VADIS PHARMACEUTICALS LIMITED	
BRAND NAME:	**VADISCLOX**
GENERIC NAME	**AMPICILLIN AND CLOXACILLIN SUSPENSION 250 MG**

Product Information

Summary of Product Characteristics (SmPC)

VADIS PHARMACEUTICALS LIMITED	
BRAND NAME:	**VADISCLOX**
GENERIC NAME	**AMPICILLIN AND CLOXACILLIN SUSPENSION 250 MG**

1. Name of the medicinal product

Vadisclox (Ampicillin and Cloxacillin Suspension 250 mg)

2. Qualitative and quantitative composition

Each 5 ml of the suspension contains

125 mg Ampicillin as Ampicillin Trihydrate BP

plus 125 mg Cloxacillin equivalent to Cloxacillin Sodium BP

3. Pharmaceutical form

Powder for suspension

4. Clinical particulars

4.1 Therapeutic indications

VADISCLOX is indicated for the treatment of the following infections including mixed Grampositive (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 VADISCLOX. 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 VADISCLOX is questionable (see Pharmacological properties, Pharmacodynamics).

VADISCLOX is indicated for the prophylaxis or treatment of bacterial infections inpremature babies or neonates, caused by known susceptible strains of bacteria.

4.2 Posology and method of administration

Adults and Elderly

Oral: - 1 to 2g every 6 hours

Intramuscular (i.m.) injection: - 500mg to1g very 4 to 6 hours

The dose of VADISCLOX may be increased for the treatment of severe infections.

Children 2 to 12 years

Oral: - Half adult dose: 5 to 10mL suspension every 6

hoursInjectable: - Half adult dose: 250mg every 8 hours

Neonates to 2 years

Neonatal oral drops: - 0.6mL (90mg) of reconstituted suspension every 4 hours. Administer 0/5 to 1 hour priorto feeding.

Renal impairment

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

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

Creatinine clearance between 50 and 10mL/minute: -

Dosage (oral or parenteral administration) initial dose: normal dose (according to indication).

- Dosage (oral or parenteral administration) maintenance dose: the normal unit dose (VADISCLOX 500 mg orally, up to 1g i.m. or i.v) three times daily.

Creatinine clearance below 10mL/minute:

- 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.

In cases of dialysis, an additional normal unit dose (VADISCLOX 500mg orally, up to 1g i.m. or i.v) is to be administered after the procedure.

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

Mode of Administration Oral route: VADISCLOX should be administered 0.5 to 1 hour before meals.

4.3 Contraindications

Hypersensitivity to the active substance, to any of the Penicillin or to any of the excipients

History of a severe immediate hypersensitivity reaction (e.g. anaphylaxis) to another beta-lactam agent (e.g. a cephalosporin, carbapenem or monobactam).

4.4 Special warnings and precautions for use

Caution should be observed when administering VADISCLOX to babies whose mothers are hypersensitive to penicillin.

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

VADISCLOX 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. VADISCLOX neonatal oral suspension and 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 VADISCLOX 500mg capsule contains 13.17mg of sodium.

VADISCLOX 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 VADISCLOX. Concurrent use with VADISCLOX may result in increased and prolonged blood levels of VADISCLOX.

In common with other antibiotics, VADISCLOX 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 VADISCLOX.

Concurrent administration of allopurinol during treatment with VADISCLOX 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

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

4.8 Undesirable effects

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).

4.9 Overdose

Overdosage with oral VADISCLOX 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

Pharmacodynamics VADISCLOX is a combination of ampicillin and cloxacillin. Cloxacillin is a narrow-spectrum antibiotic of the isoxazolyl penicillin group; it is not inactivated by staphylococcal betalactamases. 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. VADISCLOX 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 VADISCLOX. MRSA and MRCoNS are resistant to VADISCLOX. For all other indicated bacterial species, the susceptibility of VADISCLOX is similar to ampicillin including limited activity against Gram-negative organisms.

5.2 Pharmacokinetic properties

Pharmacokinetics 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. 8 The presence of food in the stomach may depress oral absorption and VADISCLOX should therefore be taken 0.5 to 1 hour before meals. Distribution VADISCLOX 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: VADISCLOX diffuses in only small proportion into the cerebrospinal fluid of subjects whose meninges are not inflamed. Crossing into breast milk: VADISCLOX 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 VADISCLOX 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

Non-clinical data reveal no special hazard for humans based on studies of safety pharmacology, repeated dose toxicity, genotoxicity and toxicity to reproduction and development.

Carcinogenicity studies have not been conducted with amoxicillin.

6. Pharmaceutical particulars

6.1 List of excipients

Sodium CMC

Aerosil

Sodium Benzoate

Vanilla Flavor

Sugar

Tartrazine yellow

Magnesium Stearate

6.2 Incompatibilities

VADISCLOX must not be dissolved in either protein or protein hydrolysate solutions or in lipid solutions, or in blood or plasma. When VADISCLOX 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

Dry Powder: 3 years

Reconstituted suspension: 7 days

Reconstituted suspensions: At 2°C-8°C in a refrigerator.

6.4 Special precautions for storage

Keep tightly closed and store in a dry place below 25°C. Once dispensed the suspension should be used within 7 days. If necessary dilute with Syrup B.P.

6.5 Nature and contents of container

1 X 100 ml PET Bottles

6.6 Special precautions for disposal and other handling

Check cap seal is intact before use.

Invert and shake bottle to loosen powder.

To prepare add the required quantity as stated on the product labels of potable water and shake until all contents are dispersed

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

7. Marketing authorisation holder
First Vadis Pharmaceutical Industries Limited
Plot IN/2 Phase 2 Extension,

Emene Industrial Layout Enugu State

Manufacturer
First Vadis Pharmaceutical Industries Limited, Enugu State.

8. Marketing authorisation number(s)

NAFDAC REG. NO.: A4-9409

9. Date of first authorisation/renewal of the authorisation

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10. Date of revision of the text
