Summary of Product Characteristics (SmPC)

1. Name of the medicinal product

NEMECLOX®

2. Qualitative and quantitative composition

NEMECLOX 500mg *Capsules*

Each capsule contains Ampicillin Trihydrate equivalent to 250mg Ampicillin and Cloxacillin Sodium equivalent to 250mg cloxacillin

Excipients …….q.s

NEMECLOX 250mg/5ml Powder for oral Suspension*:*

Each 5 ml after reconstitution contains Ampicillin trihydrate equivalent to Ampicillin 125mg and cloxacillin sodium equivalent to 125mg Cloxacillin contained in 100ml HDPE bottle or 60ml HDPE bottle.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

NEMECLOX® 500mg capsule: Black and Purple colored Hard Gelatin Capsule shell with "NEMEL" printed on one side of the shell and "NEMECLOX® 500mg" presented in tropicalized blisters and PVC blisters.

NEMECLOX 250mg/5ml Powder for oral suspension:
white to off-white powder for oral suspension available in either 100ml or 60ml HDPE bottles.

4. Clinical particulars

4.1 Therapeutic indications.

NEMECLOX is indicated for the treatment of the following infections including mixed Gram- positive (except methicillin-resistant Staphylococcus aureus (MRSA) and methicillin-resistant coagulase-negative staphylococcus (MRCoNS)) and Gram-negative infections:

***Surgery*: post-operative wound infections, post-operative pulmonary infections.**

Respiratory infections: bronchopneumonia, acute exacerbations of chronic bronchitis.

Obstetrics: puerperal fever.

Other infections such as septicaemia, bone infections e.g., osteomyelitis, ear, nose and throat infections.

Appropriate culture and susceptibility tests should be performed before treatment in order to isolate and identify organisms causing infection and to determine their susceptibility to *NEMECLOX*. Where treatment is initiated before results are available expert advice should be sought when the local prevalence of resistance is such that the utility of *AMPICLOX* is

questionable (*see Pharmacological properties, Pharmacodynamics*).

4.2 Posology and method of administration

Posology

Route	**Dosage**
Adults and Elderly	
Oral	1 to 2g every 6 hours
The dose of NEMECLOX may be increased for the treatment of severe infections.	

Children **2 to 12 years**	**Dosage**
Oral	Half adult dose: 5 to 10mL suspension every 6 hours

Renal **impairment**

In cases of renal failure, the dosage should be adapted in accordance with the following:

Creatinine clearance greater than 50mL/minute: normal dose according to indication.

Creatinine clearance between 50 and 10mL/minute:

- Dosage (oral) initial dose: normal dose (according to indication).

- Dosage (oral) maintenance dose: the normal unit dose (NEMECLOX 500mg orally) three times daily.

Creatinine clearance below 10mL/minute:

- Dosage (oral) initial dose: normal dose (according to indication).

- Dosage (oral) maintenance dose: the normal unit dose twice or once daily.

In cases of dialysis, an additional normal unit dose (NEMECLOX 500mg orally) is to be administered after the procedure.

Hepatic **impairment**

Reduce frequency of administration depending on the severity of the condition.

Method of administration

***NEMECLOX* should be administered 30minutes to 1 hour before meals.**

4.3 Contraindications

NEMECLOX should not be given to patients with a history of hypersensitivity to beta-lactam antibiotics (e.g., penicillins, cephalosporins) or excipients (*See List of Excipients*).

NEMECLOX is contraindicated for ocular administration.

4.4 Special warnings and precautions for use

Before initiating therapy with *NEMECLOX*, 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, *NEMECLOX* should be discontinued and the appropriate alternative therapy instituted. All adverse reactions should be treated symptomatically.

NEMECLOX 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*).

NEMECLOX oral suspension 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.

The sodium content of the formulation must be included in the daily allowance of patients on sodium restricted diets.

Each NEMECLOX 500mg capsule contains 13.17mg of sodium.

NEMECLOX suspension 250mg contains 12.14mg sodium per 5 mL dose.

4.5 Interaction with other medicinal products and other forms of interaction

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

In common with other antibiotics, NEMECLOX 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 NEMECLOX.

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

4.6 Fertility, 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.

4.7 Effects on ability to drive and use machines or cognitive skills

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 *NEMECLOX*. 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:	Diarrhoea and nausea
Uncommon:	Vomiting
Very rare:	Pseudomembranous colitis (*See Warnings and Precautions*) and haemorrhagic colitis

Hepatobiliary 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, 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).*

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

4.9 Overdose

Overdosage with oral NEMECLOX is unlikely to cause serious reactions if renal function is normal. Very high dosage 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

NEMECLOX 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.

***NEMECLOX* 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 *NEMECLOX*. MRSA and MRCoNS are resistant to *NEMECLOX*. For all other indicated bacterial species, the susceptibility of *NEMECLOX* 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 NEMECLOX should therefore be taken 0.5 to 1 hour before meals.

Distribution

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

Crossing into breast milk: NEMECLOX 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

NEMECLOX 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.

5.3 Preclinical Safety Data

6. Pharmaceutical particulars

6.1 List of excipients

Capsule:

Corn Starch

Talcum Powder

Magnesium stearate

Hard Gelatin shell

Powder for Oral suspension:

Sodium chloride

Corn Starch

Vanilla Flavour

Sodium Benzoate

Sodium Carboxyl methyl Cellulose (Sodium CMC)

Sodium Citrate

Sucrose

Aspartame Sweet

Magnesium Stearate

Purified Talcum Powder

Citric Acid

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

NEMECLOX® CAPSULE 500mg

3years

NEMECLOX® Powder for oral suspension 250mg/5ml

2 years

6.4 Special precautions for storage

Do not store above 30°C.

Keep in the original carton to protect from light.

6.5 Nature and contents of container

NEMECLOX ® Capsules are packed in Alu/PVC blisters of 10 capsules per blister pack. 10 blister packs are packed in a box accompanied by a patient information leaflet.

NEMECLOX® Powder for oral suspension is filled in HDPE bottles. 1 of such labelled bottle is packed in a packet accompanied by a measuring cap & patient information leaflet.

6.6 Special precautions for disposal and other handling

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

7. Marketing authorization holder

NEMEL Pharmaceuticals Limited

Plot 35 Emene Industrial Layout

Enugu, Nigeria.

8. Marketing authorization number(s)

A4-4164; A4-8510.

9. Date of first authorization/renewal of the authorization.

26th January, 2016

10. Date of revision of the text

21st January, 2021.