SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Flucloxacillin 250mg/5ml Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

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

Excipients with known effect:
Each 5ml dose contains 2.96g of sucrose and 24.09mg of sodium.
For the full list of excipients, see section 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 *Staphylococci* and *Streptococci*.

Typical indications include:

Skin and soft tissue infections:

Boils
Abscesses
Carbuncles
Furunculosis
Cellulitis
Impetigo
Infected wounds
Infected burns
Protection for skin grafts
Infected skin conditions e.g. ulcers, eczema and acne.

Respiratory tract infections:

Pneumonia
Lung abscess
Empyema
Pharyngitis
Tonsillitis
Quinsy

Sinusitis
Otitis media and externa

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

Posology

The dosage depends on the age, weight and renal function of the patient, as well as the severity of the infection.

Adults (including the elderly)
Oral: - 250mg four times daily.
In serious infections, the dosage may be doubled.

Paediatric population

2 - 10 years:	125mg four times daily
Under 2 years:	62.5mg four times daily

In cases of severe renal impairment (creatinine clearance < 10ml/min) a reduction in dosage may be 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.

Method of administration
Oral. To be administered ½ - 1 hour before meals.

4.3 Contraindications

Hypersensitivity to the active substance, to any of the excipients listed in section 6.1, or to β-lactam antibiotics (e.g. penicillins, cephalosporins).

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

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. Flucloxacillin should be used with caution in patients with evidence of hepatic dysfunction, patients >50 years or patients with underlying disease all of whom are at increased risk of hepatic reactions. The onset of these hepatic 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 (see section 4.8).

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 β-lactams. Serious and occasionally fatal hypersensitivity reactions (anaphylaxis) have been reported in patients receiving β-lactam antibiotics. Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients on oral therapy. These reactions are more likely to occur in individuals with a history of β-lactam hypersensitivity.

If anaphylaxis occurs, flucloxacillin should be discounted and the appropriate therapy instituted. Serious anaphylactic reactions may require immediate emergency treatment with adrenaline (epinephrine). Ensure adequate airway and ventilation and give 100% oxygen. IV crystalloids, hydrocortisone, antihistamine and nebulised bronchodilators may also be required.

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.

This product contains up to 2.96g sucrose per 5ml dose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption syndrome or sucrase-isomaltase deficiency should not take this medicine.

Sodium content: this medicinal product contains 24.09mg sodium per 5ml. To be taken into consideration by patients on a controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

Probenecid and sulfinpyrazone slow down the excretion of flucloxacillin.

Other drugs, such as piperacillin, which are excreted via renal tubular secretion, may interfere with flucloxacillin elimination.

Oral typhoid vaccine may be inactivated by flucloxacillin.

Flucloxacillin reduces the excretion of methotrexate which can cause methotrexate toxicity.

Flucloxacillin may reduce the response to sugammadex.

There are rare cases of altered international normalised ratio (INR) in patients taking warfarin and prescribed a course of flucloxacillin. If co-administration is necessary, the prothrombin time or international normalised ratio should be carefully monitored during addition or withdrawal of flucloxacillin.

4.6 Fertility, pregnancy and lactation

Pregnancy

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. Flucloxacillin should only be used in pregnancy when the potential benefits outweigh the risks associated with treatment.

Breastfeeding

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

Flucloxacillin has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The following convention has been utilised for the classification of undesirable effects: - Very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data).

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), 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). 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.

There is evidence that the risk of flucloxacillin-induced liver injury is increased in subjects carrying the HLA-B*5701 allele. Despite this strong association, only 1 in 500-1000 carriers will develop liver injury. Consequently, the positive predictive value of

testing the HLA-B*5701 allele for liver injury is very low (0.12%) and routine screening for this allele is not recommended.

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 the 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 was derived from clinical studies involving a total of approximately 929 adult and paediatric patients taking flucloxacillin.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the yellow card scheme at www.mhra.gov.uk/yellowcard

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

ATC Code: J01CF05

Pharmacotherapeutic group – Beta-lactamase resistant penicillins

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 bactericidal effect on streptococci, except those of group D *(Enterococcus faecalis),* and staphylococci. It is not active against methicillin-resistant staphylococci.

Risk of hepatic injury

There is evidence that the risk of flucloxacillin-induced liver injury is increased in subjects carrying the HLA-B*5701 allele. Despite this strong association, only 1 in 500-1000 carriers will develop liver injury. Consequently, the positive predictive value of testing the HLA-B*5701 allele for liver injury is very low (0.12%) and routine screening for this allele is not recommended.

5.2 Pharmacokinetic properties

Absorption: Flucloxacillin is stable in acid media and can therefore be administered either by the oral or parenteral 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.

Biotransformation: 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.

Elimination: Excretion occurs mainly through the kidney. Between 65.5% (oral route) and 76.1% (parenteral 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
Ammonium-glycyrrhizate
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

Dry powder
Bottle not in an aluminium pouch - 9 months.
Bottle in an aluminium pouch – 2 years.
Once removed from the pouch reconstitute immediately.
Once reconstituted the mixture may be stored for a maximum of 7 days when stored in the original container at 2°C - 8°C in a refrigerator.

6.4 Special precautions for storage

Dry powder: Do not store above 25^{o}C.
Store in the original container in order to protect from light and moisture.
For storage conditions of the reconstituted medicinal product, see section 6.3.

6.5 Nature and contents of container

150ml natural high density polyethylene (HDPE) bottle with polypropylene Cap, R4 Flexband with Blue Tamper Evident Band

Or

150ml natural high density polyethylene (HDPE) bottle with polypropylene Cap, PP28 Mediloc Tamper Evident Closure

Contents of the bottle after constitution: 100ml
Optional – Bottle placed in Aluminium pouch.
Hugo Meding – polypropylene spoon –article number 7229.
5ml Medispoon

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

Athlone Pharmaceuticals Limited
Ballymurray
Co. Roscommon
Ireland

8 MARKETING AUTHORISATION NUMBER

PL 30464/0168

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

16/11/2007 / 22nd Oct 2009

10 DATE OF REVISION OF THE TEXT

08 Jan 2016

SUMMARY OF PRODUCT CHARACTERISTICS CMS

1. NAME OF THE MEDICINAL PRODUCT

Flucloxacillin 250mg/5ml Oral Solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

Excipients with known effect:
Each 5ml dose contains up to 2.96g sucrose.
Each 5ml dose contains 24.09mg sodium.
For the full list of excipients, see section 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 *Staphylococci* and *Streptococci*.

Typical indications include:

Skin and soft tissue infections:

Boils	Infected burns
Impetigo	Furunculosis
Abscesses	Protection for skin grafts
Infected wounds	Cellulitis
Carbuncles	

Infected skin conditions e.g. Ulcers, eczema and acne

Respiratory tract infections:

Pneumonia	Pharyngitis
Lung abscess	Tonsillitis
Empyema	Quinsy
Sinusitis	

Otitis media and externa

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

The dosage depends on age, weight and renal function of the patient, as well as the severity of the infection.

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's dose:

- Less than 2 years: 62.5 mg four times daily
- 2-10 years: 125mg four times daily
- 10-18 years: 250mg four times daily

In cases of severe renal impairment (creatinine clearance < 10ml/min) a reduction in dosage may be 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 beta-lactam antibiotics (e.g. penicillins, cephalosporins) or 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

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. Flucloxacillin should be used with caution in patients with evidence

of hepatic dysfunction, patients >50 years or patients with underlying disease. In these patients, hepatic events may be severe and in extremely rare circumstances, deaths have been reported (see section 4.8).

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 beta-lactams. Serious and occasionally fatal hypersensitivity reactions (anaphylaxis) have been reported in patients receiving beta-lactam antibiotics. Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients on oral therapy. These reactions are more likely to occur in individuals with a history of beta-lactam hypersensitivity.

If anaphylaxis occurs flucloxacillin should be discontinued and the appropriate therapy instituted. Serious anaphylactic reactions may require immediate emergency treatment with adrenaline (epinephrine). Ensure adequate airway and ventilation and give 100% oxygen. IV crystalloids, hydrocortisone, antihistamine and nebulised bronchodilators may also be required.

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.

This product contains 2.96g sucrose per 5ml dose. Patients with hereditary problems of fructose intolerance, glucose-galactose malabsorption, or sucrase-isomaltase insufficiency should not take this medicine.

This medicinal product contains 24.09mg sodium per 5ml dose. This should be taken into consideration by patients on a controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

Probenecid and sulfinpyrazone slow down the excretion of flucloxacillin.

Other drugs, such as piperacillin, which are excreted via renal tubular secretion, may interfere with flucloxacillin elimination.

Oral typhoid vaccine may be inactivated by flucloxacillin.

Flucloxacillin reduces the excretion of methotrexate which can cause methotrexate toxicity.

Flucloxacillin may reduce the response to sugammadex.

There are rare cases of altered international normalised ratio (INR) in patients taking warfarin and prescribed a course of flucloxacillin. If co-administration is necessary, the prothrombin time or international normalised ratio should be carefully monitored during addition or withdrawal of flucloxacillin.

4.6 Fertility, pregnancy and lactation

Animal studies with flucloxacillin have shown no teratogenic effects. Flucloxacillin preparations have been in use since 1970 and the limited numbers of reported cases of use in human pregnancy have shown no evidence of untoward effect. Flucloxacillin should only be used in pregnancy when the potential benefits outweigh the risks associated with treatment.

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 following convention has been utilised for the classification of undesirable effects: Very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data).

The most common adverse effects of flucloxacillin are hypersensitivity reactions especially skin rashes.

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. Haemolytic anaemia. Coagulation disorders.

Immune system disorders
Very rare: Anaphylactic shock (see section 4.4), angioneurotic oedema.

If any hypersensitivity reaction occurs, the treatment should be discontinued. (See also Skin and subcutaneous tissue disorders).

Nervous system disorders
Very rare: Convulsions

Gastrointestinal disorders
Common: Diarrhoea, nausea
Uncommon: Sore mouth or tongue, black hairy tongue
Very rare: Pseudomembranous colitis.

Hepatobiliary disorders
Very rare: Hepatitis and cholestatic jaundice. (See section 4.4). Changes in liver function laboratory test results.

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, serum sickness-like reaction and toxic epidermal necrolysis.

Musculoskeletal and connective tissue disorders
Very rare: Arthralgia and myalgia.

Renal and urinary disorders
Very rare: Interstitial nephritis.

General disorders and administration site conditions
Very rare: Fever

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via IMB Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.imb.ie; e-mail: imbpharmacovigilance@imb.ie

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

ATC Code: J01CF05
Group – Beta-lactamase resistant penicillins

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 parenteral 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 into 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% (parenteral 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
Ammonium glycyrrhizate
Sodium citrate anhydrous
Flavour pineapple
Flavour menthol
Erythrosine (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

Dry Powder:
Bottle not placed in aluminium pouch – 9 months
Bottle in aluminium pouch – 24 months
Once removed from the pouch, reconstitute immediately.
Once reconstituted the mixture may be stored for a maximum of 7 days when stored in the original container at 2ºC - 8ºC in a refrigerator.

6.4 Special precautions for storage

Dry powder: Do not store above 25ºC. Store in the original container in order to protect from light and moisture. For storage conditions of the reconstituted medicinal product, see section 6.3.

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.

Contents of the bottle after reconstitution: 100ml

Optional – Bottle placed in aluminium pouch.

Hugo Meding – polypropylene spoon - Article number – 7229

5ml MediSpoon

6.6 Special precautions for disposal and other handling

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 of preparation.

7. MARKETING AUTHORISATION HOLDER

Athlone Laboratories Limited
Ballymurray
Co. Roscommon
Ireland

8. MARKETING AUTHORISATION NUMBER(S)

PA 298/017/004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 8th October 2010

10. DATE OF REVISION OF THE TEXT

11 Feb 2016