1.3

Product Information

1.3.1

Summary of Product Characteristics (SmPC)

1. Name of the medicinal Product

Combipack of Amoxicillin and Potassium Clavulanate Injection BP & Sterilised water for injections BP 20 ml

1.1 Strength

Each Combipack Contains:

(A) One Vial of Amoxicillin and Potassium Clavulanate Injection BP

Each Vial Contains:

Amoxicillin Sodium BP (Sterile)

Eq. to Amoxicillin……1000 mg.

Potassium Clavulanate BP

Eq. to Clavulanic acid…….200 mg

(B) One ampoule of 20 ml Sterilized Water for injection BP

2. Qualitative and Quantitative Composition

2.1 Qualitative declaration

Amoxicillin and Potassium Clavulanate injection

2.2 Quantitative declaration

Amoxicillin and Potassium Clavulanate injection

Sr. No.	Ingredients	Specifications	Standard Quantity/ (mg/vial)	Reason for Inclusion
01	Sterile Blend of Amoxicillin and Potassium Clavulanate Contains	In-House	1268.5	Anti-bacterial
A.	Amoxicillin sodium sterile Eq.to Amoxicillin		1030.2 Eq. to 1000	

B.	Potassium Clavulanate sterile Eq.to Clavulanic acid		238.25 Eq. to 200.00	

3. Pharmaceutical Form

Dry Powder Injection

4. Clinical Particulars

4.1 Therapeutic Indications

Amoxicillin and Potassium Clavulanate is indicated for the short term treatment of common bacterial infections such as:

Upper Respiratory Tract Infections (including ENT): tonsillitis, sinusitis, otitis media.

Lower Respiratory Tract Infections: acute exacerbations of chronic bronchitis, lobar and Broncho-pneumonia.

Genito-urinary Tract Infections: cystitis, urethritis, pyelonephritis, female genital infections.

Skin and Soft Tissue Infections.

Bone and Joint Infections: osteomyelitis.

Other Infections: septic abortion, puerperal sepsis, intra-abdominal sepsis, septicemia, peritonitis, post-surgical infections.

Amoxicillin and Potassium Clavulanate is indicated for Prophylaxis against infection which may be associated with major surgical procedures: gastro-intestinal, pelvic, head and neck, cardiac, renal, joint replacement and biliary tract surgery.

Infections caused by amoxicillin susceptible organisms are amenable to Amoxicillin and Potassium Clavulanate treatment due to its amoxicillin content. Mixed infections caused by amoxicillin susceptible organism in conjunction with Amoxicillin and Potassium Clavulanate - susceptible Beta-Lactamase-producing organisms may therefore be treated by Amoxicillin and Potassium Clavulanate.

4.2 Posology and Method of Administration

Dosage:

Children 0-3 months: 30mg/kg* Amoxicillin and Potassium Clavulanate injection every 12 hours in infants <4kg and 30mg/kg* Amoxicillin and Potassium Clavulanate injection every 8 hours in infants >4kg.

Children 3 months - 12 year: Usually 30mg/kg* Amoxicillin and Potassium Clavulanate injection 8 hourly. In more serious infections, increase frequency to 6 hourly intervals.

Adults and Children 40kg and over: Usually 1.2 g/8 hourly. In more serious infections, increase frequency to 6 hourly intervals.

*Each 30mg Amoxicillin and Potassium Clavulanate injection provides 5mg clavulanic acid with 25mg amoxicillin.

Dosage for surgical prophylaxis:

Surgical prophylaxis with Amoxicillin and Potassium Clavulanate injection should aim to protect patient during period of risk of infection.

Accordingly, procedures in adults lasting for less than 1 hour are successfully covered by 1.2g Amoxicillin and Potassium Clavulanate injection Intravenous given at induction of anaesthesia. Longer operations require subsequent doses of 1.2g Amoxicillin and Potassium Clavulanate injection IV (up to 4 doses in 24 hours), and this regime can be continued for several days if procedure has significantly increased risk of infection. Clear clinical signs of infection at operation requires normal course of IV Amoxicillin and Potassium Clavulanate injection post-operatively.

Dosage in renal impairment:

Adults: Dosing adjustments are based on the maximum recommended level of amoxicillin.

Route of Administration	**Mild Impairment (creatinine clearance >30mL/min)**	**Moderate Impairment (creatinine clearance 10-30mL/min)**	**Severe Impairment (creatinine clearance <10mL/min)**
Intravenous	No change in dosage	1.2g IV stat followed by 600 mg IV 12 hourly	1.2g IV stat followed by 600 mg IV 24 hourly. Dialysis decreases serum concentrations of co-amoxiclav. An additional 600 mg IV dose may be

			supplemented at the end of dialysis

Each 1.2g vial of Co-amoxiclav contains 1.0 mmoL of potassium and 3.1 mmoL of sodium. (approx.)

Children: Dosing adjustments are based on the maximum recommended level of amoxicillin.

Route of Administration	**Mild Impairment (creatinine clearance >30mL/min)**	**Moderate Impairment (creatinine clearance 10-30mL/min)**	**Severe Impairment (creatinine clearance <10mL/min)**
Intravenous	No change in dosage	30 mg/kg 12 hourly	30 mg/kg every 24 hours. Dialysis decreases serum concentrations of Co-amoxiclav. An additional 15 mg/kg may need to be supplemented at the end of dialysis, then 30 mg/kg/day.

Dosage in hepatic impairment:

Dose with caution; monitor hepatic function at regular intervals for both adults and children. There are as yet insufficient data on which to base a dosage recommendation.

Dosage in elderly:

No adjustment needed, dose as for adults. if there js evidence of renal impairment, dose should be adjusted as for renally impaired adults.

4.3 Contraindications

In patients with a history of hypersensitivity to beta-lactams, e.g. penicillins and cephalosporins.

In patients with a previous history of Amoxicillin and Potassium Clavulanate associated jaundice/hepatic dysfunction.

4.4 Special Warnings and Special Precautions for Use

Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity.

It should be avoided if infectious mononucleosis is suspected since the occurrence of a morbilliform rash has been associated with this condition following the use of amoxicillin.

Prolonged use may also occasionally result in overgrowth of non-susceptible organisms.

If the parenteral administration of high doses is necessary, the sodium content must be taken into account in patients on a sodium restricted diet.

In patients with reduced urine output crystalluria has been observed very rarely, predominantly with parenteral therapy. During administration of high doses of amoxicillin it is advisable to maintain adequate fluid intake and urinary output in order to reduce the possibility of amoxicillin crystalluria.

Hepatic impairment: Used with caution in patients with evidence of hepatic dysfunction.

Renal impairment: Dosage should be adjusted according to the degree of impairment.

Pregnancy: Safe use of Amoxicillin and Potassium Clavulanate combination during pregnancy has not been established. Due to absence of adequate controlled studies in pregnant women, the combination should not be used during pregnancy.

Lactation: Amoxicillin and Clavulanic Acid are distributed in breast milk. Hence caution should be exercised if using Amoxicillin and Potassium Clavulanate in nursing women.

4.5 Pregnancy and Lactation

Pregnancy: Safe use of Amoxicillin and Clavulanate combination during pregnancy has not been established. Due to absence of adequate controlled studies in pregnant women, the combli1ation should not be used during pregnancy.

Lactation: Amoxicil.fu1 and Clavulanic Acid are dislibuted in breast milk. Hence caution should be exercised if using Amoxicillin – Clavulanic Acid nursing women.

4.6 Undesirable Effects:

Clostridium difficile-associated diarrhoea and colitis (antibiotic-associated pseudo-membranous colitis) caused by toxin producing clostridia has been reputed.

Adverse reactions observed in pediatric patients are similar to those reported in adults.

Abdominal discomfort, anorexia and flatulence, dyspepsia, gastritis, stomatitis, glossitis, black or hairy tongue and enterocolitis also have been reported.

Moderate increases in serum concentrations of AST (SGOT) and/or ALT (SGPT), alkaline phosphatase and/or bilirubin have been observed in patients receiving amoxicillin and clavulanic acid.

Hepatic dysfunction reflected as cholestatic, hepatocellular or mixed cholestatic hepatocellular changes have been reported most frequently in geriatric patients, males, or in patients receiving long-term therapy.

4.7 Overdose

Gastrointestinal symptoms and disturbance of the fluid and electrolyte balances may be evident. They may be treated symptomatically, with attention to the water/electrolyte balance.

Amoxicillin crystalluria, in some cases leading to renal fail w-e. bas been observed.

Amoxicillin has been reported to precipitate in bladder catheters after intravenous administration of Large doses. A regular check of patency should be maintained.

Co-amoxiclav can be removed from the circulation by haemodialysis.

5. Pharmacological Properties

5.1 Pharmacodynamics Properties

Amoxicillin is a semisynthetic antibiotic with a broad spectrum of antibacterial activity against many gram positive and gram-negative micro-organisms. Amoxicillin is, however susceptible to degradation by beta lactamases and therefore the spectrum of activity of amoxicillin alone does not include organisms which produce these enzymes.

Clavulanic acid is a beta-lactam, structurally related to the Penicillins, which possesses the ability to inactivate a wide range of beta-lactamase enzymes commonly found in micro-organisms resistant to Penicillins and cephalosporins. In particular, it has good activity against the clinically important plasmid mediated beta-lactamases frequently responsible for transferred drug resistance. It is generally less effective against chromosomally-mediated type I beta-lactamases.

The presence of clavulanic acid in Co-amoxiclav formulations protect amoxicillin from degradation by beta-lactamase enzymes and effectively extends the antibacterial spectrum of amoxicillin to include many bacteria normally resistant to amoxicillin and other Penicillins and cephalosporins. Thus Co-amoxiclav possesses the distinctive properties of a broad spectrum antibiotic and a beta-lactamase inhibitor.

5.2 Pharmacokinetic Properties

Absorption: Amoxicillin and Clavulanic Acid are fully dissociated in aqueous solution at physiological pH.

Distribution: Following intravenous administration therapeutic concentrations of both amoxicillin and clavulanic acid may be detected in the tissues and interstitial 1luid. Therapeutic concentrations of both medicines have been found in gall bladder. abdomi11al tissue, skin. fat, and muscle tissues: fluids found to have therapeutic levels include synovial and peritoneal fluids, bile and pus.

Neither amoxicillin nor clavulanic acid is highly protein bound. studies show that about 13% to 25% of total plasma drug content of each compound is bound to protein.

Amoxicillin, like most penicillin can be detected in breast milk. Trace quantities of Clavulanate can also be detected in breast milk. With the exception of the risk of Sensitisation associated with this excretion. there are no known detrimental effects for the breastfed infant.

Elimination: As with other Penicillins. the major route of elimination for amoxicillin is via the kidney, whereas for Clavulanate it is by both renal and non-renal mechanisms. Approximately 60-70% of the amoxicillin and approximately 40-65% of the clavulanic acid are excreted unchanged in urine during the first 6 hours after administration of a 1000/200mg bolus intravenous injection.

Amoxicillin is also partly excreted in the urine as the inactive penicilloic acid in quantities equivalent to 10- 25% of the initial dose. Clavulanic acid is extensively metabolised in man to 2,5-dihydro-4-(2-bydroxycthyl)-5-oxo-1H-pyrrole-3-carboxylic acid and 1-amino-4-hydroxy-butan-2-one and eliminated in urine and faeces as carbon dioxide in expired air.

5.3 Preclinical Safety Data

Not applicable.

6. Pharmaceutical Particulars

6.1 List of Excipients

Not applicable

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

24 months

6.4 Special Precautions for Storage

Store below 30°C. Protect from light and moisture.

6.5 Nature and Contents of Container

Off white to faintly yellow coloured powder filled in 20 ml transparent USP type-III Vial having 20 mm gray butyl rubber stopper with 20 mm flip off seal. Such one vial is packed in a Tray Pack with one ampoule of 20 ml diluent. such one Tray is packed in a Printed Carton with Packaging Insert.

6.6 Special precaution for disposal and other handling

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

7. Registrant (Marketing Authorization Holder and Manufacturing Site Addresses)

7.1 Name and Address of Marketing Authorization Holder

GENERICS AND SPECIALITIES LTD.

31, AWONIYI ELEMO STREET,

OFF LATEEF SALAMI STREET.

AJAO ESTATE, LAGOS,

NIGERIA.

7.2 Name and Address of manufacturing site(s)

Lincoln Pharmaceuticals Limited

Trimul Estate, Khatraj, Taluka: Kalol,

District: Gandhinagar Gujarat, India.

Telephone no.: +91-079-4107-8096

Fax: +91-079-4107-8062

Email: hiren@lincolnpharma.com

Website: www.lincolnpharma.com

7.3 Marketing Authorization Number

To be included after obtaining first registration.

7.4 Date of First <Registration> / Renewal of The <Registration>

It will be applicable after registration of this product.

8. Date of Revision of the Text

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9. Dosimetry (If Applicable)

Not Applicable

10. Instructions for preparation of radiopharmaceuticals (if Applicable)

Not Applicable