Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

VABIOTIC 125MG

2. Qualitative and quantitative composition

Each 5ml contains 125mg Flucloxacillin Sodium
Excipient(s) with known effects:
Aspartame
Sodium

3. Pharmaceutical form

Oral Suspension
Before Reconstitution: Light orange Coloured powder
After Reconstitution: Orange Coloured Suspension

4. Clinical particulars

4.1 Therapeutic indications

Pharmacological Classification: Beta-Lactamase Resistant Penicillins Flucloxacillin Oral Solution BP 250 mg/5 ml PAGE 2 Indication: Flucloxacillin Sodium is 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, e.g. ulcer, eczema, and acne, Protection for skin grafts, Carbuncles, Furunculosis, Infected wounds and Impetigo Respiratory tract infections: Pneumonia, Lung abscess, Empyema, Sinusitis, Pharyngitis, Otitis media and externa, Tonsillitis and Quinsy Other infections caused by Flucloxacillin-sensitive organisms: Osteomyelitis, Urinary tract infection, Enteritis, Meningitis, Endocarditis and Septicaemia Flucloxacillin Sodium 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.

4.2 Posology and method of administration

Premature infants, neonates, sucklings and infants Other pharmaceutical forms/strengths may be more appropriate for administration to this population.

Posology

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

Under 2 years: 2.5ml (62.5mg) four times daily
Usual children's dosage 2-10 years: 5ml (125mg) four times daily
Usual adult dosage (including elderly patients)
Oral- 10ml (250mg) four times daily
Osteomyelitis or endocarditis: Up to 8 g daily, in divided doses six to eight hourly
Surgical prophylaxis - 1 to 2 g IV at induction of anaesthesia followed by 500 mg six hourly IV, IM or orally for up to 72 hours
Abnormal renal function: In patients with renal insufficiency, excretion of flucloxacillin is slowed. In the presence of severe renal insufficiency (creatinine clearance < 10 ml/min) a reduction in dose or an extension of dose interval should be considered. The maximum recommended dose in adults is 1g every 8 to 12 hours. 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 Hepatic impairment: Dose reduction in patients with reduced hepatic function is not necessary. Administration Oral: Oral doses should be administered half to one hour before meals.

4.3 Contraindications

Flucloxacillin should not be given to patients with a history of hypersensitivity to β-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

Before initiating therapy with flucloxacillin, careful enquiry should be made concerning previous hypersensitivity reactions to β-lactams. 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. Cross-sensitivity between penicillins and cephalosporins is well documented. 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 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. 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). 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 (see section 4.2). 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. 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.
Prolonged use may occasionally result in overgrowth of non-susceptible organisms.
The occurrence at the treatment initiation of a feverish generalised erythema associated with pustule may be a symptom of acute generalised exanthematous pustulosis (AGEP) (see section 4.8). In case of AGEP diagnosis, flucloxacillin should be discontinued and any subsequent administration of flucloxacillin contra-indicated.
Caution is advised when flucloxacillin is administered concomitantly with paracetamol due to the increased risk of high anion gap metabolic acidosis (HAGMA). Patients at high risk of HAGMA are in particular those with severe renal impairment, sepsis or malnutrition especially if the maximum daily doses of paracetamol are used. After co-administration of flucloxacillin and paracetamol, a close monitoring is recommended in order to detect the appearance of acid-base disorders, namely HAGMA, including the search of urinary 5-oxoproline. If flucloxacillin is continued after cessation of paracetamol, it is advisable to ensure that there are no signals of HAGMA, as there is a possibility of flucloxacillin maintaining the clinical picture of HAGMA (see section 4.5).
Patients with rare hereditary problems of fructose intolerance, glucose galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Probenecid and sulfinpyrazone decreases the renal tubular secretion of flucloxacillin. Other drugs such as piperacillin, which are excreted via renal tubular secretion, may interfere with flucloxacillin elimination. Concurrent administration of probenecid delays the renal excretion of flucloxacillin. 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.
Bacteriostatic drugs may interfere with the bactericidal action of flucloxacillin. 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 normalized ratio should be carefully monitored during addition or withdrawal of flucloxacillin. Caution should be taken when flucloxacillin is used concomitantly with paracetamol as concurrent intake has been associated with high anion gap metabolic acidosis, especially in patients with risk factors. (see section 4.4.)

4.6 Fertility, pregnancy, and lactation

Pregnancy: Animal studies with flucloxacillin 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 have shown no evidence of untoward effects. The decision to administer any drug during pregnancy should be taken with the utmost care. Therefore flucloxacillin should only be used in pregnancy when the potential benefits outweigh the potential risks associated with treatment.
Lactation: Trace quantities of flucloxacillin can be detected in breast milk. The possibility of hypersensitivity reactions must be considered in breast-feeding infants. 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.

Adverse effects on the ability to drive or operate machinery have not been observed.

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(≥1/10000 to <1/1000),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. Eosinophilia, 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). Hepatitis and cholestatic jaundice 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).
Frequency not known: AGEP – acute generalized exanthematous pustulosis (see section 4.4)

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.

Metabolism and nutrition disorders
Post marketing experience: very rare case of high anion gap metabolic acidosis, when flucloxacillin is used concomitantly with paracetamol, generally in the presence of risk factors.

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

Pharmacotherapeutic Group: Beta-Lactamase Resistant Penicillins
ATC CODE: J01CF05
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) 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 into the cerebrospinal fluid of subjects whose meninges are not inflamed.
Crossing into mothers' milk: Flucloxacillin is excreted in small quantities in mothers' 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

Not Applicable.

6. Pharmaceutical particulars

6.1 List of excipients

Kyron T-135
Citric Acid Anhydrous
Sodium Methyl Paraben
Sodium Propyl Paraben
Xanthan Gum
Aspartame
Sucralose
Orange Flavour
Sunset Yellow
Sugar

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Dry Powder:24 months
Reconstituted Suspension: 7 days.

6.4 Special precautions for storage:

Store below 30°C. Protect from light and moisture
Tap the bottle to loosen the Powder.
Keep cap tightly closed. Shake well before use. Use within 7 days preparation

6.5 Nature and contents of container

100 ml glass bottle
100 ml bottles packed in one carton pack along with package insert.
Pack size: 1 x 100 ml bottles in one carton box along with packing leaflet.

6.6 Special precautions for disposal and other handling:

No special requirements.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorization holder and manufacturing site addresses

Marketing authorization holder:

EASTLEIGH PHARMACEUTICAL COMPANY LIMITED
Address: P.O Box 167-00610 Nairobi, Kenya

Manufacturing site address:

MARS REMEDIES PVT LTD
Address: 635, GIDC Estate, Waghodia-391760, Vadodara, GUJARAT INDIA

8. Marketing authorization number

CTD9587

9. Date of first registration
11/11/2022

10. Date of revision of the text:
15/09/2023

11. Dosimetry:
Not Applicable

12. Instructions for Preparation of Radiopharmaceuticals:
Not Applicable