# National Agency for Food & Drug Administration & Control (NAFDAC)

# Registration & Regulatory Affairs (R & R) Directorate

# SUMMARY OF PRODUCT CHARACTERISTICS (SmPC) TEMPLATE

## 1. NAME OF THE MEDICINAL PRODUCT
Avroclox Suspension

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION
When reconstituted, each 5ml contains 125mg Ampicillin as Ampicillin Trihydrate and 125mg Cloxacillin as Cloxacillin Sodium

## 3. PHARMACEUTICAL FORM
Powder for oral Suspension

Avroclox Suspension is presented as a white flavoured dry powder for reconstitution.

## 4. CLINICAL PARTICULARS
### 4.1 Therapeutic indications
Avroclox suspension is indicated for the treatment of sensitive bacteria in:

- Respiratory Tract Infections
  Sinisitis, Otitis media, pneumonia, acute excerbation of chronic bronchitis and epiglottis.
- Urinary Tract Infections
- Genital Infections:
  Gonorrhea and pelvic infections.
- Gastro-intestinal Tract Infections:
  Gastro enteritis (including salmonella enteritis and shigellosis), typhoid and paratyphoid fever, peritonitis and biliary tract infections.
- Skin and soft tissue Infections.
- Meningitis
- Ear, Nose and Throat Infections
- Perinatal streptococcal Infections
- Septicaemia
- Endocarditis
- Orthopaedic Infections.

### 4.2 Posology and method of administration
STANDARD DOSE
Children: 1 month – 2 years: 125 - 250mg (5 -10ml) every 6 hours

Children: 2 - 10 years: 250 - 500mg (10 - 20ml) every 6 hours

The product should be taken 30 minutes to 1 hour before food or 2 hours after food.

Take at regular intervals around-the-clock to maintain adequate blood levels. Prescribed course of treatment should be completed unless otherwise directed. Majority of patients will require treatment for at least 2 weeks.

### 4.3 Contraindications
- Avroclox should be avoided in patients with known history of hypersensitivity to beta-lactam antibiotics (e.g. ampicillin, penicillins, cephalosporins) or excipients.
- It should not be given to patients with infectious mononucleosis, lymphatric leukaemia or possibly HIV infection since they are susceptible to Ampicillin-induced skin rashes.
- Cloxacillin has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

### 4.4 Special warnings and precautions for use
Before initiating therapy with ampicillin, careful enquiry should be made concerning previous hypersensitivity reactions to beta-lactam antibiotics.

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 penicillins. These reactions are more likely to occur in individuals with a history of beta-lactam hypersensitivity.

Ampicillin should be avoided if infectious mononucleosis and/or acute or chronic leukaemia of lymphoid origin are suspected. The occurrence of a skin rash has been associated with these conditions following the administration of ampicillin.

Prolonged use may occasionally result in overgrowth of non-susceptible organisms.

Dosage should be adjusted in patients with renal impairment (see section 4.2).

**4.5 Interaction with other medicinal products and other forms of interaction**
Ampicillin may also interact with bacteriostatic antibacterials such as chloramphenicol and tetracycline. It may also interact with oral contraceptives, sulphonamides, acetyl Salicylate and methotrexate.

In common with other oral broad-spectrum antibiotics, ampicillin may reduce the efficacy of oral contraceptives and patients should be warned accordingly.

Probenecid decreases the renal tubular secretion of ampicillin. Concurrent use with ampicillin may result in increased and prolonged blood levels of ampicillin.

Concurrent administration of allopurinol during treatment with ampicillin can increase the likelihood of allergic skin reactions.

It is recommended that when testing for the presence of glucose in urine during ampicillin treatment, enzymatic glucose oxidase methods should be used. Due to the high urinary concentrations of ampicillin, false positive readings are common with chemical methods.

The absorption of Ampicillin is reduced in the presence of chloroquine.

The possibility of a prolonged bleeding time following oral treatment with a broad-spectrum drug like ampicillin should be borne in mind in patients receiving anticoagulants.

Cloxacillin has been reported to be incompatible with aminoglycosides and a number of other antimicrobials.

**4.6 Pregnancy and lactation**
Pregnancy:
Animal studies with Ampicillin have shown no teratogenic effects. The product has been in extensive clinical use since 1961 and its use in human pregnancy has been well documented in clinical studies. When antibiotic therapy is required during pregnancy, Ampicillin may be considered appropriate.

Lactation:
During lactation, trace quantities of penicillins can be detected in breast milk.
Adequate human and animal data on use of Ampicillin during lactation are not available.

**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**
Hypersensitivity reactions:
If any hypersensitivity reaction occurs, the treatment should be discontinued.

Skin rash, pruritis and urticaria have been reported occasionally. The incidence is higher in patients suffering from infectious mononucleosis and acute or chronic leukaemia of lymphoid origin. Purpura has also been reported. Rarely, skin reactions such as erythema multiforme and Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported.

As with other antibiotics, anaphylaxis (see Item 4.4 – Warnings) has been reported rarely.

Renal effects:
Interstitial nephritis can occur rarely.

Gastrointestinal reactions:
Effects include nausea, vomiting and diarrhoea. Pseudomembraneous colitis and haemorrhagic colitis have been reported rarely.

Hepatic effects:
As with other beta-lactam antibiotics, hepatitis and cholestatic jaundice have been reported rarely. As with most other antibiotics, a moderate and transient increase in transaminases has been reported.

Haematological effects:
As with other beta-lactams, haematological effects including transient leucopenia, transient thrombocytopenia and haemolytic anaemia have been reported rarely.

Prolongation of bleeding time and prothrombin have also been reported rarely.

**4.9 Overdose**
Neutropenia has been reported in patients receiving high doses of beta-lactams. Warning signs include fever, rash and eosinophilia. Monitoring of the leucocyte count is recommended during long-term treatment with high doses.

Hypersensitivity reactions due to overdosage give rise to a wide variety of clinical symptoms. Immediate reactions include anaphylaxis, angioedema, urticaria and some maculopapular rashes. Late reactions may include serum sickness-like reactions and haemolytic anaemia.

Prolongation of bleeding time and defective platelet function; convulsions and other symptoms of CNS toxicity have also been reported.

After acute overdosage, gastro-intestinal symptoms and disturbances of the fluid and electrolyte balance may be treated symptomatically with attention to water and electrolyte balance.
Ampicillin may be removed from the circulation by haemodialysis.

**5. PHARMACOLOGICAL PROPERTIES**
**5.1 Pharmacodynamic properties**

**Ampicillin:**
Ampicillin is a beta-lactam antibiotic with a bactericidal action. It is an aminopenicillin with an amino group side chain attached to the basic penicillin structure, this makes ampicillin better able to penetrate the outer membrane of some gram-positive bacteria and thus has a broader spectrum of activity than benzyl penicillin.
There is synergy against some beta-lactamase producing organisms between ampicillin and beta-lactamase inhibitors such as clavulanic acid or sulbactam and also penicillinase-stable drugs such as cloxacillin or flucloxacillin. Synergy has also been demonstrated between ampicillin and aminoglycosides against a range of organisms, including enterococci. Variable effects ranging from synergy to antagonism have been reported between ampicillin and other beta-lactam bacteriostatic drugs such as chloramphenicol and rifampicin.
Ampicillin is the drug of choice for treatment of infections due to sensitive strains of strep Group B, Enterococcus faecalis (combined with gentamycin), Listeria monocytogenes (with or without gentamycin), E.coli (with or without gentamycin) and Proteus mirabilis and salmonella (not typhi). It is poorly effective against penicillinase producing organisms.

**Cloxacillin:**
Cloxacillin is an isoxazoyl penicillin which are potent inhibitors of the growth of most penicillinase-producing staphylococci. It is bactericidal.
It is used in the treatment of infections due to staphylococci and is active against both penicillinase-producing and non-penicillinase-producing staphylococci. It is stable in acid medium and is resistant to cleavage by penicillinase.

It may be used with other antibiotics including ampicillin to produce a wider spectrum of activity.

**5.2 Pharmacokinetic properties**

**Ampicillin:**

Ampicillin is relatively resistant to inactivation by gastric acid and is moderately well absorbed from the GIT after oral administration. Food can interfere with the absorption of ampicillin so doses should preferably be taken at least 30 minutes before meals. Peak plasma concentrations are attained in about 1-2 hours and after a 500mg oral dose are reported to range from 3-6mcg/ml.

Ampicillin is widely distributed and therapeutic concentrations can be achieved in ascitic, pleural and joint fluids. It can cross the placenta and small amount are distributed into breast milk. There is little diffusion into the CSF except when the meninges are inflamed. About 20% is bound to plasma proteins and the plasma half-life is about 1 to 1.5 hours, but this may be increased in neonates, the elderly and patients with renal impairment.

Ampicillin is metabolised to some extent to penicilloic acid, which is excreted in the urine.

Renal clearance of Ampicillin occurs partly by glomerular filtration and partly by tubular secretion. It is reduced by probenecid. About 20-40% of an oral dose may be excreted unchanged in the urine in 6 hours; urinary concentrations have ranged from 0.25-1mg/ml following a 500mg dose. Ampicillin is removed by haemodialysis. High concentrations are reached in bile, it undergoes enterohepatic recycling and some are excreted in the faeces.

**Cloxacillin:**

Cloxacillin is rapidly but incompletely absorbed from the GIT (30-80%), and absorption is reduced by the presence of food in the stomach so it should be preferably administered 1 hour before or 2 hours after meals to ensure better absorption. After oral dose of 500mg, a peak plasma concentration of 7-15mcg/ml is attained in fasting subjects in 1-2 hours.

About 94% of cloxacillin in the circulation is bound to plasma proteins. It has been reported to have a plasma half-life of 0.5-1 hour. The half-life is prolonged in neonates. Cloxacillin crosses the placenta and is distributed into breast milk. There is little diffusion into the CSF except when the meninges are inflamed. Therapeutic concentrations can be achieved in pleural and synovial fluids and in bile.

Cloxacilin is metabolised to a limited extent and the unchanged drug and metabolites are excreted in the urine by glomerular filtration and renal tubular secretion.

About 35% of an oral dose is excreted in the urine and up to 10% in the bile. Cloxacillin is not removed by haemodialysis.

**5.3 Preclinical safety data**

No further information of relevance to add.

**6. PHARMACEUTICAL PARTICULARS**

**6.1 List of excipients**

Sucrose
Sodium Benzoate
Sodium carboxymethyl cellulose
Citric Acid
Methyl Hydroxybenzoate
Propyl Hydroxybenzoate
Aerosil
Peppermint Flavour
Sodium Citrate
Talc

**6.2 Incompatibilities**

None.

**6.3 Shelf life**
3 years

**6.4 Special precautions for storage**
Store below 30°C. Protect from light

**6.5 Nature and contents of container**
Avroclox Suspension is available in 100ml amber bottle with aluminium screw cap

**6.6 Special precautions for disposal and other handling**
None.

**7. APPLICANT/MANUFACTURER**
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