SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. Name: Euroclox 500mg Capsule

2. Quantitative and qualitative composition:

Each 500 mg Capsule contains:

Ampicillin trihydrate equivalent to Ampicillin	250 mg
Cloxacillin sodium equivalent to Cloxacillin	250 mg

3. Pharmaceutical form: 500mg gelatin capsule containing Ampicillin Trihydrate BP equivalent to 250mg and Cloxacillin Sodium BP equivalent to 250mg
4. Clinical particulars:

4.1 Therapeutic indications:

EUROCLOX can be used to treat infections of the respiratory tract, ear, nose and throat, urinary tract, gastrointestinal tract, skin and soft tissues, septicaemia, pelvic infections, endocarditis and orthopaedic infections involving ampicillin-susceptible bacteria (such as Gram-positive organisms like S. pneumoniae and other Streptococci, L. monocytogenes as well as Gram-negative organisms like M. catarrhalis, N. gonorrhea, N. meningitidis, E. coli, P. mirabilis, Salmonella, Shigella and H. influenza) and Cloxacillin-susceptible Gram-positive organisms including Penicillinase producing strains of Staphylococci. It is highly active against Staphylococcus aureus, Streptococcus pyogenes, Streptococcus viridans, Streptococcus pneumoniae, N. meningitidis, H. influenzae

4.2 Posology and method of administration:

Best taken at least 30 minutes to 1 hour before meals, 1-2 capsules every 6 hours. 'OR' As directed by the physician.

4.3 Contraindications:

EUROCLOX Capsule is contraindicated in individuals with a history of hypersensitivity reaction to Penicillin, Cephalosporins, Penicillin derivatives or other beta-lactams.

4.4 Special warnings and precaution for use:

To reduce the incidence of relapse, the development of resistance or failure of treatment, take at regular intervals and complete the prescribed course unless otherwise directed. History of gastrointestinal diseases especially antibiotic-associated colitis (Ampicillin like other Penicillins may cause pseudomembranous colitis). Care should be taken when treating patients with syphilis, as the Jarisch Herxheimer reaction may occur shortly after starting treatment. This reaction, manifesting as fever, chills, headache and reaction at the site of the lesion, can be

dangerous in cardiovascular syphilis or where there is a serious risk of increased local damage such as with optic atrophy. EUROCLOX contains Ampicillin and should preferably not be given to patients with infectious mononucleosis, lymphatic leukaemia and renal patients receiving Allopurinol treatment because of an increased risk of developing skin rashes.

4.5 Interaction with other medicinal products:

Co-administration with bacteriostastic antibiotics such as Tetracyclines, Erythromycins or Sulphonamides may antagonize the bactericidal effect of Penicillins. Probenecid decreases renal tubular secretion of Penicillins resulting in increased and more prolonged Penicillin concentrations. Co-administration with Allopurinol leads to increased incidence of skin rash. It may decrease the efficacy of oestrogen-containing oral contraceptives.

4.6 Fertility, Pregnancy and lactation:

Animal studies show no teratogenic effect when used in pregnancy. Trace amounts of penicillins are excreted in breast milk.

4.7 Effects on ability to drive and use machines

Patients experiencing seizure or other forms of CNS disturbances when taking this drug should refrain from operating machines.

4.8 Undesirable effects

Gastrointestinal reactions such as diarrhoea, nausea and heartburn. Allergic reaction which may include exfoliative dermatitis other skin rashes, interstitial nephritis and vasculitis may occur. In this event, EUROCLOX should be withdrawn and an antihistamine administered. Should a serious anaphylactic reaction occur, it should be discontinued and the patient treated with the usual agents (adrenaline, corticosteroids or antihistamines). A generalized sensitivity reaction with urticaria, fever, joint pains and eosinophilia can develop within a few hours to several weeks after starting treatment. Superinfections by resistant species, such as Pseudomonas or Candida, which do not respond to Penicillin therapy may occur. A sore mouth or tongue and a black hairy tongue have been reported. Increase in liver enzyme values have been reported.

4.9 Tabulated summary of adverse reaction : N/A

4.10 Overdose:

Care should be taken when high doses are given to patients with renal impairment (because of the risk of neurotoxicity), or congestive heart failure. Renal and Haematological systems should be monitored during prolonged and high dose therapy. Haemolytic anaemia and leucopenia, prolongation of bleeding time and defective platelet function have been observed usually following high intravenous doses. Convulsions and other signs of toxicity to the central nervous system may occur particularly with intravenous administration or in patients with renal failure. EUROCLOX contains Cloxacillin Sodium, therefore disturbances of blood electrolytes may follow the administration of large doses. Treatment is symptomatic and supportive.

5. Pharmacological properties:

ATC code: JO1CR

Pharmacodynamics: EUROCLOX is a combination of Ampicillin and Cloxacillin. Ampicillin, an amino Penicillin and Cloxacillin, an isoxazoyl Penicillin have an identical mode of action. i.e., they inhibit bacterial cell wall synthesis. This results in the weakening of the bacterial cell wall and cell lysis. Ampicillin is susceptible to degradation by beta-lactamases and is therefore inactive against strains producing this enzyme. The combination displays synergy against some beta-lactamase-producing organisms as Cloxacillin protects Ampicillin from enzymatic destruction by binding them. Cloxacillin forms a relatively stable enzyme-substrate complex with a beta-lactamase and competitively inhibits the activity of beta-lactamases; thus Cloxacillin when given in combination with Ampicillin protects the latter from destruction by beta lactamase. The sparing of Ampicillin by this mechanism increases the availability of Ampicillin at the site of infection. This serves to retain the broad antibacterial spectrum of Ampicillin against Gram positive and Gram negative organisms including those that produce beta-lactamase.

Pharmacokinetics: Ampicillin and Cloxacillin are individually acid stable and easily absorbed when administered before meals to produce good serum and urine concentrations. Higher and more prolonged levels may be achieved in patients with normal renal function by the concurrent administration of Probenecid. EUROCLOX is predominantly excreted by glomerular filtration and renal tubular secretion.

6. Preclinical safety data/ Pharmaceutical particulars:

In mice, rats and dogs, penicillin G, the phenoxypenicillins, methicillin, the isoxazoles and ampicillin are all tolerated intravenously in doses of 2 g/kg. or more, and in twice that dosage subcutaneously or orally. With some derivatives (e.g. ampicillin) it is difficult to establish a toxic dose within the limits of solubility. Extremely high doses (5 g/kg) may cause convulsions if given intravenously: this would be equivalent to about half a kilogram by injection or a kilogram by mouth to man. At about half this dose level, the isoxazoles cause transient hypotension but in other respects there is no interference with vital functions. The toxic level in man has never been established but it is known that methicillin and penicillin G can be given intravenously in doses of 20 g per day for weeks on end, and that ampicillin and the isoxazoles can be given in doses of at least 4 g/day (80 mg/kg) without any signs of immediate or delayed toxicity. This means that concentrations of penicillin G and methicillin of 50 mg%

can circulate harmlessly in the blood and tissues; in other words, that penicillin is no more toxic than glucose or urea, and much less toxic than many other physiological substances. When such large doses are being given, it is best to use the sodium salt as the potassium cation can be toxic: 15 mega units of penicillin G supplies 25 mEq of K+ which may cause cardiac dilation, especially if the heart is already damaged, as in bacterial endocarditis, which is the main disease requiring such high doses. Even the sodium cation may rise if there is any renal impairment (Stewart, G.T).

Tolerance of various species to Penicillins

Dose tolerated in mg/kg/day					
Drug	Mouse	Rat	Guinea Pig	Rabbit	Dog
Peniciilin G	3,000	3,500	5	500	500
Methicillin	3,000	4,000	10	500	250
Ampicillin	5,000	5,000			
Cloxacillin	2,000	500	10	200	

6.1 List of excipients

1. Ampicillin Trihydrate BP
2. Cloxacillin sodium BP
3. Magnesium Stearate

6.2 Incompatibilities: Check USP

6.3 Shelf life: Two years from the date of manufacturing

6.4 Special Precautions for storage: Store the drug capsule below 30^0C in a cool and dry place, away from direct sunlight. Keep all medicines out of the reach of children

6.5 Nature and contents:

1. 10 capsules in one regular blister and 10 regular blisters in one carton.
2. 10 capsules in one tropical blister and 2 such tropical blisters in one clinical box.

6.6 Special Precautions for disposal: dispose empty cartons placed in secondary package in a waste bin.

7. Marketing Authorization Holder (MAH):
   Address: CHRIS-EJIK PHARMACEUTICALS AND HEALTHCARE PRODUCTS LTD
   3, Oje-Imianvan Street, Oregun, Ikeja, Lagos

8. MAH No/License: Not applicable
9. Date of first authorization/ renewal of the authorization: Not applicable
10. Date of revision of the text: Not applicable
11. Dosimetry: Not applicable
12. Instructions for preparation of radiopharmaceutical: Not applicable