cocci.

5.2 Pharmacokinetic properties

Flucloxacillin provides good absorption after oral administration (30 - 80% absorbed from GI tract). Absorption of the drug is more efficient when taken on an empty stomach. Peak plasma levels are attained at 1 hour after administration and 1g dose provides peak plasma levels of 15mcg/ml. The drug is rapidly excreted by the kidney, about 50% within 6 hours of administration. T½ = 30 - 60 minutes.

About 95% of flucloxacillin in circulation is bound to plasma proteins.

5.3 Preclinical safety data

Not relevant

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Benzoate Ph Eur

Disodium edetate Ph Eur

Saccharin Sodium Ph Eur

Mono-ammonium-glycyrrhizinate

Sodium citrate (dried) Ph Eur

Flavour pineapple

Flavour menthol

Red FD & C No.3 (E127)

Sucrose Ph Eur

6.2 Incompatibilities

As for penicillins. Incompatibilities with colistin polymyxin B sulphate. Loss of potency after mixing with streptomycin has also been reported.

6.3 Shelf life

36 months

Once reconstituted the mixture should be used within 7 days.

6.4 Special precautions for storage

Dry powder: Do not store above 25°C.

Reconstituted Solution: Store at 2°C-8°C in a refrigerator.

6.5 Nature and contents of container

150ml amber glass Beatson Clark container with polypropylene screw cap.

Or

150ml high density polyethylene bottle with tamper evident cap.

Or

125ml high density polyethylene bottle with a tamper evident/child resistant cap.

Or

175ml high density polyethylene bottle with a tamper evident/child resistant cap.

6.6 Special precautions for disposal

To the pharmacist: 100ml: Add 58ml of potable water and shake until all contents are dissolved

140ml: Add 79ml of potable water and shake until all contents are dissolved

To the patient: Keep cap tightly closed. Shake well before use. Use within 7 days preparation

7 MARKETING AUTHORISATION HOLDER

Kent Pharmaceutical Limited,

Wotton Road,

Ashford,

Kent TN23 6LL

8 MARKETING AUTHORISATION NUMBER(S)

PL 08215/0086

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

16/11/2007

10 DATE OF REVISION OF THE TEXT

16/11/2007

FLUCLOXACILLIN 250MG/5ML ORAL SOLUTION BP
PL 08215/0087-88

SUMMARY OF PRODUCT CHARACTERISTICS

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

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Qualitative composition

Flucloxacillin as Flucloxacillin Sodium

Quantitative composition

When reconstituted each 5ml contains 250mg flucloxacillin as flucloxacillin sodium.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM
Powder for Oral Solution. Free flowing pink coloured powder.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Treatment of infections due to sensitive Gram-positive organisms, including infections caused by β-lactamase-producing *Staphloccoci*.

Typical indications include:

Skin and soft tissue infections:

Boils	Impetigo
Abscesses	Infected wounds
Carbuncles	Infected burns
Furunculosis	Protection for skin grafts
Cellulitis	Otitis media and externa

Infected skin conditions e.g. ulcers,

eczema and acne.

Respiratory tract infections:

Pneumonia	Pharyngitis
Lung abscess	Tonsillitis
Empyema	Quinsy
Sinusitis	

Other infections caused by Flucloxacillin sensitive organisms:

Osteomyelitis	Septicaemia
Enteritis	Meningitis
Endocarditis	Urinary-tract infection

Flucloxacillin is also indicated for use as a prophylactic during major surgical procedures such as 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.

4.2 Posology and method of administration

Route of administration

Oral. To be administered ½ - 1 hour before meals.

Adults (including the elderly)

Oral: - 250mg four times daily.

In serious infections, the dosage may be doubled.

Children

2 - 10 years : half the adult dose.

Under 2 years: quarter the adult dose.

Depends on age, weight and renal function of the patient, as well as the severity of the infection.

In cases of severe renal impairment (creatinine clearance < 10ml/min) a reduction in dosage maybe necessary. Flucloxacillin is not significantly removed by dialysis and hence no supplementary dosages need to be administered either during, or at the end of the dialysis period.

Endocarditis or osteomyelitis

Up to 8g daily in divided doses six to eight hourly.

Surgical prophylaxis

1 to 2g IV at induction of anaesthesia followed by 500mg six hourly IV, IM or orally for up to 72 hours.

4.3 Contraindications

Flucloxacillin should not be given to patients with a history of hypersensitivity to ∃- lactam antibiotics (e.g. penicillins, cephalosporins) or excipients.

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

As this product contains up to 3.05g sucrose per 5ml dose it is unsuitable in hereditary fructose intolerance, glucose-galactose malabsorption syndrome, or sucrase-isomaltase deficiency.

4.4 Special warnings and precautions for use

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 because of the risk of neurotoxicity.

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.

As for other penicillins contact with the skin should be avoided as sensitisation may occur.

Patients with a known history of allergy are more likely to develop a hypersensitivity reaction.

Prolonged use of an anti-Infective agent may occasionally result in overgrowth of non-susceptible organisms.

Before initiating therapy with flucloxacillin, careful enquiry should be made concerning previous hypersensitivity reactions to ∃-lactams. Serious and occasionally fatal hypersensitivity reactions (anaphylaxis) have been reported in patients receiving ∃-lactam antibiotics. Although anaphylaxis is more frequent following parental therapy, it has occurred in patients on oral therapy. These reactions are more likely to occur in individuals with a history of ∃-lactam hypersensitivity.

Flucloxacillin should be used with caution in patients with evidence of hepatic dysfunction (see section 4.8).

Special caution is essential in the newborn because of the risk of hyperbilirubinaemia. 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. During prolonged treatments (e.g. osteomyelitis, endocarditis), regular monitoring of hepatic and renal functions is recommended.

4.5 Interaction with other medicinal products and other forms of interaction

Probenecid slows down the excretion of flucloxacillin

4.6 Pregnancy and lactation

Animal studies with Flucloxacillin have shown no teratogenic effects. Flucloxacillin preparations have been in use since 1970 and the limited number of reported cases of use in human pregnancy have shown no evidence of untoward effect. The use of Flucloxacillin in pregnancy should be reserved for cases considered essential by the clinician.

Flucloxacillin is secreted into mother=s milk and may occasionally cause sensitisation of the infant. *Therefore flucloxacillin should only be administered to a breast-feeding mother when the potential benefits outweigh the potential risks associated with the treatment.*

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

The most common adverse effects of Flucloxacillin are hypersensitivity reactions, especially skin rashes. If a skin rash occurs treatment should be discontinued. Other hypersensitivity reactions that may occur include urticaria, fever, joint pains, rashes,

angioedema, anaphylaxis, serum sickness-like reactions, haemolytic anaemia and interstitial nephritis.

Gastrointestinal effects such as diarrhoea and nausea are common. A sore mouth or tongue or a black hairy tongue have occasionally been reported. *Pseudomembranous colitis has been reported rarely and has usually associated with the use of Flucloxacillin in combination with other antibiotics.*

Other adverse effects have generally been associated with high doses or in cases of severe renal impairment. These adverse effects include haemolytic anaemia and neutropenia, thrombocytopenia, coagulation disorders and central nervous system toxicity including convulsions.

Rarely, hepatitis and cholestatic jaundice have been reported, these are 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. In very rare cases, a fatal outcome has been reported, almost always in patients with serious underlying disease.

4.9 Overdose

With high doses (mainly parenteral) neurotoxicity may develop.

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

Properties: Flucloxacillin is a narrow-spectrum antibiotic of the group of isoxazolyl penicillins; it is not inactivated by staphylococcal β-lactamases.

Activity: Flucloxacillin, by its action on the synthesis of the bacterial wall, exerts a bacterial effect on streptococci, except those of group D *(Enterococcus faecalis)*, and staphylococci. It is not active against methicillin-resistant staphylococci.

5.2 Pharmacokinetic properties

Absorption: Flucloxacillin is stable in acid media and can therefore be administered either by the oral or parental route. The peak serum levels of flucloxacillin reached after one hour are as follows.

- After 250mg by the oral route (in fasting subjects): Approximately 8.8mg/l.
- After 500mg by the oral route (in fasting subjects): Approximately 14.5mg/l.
- After 500mg by the IM route: Approximately 16.5mg/l.

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

Distribution: Flucloxacillin diffuses well into most tissue. Specifically, active concentrations of flucloxacillin have been recovered in bones: 11.6mg/l (compact bone) and 15.6mg/l (spongy bone), with a mean serum level of 8.9mg/l.

Crossing the meningeal barrier: Flucloxacillin diffuses in only small proportion in to 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.

Metabolism: 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 minutes.

Excretion: Excretion occurs mainly through the kidney. Between 65,5% (oral route) and 76.1% (parental route) of the dose administered is recovered in unaltered active form in the urine within 8 hours. A small portion of the dose administered is excreted in the bile. The excretion of flucloxacillin is slowed in cases of renal failure.

Protein binding: The serum protein-binding rate is 95%.

5.3 Preclinical safety data

No relevant information additional to that already contained elsewhere in the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Benzoate

Disodium edetate

Saccharin Sodium

Mono-ammonium-glycyrrhizinate

Sodium citrate

Flavour pineapple

Flavour menthol

Red FD & C No.3 (E127)

Sucrose

6.2 Incompatibilities

As for penicillins, incompatibilities with Colistin Polymyxin B sulphate. Loss of potency after mixing with streptomycin has also been reported.

6.3 Shelf life

18 months unopened.

Once reconstituted the mixture should be used within 7 days.

6.4 Special precautions for storage

Dry powder: Do not store above 25^{o}C.

Reconstituted Solution: Store at 2^{o}C-8^{o}C in a refrigerator.

6.5 Nature and contents of container

150ml natural high density polyethylene (HDPE) bottle with tamper evident cap.

or

150ml natural high density polyethylene (HDPE) bottle with tamper evident/child resistant (CRC) cap

6.6 Special precautions for disposal

To the pharmacist:

100ml: Add 58ml of potable water and shake until all contents are dissolved

To the patient:

Keep cap tightly closed. Shake well before use. Use within 7 days preparation

7 MARKETING AUTHORISATION HOLDER

Kent Pharmaceutical Limited,

Wotton Road,

Ashford,

Kent TN23 6LL,

UK.

8 MARKETING AUTHORISATION NUMBER(S)

PL 08215/0087
PL 08215/0088

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

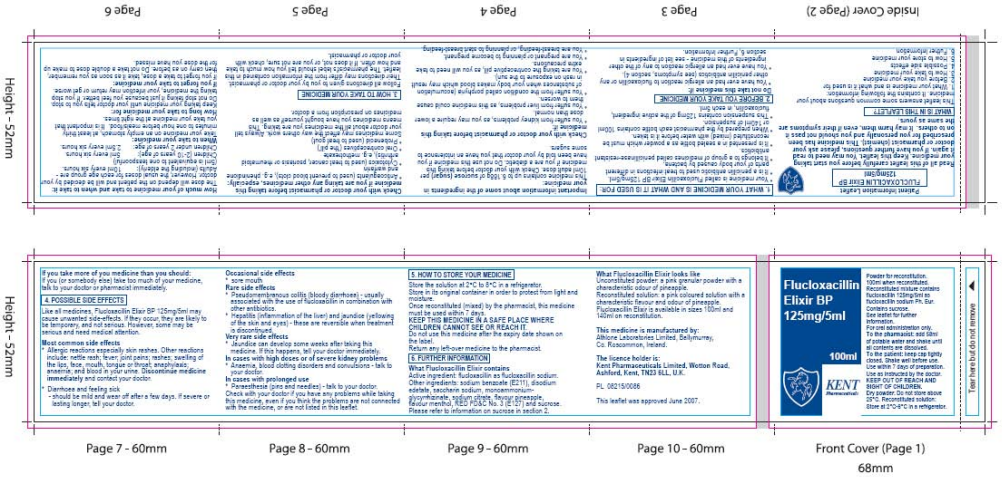
16/11/2007

10 DATE OF REVISION OF THE TEXT

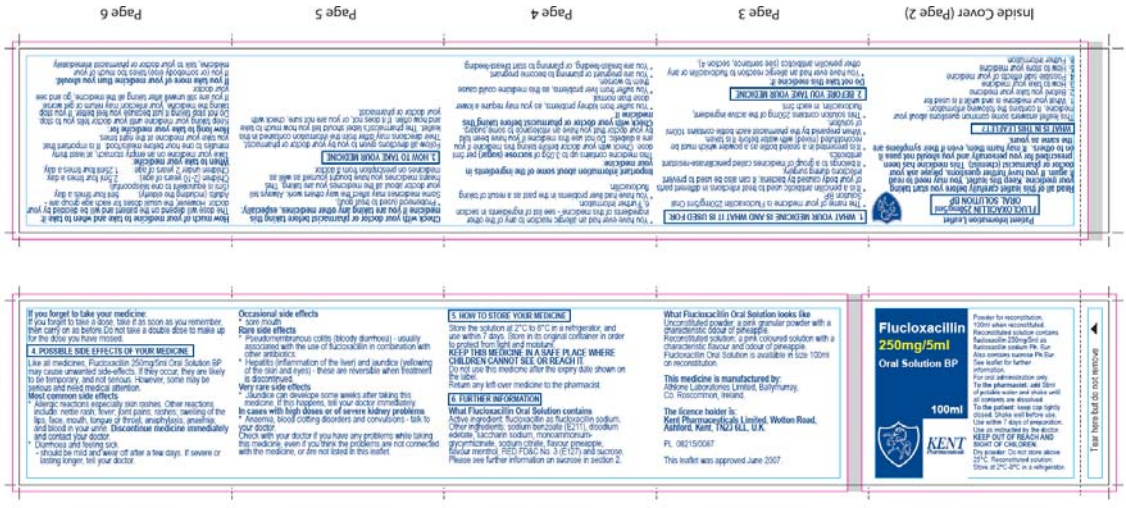
16/11/2007

PATIENT INFORMATION LEAFLET

FLUCLOXACILLIN ELIXIR BP 125MG/5ML
PL 08215/0086



FLUCLOXACILLIN 250MG/5ML ORAL SOLUTION BP
PL 08215/0087-88

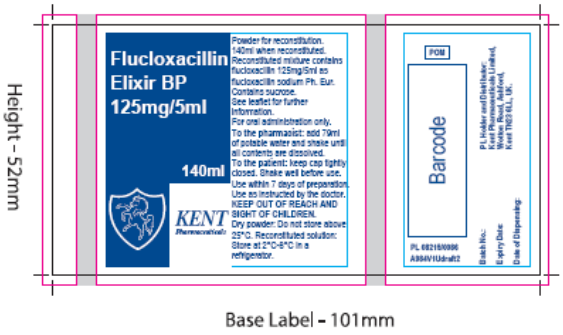


LABELLING

FLUCLOXACILLIN ELIXIR BP 125MG/5ML
PL 08215/0086

Bottle Label- 100ml

Bottle Label- 140ml



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