1.5.1 Prescribing information (Summary of Product Characteristics)

1. NAME OF THE MEDICINAL PRODUCT

Proprietary name: Ampimax Plus Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains Ampicillin Sodium BP equivalent to ampicillin 250mg and Cloxacillin Sodium BP equivalent to Cloxacillin 250mg
No any excipients are contained in this product.

3. PHARMACEUTICAL FORM

Powder for injection.
A white or almost white powder or crystalline powder.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Ampicillin 250mg & Cloxacillin 250mg powder for injection is indicated for the treatment of infections in which susceptible organisms have been detected or are suspected (see Section 5.1):
- Surgery: post-operative wound infections, post-operative pulmonary infections
- Respiratory infections: bronchopneumonia, acute exacerbations of chronicbronchitis
- Obstetrics: puerperal fever
- Bacteraemia when associated with, or suspected to be associated with, any of the infections listed in 4.1.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2. Posology and method of administration

Intramuscular/ Intravenous Adult
dosage (including Elderly):
One to two vials every four to six hours.
Children's dosage:
Up to two years: Quarter adult dose
Two to Ten years: Half adult dose.
Dosage may be further increased where necessary.ADMINISTRATION
500 mg vials
Intramuscular
Dissolve vial contents in 1.5 ml Water for Injections BP.
Intravenous
Dissolve vial contents in 10 ml Water for Injections BP and administer slowly (three to four minutes). AMPICILLIN AND CLOXACILLIN FOR INJECTION may also be added to infusion fluids or injected, suitably diluted, into the drip tube over a period of three to four minutes.
Renal Impairment:
In cases of renal failure, the dosage should be adapted in accordance with thefollowing:

	Dosing recommendation
Creatinine Clearance >50 mL/min	Normal dosing according to indication
Creatinine Clearance 50 to 10 mL/min	Dosage (oral or parenteral administration) initial dose: normal dose according to indication Dosage (oral or parenteral administration) maintenance dose: the normal unit dose (ampicillin- cloxacillin 500 mg orally up to 1 g IM or IV) three times daily
Creatinine Clearance <10 mL/min	Dosage (oral or parenteral administration) initial dose: normal dose according to indication Dosage (oral or parenteral administration) maintenance dose: the normal unit dose twice or once daily
Haemodialysis	In case of dialysis, an additionalnormal unit dose (ampicillin - cloxacillin 500 mg orally, up to 1 g IM. or IV) isto be administered after the procedure

Hepatic impairment

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

4.3. Contraindications

Penicillin hypersensitivity; ocular administration. Attention should be paid to possible cross-sensitivity with other beta-lactam antibiotics, e.g. cephalosporins, penicillins.

4.4. Special warnings and precautions for use

Before initiating therapy with AMPICILLIN AND CLOXACILLIN FOR INJECTION, careful enquiry should be made concerning previous hypersensitivity reactions to beta-lactams.
Caution should be observed when administering AMPICILLIN AND CLOXACILLIN FOR INJECTION to babies whose mothers are hypersensitive to penicillin.
AMPICILLIN AND CLOXACILLIN FOR INJECTION should be avoided if infectious mononucleosis is suspected.
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 investigatedfurther.
Dosage should be adjusted in patients with renal impairment (see section 4.2). Sodium Content

One gram of this medicinal product contains 60 mg of sodium. To be taken into consideration by patients on a controlled sodium diet.

4.5. *Interaction with other medicinal products and other forms of interaction*

Concomitant use of allopurinol during treatment with ampicillin can increase the likelihood of allergic skin reactions. There are no data on the concomitant use of AMPICILLIN AND CLOXACILLIN FOR INJECTION and allopurinol.
In common with other antibiotics, AMPICILLIN AND CLOXACILLIN FOR INJECTION may

affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral contraceptives. Therefore, alternative non-hormonal methods of contraception are recommended.
Concurrent use with probenecid may result in increased and prolonged blood levels of AMPICILLIN AND CLOXACILLIN FOR INJECTION.
Penicillins may reduce the excretion of methotrexate causing a potential increase in toxicity.

4.6. Fertility, pregnancy and lactation

Animal studies have shown no teratogenic effects. The product has been in clinicaluse since 1968 and the limited number of reported cases of use in human pregnancy has shown no evidence of untoward effect. The use of AMPICILLIN AND CLOXACILLIN FOR INJECTION in pregnancy should be reserved for cases considered essential by the clinician. During lactation, trace quantities of penicillins can be detected in breast milk.

4.7. Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

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 and Cloxacillin for Injection. The majority of the adverse reactions listed below are not unique to AMPICILLIN AND CLOXACILLIN FOR INJECTION 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 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 and agranulocytosis.
Immune system disorders
Very rare: Anaphylaxis (see item 4.4 Warnings) and other hypersensitive reactions. Skin disorders and interstitial nephritis have been reported ashypersensitivity 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 intransminases.
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 oflymphoid 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 of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product isimportant.
It allows continued monitoring of the benefit/risk balance of the medicinal product

4.9. Overdose

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.
Gastrointestinal effects should be treated symptomatically. Further management should be as clinically indicated or as recommended by the national poisons centre,where available.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Penicillins with extended spectrum ATC code: J01CA51

Ampicillin and cloxacillin for injection is a combination of ampicillin, a broad spectrum antibiotic and cloxacillin, a semi-synthetic beta-lactamase resistant penicillin with activity against gram-negative and gram-positive bacteria including beta-lactamase producing staphylococci.

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

Mechanism of resistance

The main mechanism of resistance to ampicillin/cloxacillin is alteration of pencillin-binding proteins (PBPs), which reduce the affinity of the antibacterial agent for the target.

AMPICILLIN AND CLOXACILLIN FOR INJECTION Breakpoints

EUCAST Interpretive Criteria

	Ampicillin MIC breakpoint (mg/L)		Ampicillin Zone diameter		Cloxacillin MIC breakpoint		Cloxacillin Zone diameter		Cefoxitin Zone Diameter	
			breakpoint(mm) (2 µg disk)		(mg/L)		breakpoint(mm)		breakpoint(mm) (30 µg disk)	
	S ≤	R >	S≥	R <	S ≤	R >	S≥	R <		
Enterobacteriaceae	8	8	14	14	-	-	-	-	-	-
Staphylococcus saprophyticus	Note 1	Note 1	18	18	Note 1	Note1	Note1	Note1	22	22
Staphylococcus aureus, Staphylococcus lugdunensis	-	-	-	-	-	-	-	-	22	22
Coagulase- negative Staphylococci other than S. saprophyticus and S.lugdunensis	-	-	-	-	-	-	-	-	25	25

[1] Most staphylococci are penicillinase producers, which are resistant to benzylpenicillin, phenoxymethylpenicillin, ampicillin, amoxicillin, piperacillin and ticarcillin. Isolates negative for penicillinase and susceptible to methicillin can be reported susceptible to these agents. Isolates positive for penicillinase and methicillin susceptible are susceptible to beta-lactamase inhibitor combinations and isoxazolylpenicillins (oxacillin, cloxacillin, dicloxacillin and flucloxacillin).Methicillin resistant isolates are, with few exceptions, resistant to all beta-lactam agents.

Pharmacodynamic Effects

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

The cloxacillin component of Ampicillin and cloxacillin for injection covers exclusively the suspected or demonstrated presence of *Staphylococcus aureus*. Methicillin-susceptible Staphylococcus aureus (MSSA) and methicillin susceptible coagulase- negative staphylococcus (MSCoNS) are commonly susceptible to cloxacillin. MRSA and MRCoNS are resistant to cloxacillin. For all other indicated bacterial species, the susceptibility of ampicillin/cloxacillin is similar to ampicillin including limited activity against Gram-negative organisms.

***In vitro* susceptibility of micro-organisms to Ampicillin**
Commonly Susceptible Species
Gram-positive aerobes: *Bacillus anthracis* Beta-hemolytic streptococci *Enterococcus faecalis Listeria monocytogenes*
Gram-negative aerobes: *Bordetella pertussis*
Species for which acquired resistance may be a problem
Gram-negative aerobes: *Escherichia coli Haemophilus influenzae Salmonella* spp. *Shigella* spp. *Neisseria gonorrhoeae Pasteurella* spp. *Proteus mirabilis Vibrio cholerae*
Gram-positive aerobes: *Corynebacterium* spp. *Staphylococcus* spp. including *Staphylococcus aureus Streptococcus pneumoniae* Viridans group streptococcus
Gram-positive anaerobes: *Clostridium spp.*
Gram-negative anaerobes: *Prevotella* spp.
Inherently resistant organisms
Gram-negative aerobes: *Acinetobacter baumanii, Burkholderia cepacia, Citrobacter freundii, Citrobacter koseri, Enterobacter aerogenes, Enterobacter cloacae, Escherichia hermanii, Hafnia alvei, Klebsiella pneumoniae, Morganella morganii, Proteus penneri, Proteus vulgaris , Providencia rettgeri, Providencia stuartii, Pseudomonas aeruginosa, Serratia marcescens, Stenotrophomonas maltophilia, Yersinia enterocolitica*

5.2. Pharmacokinetic properties

Ampicillin has a plasma half-life of approximately 1-2 hours and is excreted mainly in the bile and urine.
Cloxacillin is excreted in the urine and bile with a serum half-life of approximately 30 minutes.

5.3. Pre-clinical Safety Data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Not applicable.

6.2. Incompatibilities

Ampicillin and cloxacillin for injection should not be mixed with blood products or other

proteinaceous fluids (e.g. protein hydrolysates) or with intravenous lipid emulsions.
If Ampicillin and cloxacillin for injection is prescribed concurrently with an aminoglycoside, the antibiotics should not be mixed in the syringe, intravenous fluid container or giving set because loss of activity of the aminoglycoside and possibly precipitation can occur under these conditions.

6.3. Shelf life

36 months

6.4. Special precautions for storage

Do not store above 30°C. Store in the original package.

6.5. Nature and contents of container

Clear glass vials supplied in boxes of 50 vials with instructions for use.

6.6. **Special precautions for disposal and other handling of the product**

Ampicillin and cloxacillin for injection 500 mg may be added to most intravenous fluids (e.g., Water for Injections, sodium chloride 0.9%, glucose 5%, sodium chloride 0.18% with glucose 4%). In intravenous solutions containing glucose or other carbohydrates, Ampicillin and cloxacillin for injection should be infused within one hour of preparation. Intravenous solutions of Ampicillin and Cloxacillin in Water for Injections or sodium chloride 0.9% should be infused within 24 hours of preparation. Preparation of Ampicillin and cloxacillin infusion solutions must be carried out under appropriate aseptic conditions if these extended storage periods are required.

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESSES

ABACUS Pharma (Africa) Ltd
P.O. Box 12294, Dar Es Salaam, Tanzania Manufacturer:
Reyoung pharmceutical Co., Ltd.
Manufacturing site physical address: No.1 Ruiyang Road, Yiyuan County, Shandong Province, China

8. MARKETING AUTHORIZATION NUMBER

TAN 21 HM 0298

9. DATE OF FIRST REGISTRATION

20th August, 2021

10. DATE OF REVISION OF THE TEXT