1. Name of the medicinal product

Compi-clox Capsules (Ampicillin Trihydrate 125mg, Cloxacillin Sodium 125mg)

2. Qualitative and quantitative composition

Each 100ml bottle contains Ampicillin Trihydrate 125mg, Cloxacillin Sodium 125mg.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Powder for Oral Suspension

4.1 Therapeutic indications

Ampicillin

Ampicillin is used in the treatment of a variety of infections due to susceptible organisms. These infections include; bronchitis, endocarditis, epiglotitis, gastro-enteritis, gonorrhea, meningitis, pneumonia and urinary tract infections. Resistant to ampicillin is increasingly a problem in some infections e,g gonorrhea and respiratory tract infections. If beta lactamase producing organisms are present, ampicillin can be administered with a beta-lactamase inhibitor e.g. Sulbactam or Penicillase resistant antibiotics such as Cloxacillin.

Cloxacillin

Cloxacillin is isoxazolyl penicillin used in the treatment of infections due to staphylococci resistant to benzyl penicillin.

Ampicillin plus Cloxacilin

Ampicillin and Cloxacillin have identical mode of action i.e. they Inhibit bacteria cell wall synthesis. Ampicillin is susceptible to degradation by B-lactamase and is therefore inactive against strains producing the enzyme. The combination displays synergy against some B-lactamase producing organisms as cloxacillin protects ampicillin from enzymatic destruction by B-lactamase. The combination is used for infections of the respiratory tract, ears, nose, throat, orthopaedic infections, and pelvic infections.

4.2 Posology and method of administration

Dosage: Oral

By mouth, 0.5 – 1g 6hourly or more frequently is according to the severity of the infection.

Child:

1 month – 2 years, by mouth ¼ adult dose,

2 – 10 years, ½ adult dose

4.3 Contraindications

History of hypersensitivity to penicillins, cephalosporins, penicillin derivative or penicillamin.

4.4 Special warnings and precautions for use

History of gastrointestinal disease especially antibiotic associated colitis(Ampicillin like other penicillins may cause pseudomembraneous colitis).may cause skin rash in patients with infectious mononucleosis.

4.5 Interaction with other medicinal products and other forms of interaction

Probenecid decreases the renal tubular excretion of AMPICLOX. Concurrent use with Compi-clox may result in increased and prolonged blood levels of AMPICLOX.

In common with other antibiotics, Compi-clox may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral contraceptives. Sulphonamides and acetylsalicylic acid inhibit serum protein binding of cloxacillin in vitro. This may result in increased levels of free cloxacillin in serum in vivo. Bacteriostatic drugs may interfere with the bactericidal action of Compi-clox. Concurrent administration of allopurinol during treatment with Compi-clox can increase the likelihood of allergic skin reactions.

4.6 Fertility, pregnancy and lactation

Pregnancy and Lactation

Adequate human data on use during pregnancy are not available. However, animal studies have not identified any risk to pregnancy or embryo-foetal development.

Adequate human and animal data on use during lactation are not available.
Ability to perform tasks that require judgment, motor or cognitive skills

4.7 Effects on ability to drive and use machines

No adverse effects on the ability to drive or operate machinery have been observed.

4.8 Undesirable effects

Adverse Reactions
The following statements reflect the information available on the adverse reaction profile of the individual constituents (ampicillin and cloxacillin) and/or the combination in Compi-clox. The majority of the adverse reactions listed below are not unique to ampicillin - cloxacillin and may occur when using other penicillins.

Adverse reactions are listed below by system organ class and frequency. Frequencies are defined as: very common (>1/10), common (>1/100, <1/10), uncommon (>1/1000, <1/100), rare (>1/10,000, <1/1000), very rare (<1/10,000), including isolated reports. Common and uncommon adverse reactions were generally determined from pooled safety data from a clinical trial population of 1210 treated patients. Rare and very rare adverse reactions were generally determined from more than 32 years of post-marketing experience data and refer to reporting rate rather than true frequency.

Blood and lymphatic system disorders
Very rare: Hemolytic anemia, leucopenia, thrombocytopenia, agranulocytosis

Immune system disorders

Very rare: Anaphylaxis

(See Warnings and Precautions) and other hypersensitivity reactions

Skin disorders and interstitial nephritis have been reported as hypersensitivity reactions. (See also Skin and subcutaneous tissue disorders and Renal and urinary disorders).

If any hypersensitivity reaction occurs, the treatment should be discontinued.

Nervous system disorders
Very rare: Myoclonus and convulsions

Gastrointestinal disorders
Common: Diarrhoeaand nausea
Uncommon: Vomiting
Very rare: Pseudomembranouscolitis

(See Warnings and Precautions) and haemorrhagic colitis

Hepatobiliary disorders
Very rare: Hepatitisandcholestatic jaundice. A moderate and transient increase in transaminases
Skin and subcutaneous tissue disorders
Common: Skin rash, urticarial and pruritus

The incidence of skin rash, pruritus and urticaria is higher in patients suffering from infectious mononucleosis and acute or chronic leukaemia of lymphoid origin.

Very rare: Bullous reactions(including erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis), exfoliative dermatitis and purpura

Skin disorders have also been reported as hypersensitivity reactions
(See Immune system disorders).

Renal and urinary disorders

Very rare: Interstitial nephritis

Interstitial nephritis has also been reported as a hypersensitivity reaction (See also Immune system disorders).

4.9 Overdose
Overdosage with oral Compi-clox is unlikely to cause serious reactions if renal function is normal. Very high dosage of i.v. administered ampicillin and/or high dosage of cloxacillin in renal failure may provoke neurotoxic reactions similar to those seen with benzylpenicillin in excess.

Gastrointestinal effects such as nausea, vomiting, and diarrhoea may be evident. These symptoms should be treated symptomatically.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Compi-clox is a combination of ampicillin and cloxacillin. Cloxacillin is a narrow-spectrum antibiotic of the isoxazolyl penicillin group; it is not inactivated by staphylococcal beta-lactamases. Ampicillin is a broad-spectrum antibiotic of the aminopenicillin group; it is not resistant to beta-lactamases.

Both ampicillin and cloxacillin are bactericidal antibiotics and act by interfering with the formation of new bacterial cell wall by dividing organisms.

The prevalence of acquired resistance is geographically variable and for select species may be very high. Local information on resistance is desirable, particularly when treating severe infections.

Compi-clox susceptibility rates are higher than ampicillin rates due to the cloxacillin activity against β-lactamase producing staphylococci. Methicillin-susceptible Staphylococcus aureus (MSSA) and methicillin-susceptible coagulase-negative staphylococcus (MSCoNS) are commonly susceptible to Compi-clox. MRSA and MRCoNS are resistant to Compi-clox. For all other indicated bacterial species, the susceptibility of Compi-clox is similar to ampicillin including limited activity against Gram-negative organisms.

5.2 Pharmacokinetic properties

Absorption

Both ampicillin and cloxacillin are stable in the gastric environment resulting in good absorption. Neither component of the combination of ampicillin and cloxacillin interferes with the absorption or excretion of the other.

The total quantity absorbed by the oral route represents 50% (cloxacillin) and 40% (ampicillin) of the quantity administered.

The presence of food in the stomach may depress oral absorption and Compi-clox should therefore be taken 0.5 to 1 hour before meals.

Distribution

Compi-clox diffuses well into most tissues and body fluids including, among others, bronchial secretions, sinuses, saliva, cerebrospinal fluid (variable percentage depending on the degree of meningeal inflammation), bile, serous membranes and middle ear.

Crossing the meningeal barrier: Compi-clox diffuses in only small proportion into the cerebrospinal fluid of subjects whose meninges are not inflamed.

Crossing into breast milk: Compi-clox is excreted in small quantities in breast milk.

Plasma half-life for cloxacillin is 0.5 to 1 hour and 1 to 1.5 hour for ampicillin. Protein binding: the serum protein binding proportion is approximately 94% for cloxacillin and 18% for ampicillin.

Metabolism
In normal subjects approximately 20% (cloxacillin) and 40% (ampicillin) of the dose administered is metabolised.

Excretion
Compi-clox is eliminated mainly through the kidney. Approximately 30% of the dose administered orally and over 60% of the ampicillin dose administered parenterally is eliminated in active form in the urine within 24 hours. The equivalent percentages for cloxacillin are approximately 20% and 30% respectively. A small proportion (10%) of the dose administered is excreted in bile.

PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

- Dextrose Monohydrate
- Cornstarch
- Sodium CMC
- Vanilla Powder
- Aspartame
- Aerosil
- Talcum Powder
- Benzoic Acid
- Tartrazine Yellow

6.2 Incompatibilities
Compi-clox must not be dissolved in either protein or protein hydrolysate solutions or in lipid solutions, or in blood or plasma. When Compi-clox is prescribed together with an aminoglycoside, the two antibiotics should not be mixed in the same container as the one containing the infusion solution because a loss of activity may occur.

6.3 Shelf life

3years

6.4 Special precautions for storage

Bottle should be tightly closed in a cool dry place. Once reconstituted should be used within 7 days if stored in a cool place (below 25^0C) or 14days if stored in a refrigerator.

6.5 Nature and contents of container
250mg per 5ml: original pack of 100ml with patient information leaflet measuring spoon with filling marks at 2.5ml, 5ml.

.

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

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

7.0 APPLICANT/MANUFACTURER

Drugfield Pharmaceuticals Limited
Lynson Chemical Avenue Km38,
Lagos-Abeokuta Expressway
Sango-Otta, Ogun State, Nigeria
Tel: +2348033513989
Email:Info@drugfieldpharma.com.

8.0 MARKETING AUTHORISATION NUMBER

04-2350

9.0 DATE OF FIRST AUTHORISATION

15/05/2001

10. DATE OF REVISION OF THE TEXT

20/09/2022