Summary of Product Characteristics (SmPC)

1. NAME OF THE MEDICINAL PRODUCT

1.1 Name of the Medicinal Product

CLIMPICLOX DROPS

(Ampicillin and Cloxacillin Oral Suspension)

1.2 Strength

Ampicillin Trihydrate BP 60 mg

Cloxacillin Sodium BP 30 mg

1.3 Pharmaceutical Form

Oral Suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 0.6 ml of reconstituted suspension contains:

Ampicillin Trihydrate BP

Equivalent to Ampicillin …….60 mg

Cloxacillin Sodium BP

Equivalent to Cloxacillin …….30 mg

Excipients…….....q. s.

Contains approved flavour

3. PHARMACEUTICAL FORM

Oral Suspensions.

4. Clinical particulars

4.1 Therapeutic indications

Ampicillin - Cloxacillin suspension are indicated for the prophylaxis or treatment of bacterial infections in premature babies or neonates, caused by known susceptible strains of bacteria.

4.2 Posology and method of administration

0.6 ml (containing 60 mg Ampicillin and 30 mg Cloxacillin) of reconstituted suspension every 4 hours. Administer 0.5 to 1 hour prior to feeding.

4.3 Contraindications

Ampicillin - Cloxacillin should not be given to patients with a history of hypersensitivity to beta-lactam antibiotics (e.g. penicillins, cephalosporins) or excipients (see Excipients).

4.4 Special warnings and precautions for use

Caution should be observed when administering ampicillin - cloxacillin neonatal suspension to babies whose mothers are hypersensitive to penicillin.

Before initiating therapy with ampicillin - cloxacillin, careful inquiry should be made concerning previous hypersensitivity reactions to beta-lactams.

Cross-sensitivity between penicillins and cephalosporins is well documented.

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.

If an allergic reaction occurs, ampicillin - cloxacillin should be discontinued and the appropriate alternative therapy instituted. All adverse reactions should be treated symptomatically.

Ampicillin - cloxacillin 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.

Pseudomembranous colitis has been reported with the use of antibiotics and may range in severity from mild to life-threatening. Therefore, it is important to consider its diagnosis in patients who develop diarrhoea during or after antibiotic use. If prolonged or significant diarrhoea occurs or the patient experiences abdominal cramps, treatment should be discontinued immediately and the patient investigated further.

Dosage should be adjusted in patients with renal impairment (see Dosage and Administration, Renal Impairment).

Cloxacillin can displace bilirubin from protein-binding sites. Normal caution should therefore be exercised in the treatment of jaundiced neonates.

Ampicillin - cloxacillin neonatal suspension and syrup contain sodium benzoate which is a mild irritant to the skin, eyes and mucous membrane. It may increase the risk of jaundice in newborn babies

4.5 Interaction with other medicinal products and other forms of interaction

Probenecid decreases the renal tubular excretion of ampicillin - cloxacillin. Concurrent use with ampicillin – cloxacillin may result in increased and prolonged blood levels of ampicillin - cloxacillin.

In common with other antibiotics, ampicillin-cloxacillin 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 ampicillin - cloxacillin.

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

4.6 Fertility, pregnancy and lactation

Pregnancy

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

Breastfeeding

Adequate human and animal data on use during lactation are not available.

Fertility

There is no information on the effects of salbutamol on human fertility.

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

The following statements reflect the information available on the adverse reaction profile of the individual constituents (ampicillin and cloxacillin) and/or the combination in ampicillin - cloxacillin. 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: Haemolytic anaemia, 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: Diarrhoea and nausea.

Uncommon: Vomiting.

Very rare: Pseudomembranous colitis (See Warnings and Precautions) and haemorrhagic colitis.

Hepato-biliary disorders

Very rare: Hepatitis and cholestatic jaundice. A moderate and transient increase in transaminases.

Skin and subcutaneous tissue disorders

Common: Skin rash, urticaria 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, StevensJohnson 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

Symptoms and Signs

Overdosage with oral ampicillin - cloxacillin 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.

Treatment

Gastrointestinal effects should be treated symptomatically.

5. Pharmacological properties

5.1 Pharmacodynamic properties

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.

Mechanism of Action

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

Pharmacodynamic Effects

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.

Ampicillin - cloxacillin 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 ampicillin/cloxacillin. MRSA and MRCoNS are resistant to ampicillin/cloxacillin. For all other indicated bacterial species, the susceptibility of ampicillin/cloxacillin 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 ampicillin - cloxacillin should therefore be taken 0.5 to 1 hour before meals.

Distribution

Ampicillin - cloxacillin 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: Ampicillin - cloxacillin diffuses in only small proportion into the cerebrospinal fluid of subjects whose meninges are not inflamed.

Crossing into breast milk: Ampicillin - cloxacillin is excreted in small quantities in breast milk.

Plasma half-life for cloxacillin is 0.5 to 1 hour and 1 to 1.5 hours 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.

Elimination

Ampicillin - cloxacillin is eliminated mainly through the kidney. Approximately 30% of the dose administered orally and over 60% of the ampicillin dose administered parenterally are 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.

5.3 Preclinical safety data

Not Available.

6. Pharmaceutical particulars

6.1 List of excipients

No.	Name of the Excipients	Excipients reference	Function
1	Sugar	BP	Sweetener
2	Sodium Benzoate	BP	Preservative
3	Sodium Citrate	BP	Preservative
4	Sodium CMC	BP	Disintegrate
5	Citric Acid	BP	Preservative
6	Essence Pineapple DC	IH	Flavour
7	Magnesium Stearate	BP	Lubricant
8	Colloidal Silicon Dioxide	BP	Lubricant
9.	Purified Talc	BP	Lubricant

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store below 30°C & dry place. Protect from light.

For reconstituted suspension: Store in refrigerator (2-8^{0}C)

6.5 Nature and contents of container

Amber coloured round glass bottle 18 ml.

6.6 Special precautions for disposal and other handling

Not applicable

7. Marketing Authorization Holder

MAXHEAL PHARMACEUTICALS (INDIA) LIMITED,

Plot No. – 95/6, MIDC Satpur,

Dist- Nashik, Maharashtra- 422007, INDIA.

8. Marketing Authorization Number

Not Applicable.

9. Date of First Authorization /Renewal of the Authorization

Not Applicable.

10. Date of Revision of the Text

Not Applicable