BRAND NAME:	**MEDNOCLAV**
GENERIC NAME:	**AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM**

MODULE-1 ADMINISTRATIVE INFORMATION

1.3.1 Summary Of Product Characteristics (Smpc)

1. Name of drug product

AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM

1.1 (Trade) name of product

MEDNOCLAV

1.2 Strength

Each vial contains:

Amoxicillin sodium (Sterile) BP

Eq. to Amoxicillin ……..…1000 mg

Potassium Clavulanate (Sterile) BP

Eq. to Clavulanic Acid ……...200 mg

1.3 Pharmaceutical Dosage Form

Powder for injection

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MODULE-1 ADMINISTRATIVE INFORMATION

2. Qualitative & Quantitative composition

2.1 Qualitative Declaration

Each vial contains:

Amoxicillin sodium (Sterile) BP

Eq. to Amoxicillin ……..…1000 mg

Potassium Clavulanate (Sterile) BP

Eq. to Clavulanic Acid ……...200 mg

2.2 Quantitative Declaration

Batch Formula:

Batch size: 10,000 Vial

Sr. No.	Ingredients	Specifications	Reason For Inclusion	Label Claim	Overages	Quantity / unit (mg)	Quantity/ Batch (kg)
1.	Amoxicillin sodium Equivalent to Amoxicillin	BP	Active	1000 mg	10.0%	1100.00	11.00
2.	Potassium Clavulanate Equivalent to Clavulanic Acid	BP	Active	200 mg	20.0%	240.00	2.40

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MODULE-1 ADMINISTRATIVE INFORMATION

3. Pharmaceutical dosage form

IV

4. Clinical Particulars

4.1 Therapeutic Indications

AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM should be used in accordance with local official antibiotic-prescribing guidelines and local susceptibility data.

AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM is indicated for the short term treatment of bacterial infections at the following site:

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

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

Genito-urinary Tract Infections: e.g. cystitis, urethritis, pyelonephritis,

Skin and Soft Tissue Infections, e.g boils, abscesses, cellulities, wound infections.

Bone and Joint Infections: e.g. osteomyelitis

Other Infections: e.g., intra-abdominal sepsis

AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM intravenous is also indicated for prophylaxis against infection which may be associated with major surgical procedures such as gastro-intestinal, pelvic, head and neck, cardiac, renal, joint replacement and biliary tract.

Susceptibility to AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM will vary with geography and time (see pharmacological properties, pharmacodynamics for further information) Local susceptibility data should be consulted where available, and microbiological sampling and susceptibility testing performed where necessary.

Infections caused by amoxicillin susceptible organisms are amenable to AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM treatment due to its amoxicillin content. Mixed infections caused by amoxicillin susceptible organism in conjunction with AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM -susceptible beta- lactamase-producing organisms may therefore be treated with AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM

BRAND NAME:	MEDNOCLAV
GENERIC NAME:	AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM

MODULE-1 ADMINISTRATIVE INFORMATION

4.2 Posology and Method of Administration

Dosage for treatment of infections:

Adults and children over 12 years	Usually 1.2 g eight-hourly. In more serious infections, increase frequency to six-hourly intervals.
Children 3 months - 12 year:	Usually 30mg/kg. In more serious infections, increase frequency to six-hourly intervals.

Adults dosage for surgical prophylaxis

The usual dose is 1.2 g AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM intravenous given at the induction of anaesthesia. Operation where is a high risk of infection, e.g. colorectal surgery, may reuire three is a high risk of infection, e.g colorectal surgery, may require three, and up to four, dosea of 1.2 g AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM intravenous therapy post-operatively.

Dosage in renal impairment

Adults

Mild Impairment (creatinine clearance >30mL/min	Moderate Impairment (creatinine clearance 10-30mL/min)	Severe Impairment (creatinine clearance
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 OXYNIC. An additional 600 mg IV dose may be supplemented at the end of dialysis

Children

Similar reductions in dosage should be made for children.

Dosage in hepatic impairment

Dose with caution; monitor function at regular intervals.

Each 1.2g vial of AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM contains 1.0 mmoL of potassium and 3.1 mmoL of sodium.

(approx.)

Administration:

AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM intravenous may be administered either by intravenous injection or by intermittent infusion. It is not suitable for intramuscular administration.

MODULE-1 ADMINISTRATIVE INFORMATION

4.3 Contraindications

AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM is contraindicated in patients with a history of hypersensitivity to beta-lactams, e.g. penicillins and cephalosporins.

AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM is contraindicated in patients with a previous history of AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM associated jaundice/hepatic dysfunction.

4.4 Special Warnings and Precautions for Use

Before initiating therapy with AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM, careful enquiry should be made concerning previous hypersensitivity reactions, cephalosporins, or other allergens.

Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions) have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity (see contraindication). If an allergic reaction occurs, AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM therapy should be discontinued and appropriate alternative therapy instituted. Serious anaphylactic reactions require immediate emergency treatment with adrenaline. Oxygen, intravenous (i.v) steroids and airway management, including intubation may also be required.

Change in liver function tests have been observed in some patients receiving AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM. The clinical significance of these changes is uncertain but AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM should be used with caution in patients with evidence of hepatic dysfunction.

Cholestatic jandiec, which may be become apparent for up to six weeks after treatment has csased.

In patients with renal impairment AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM dosage should be adjusted as recommended in dosage and administration section.

AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM 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 overgrowths of non-susceptible oraganisms.

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 diarrhea during or after antibiotic use. If prolonged or significant diarrhea occurs or the patient experiences abdominal cramps, treatment should be discontinued immediately and the patient investigated further.

Abnormal prolongation of prothrombin time (increased INR0 has been reported rarely in patients receiving AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM and Intravenous anticoagulants. Appropriate monitoring should be undertaken when anticoagulants are prescribed concurrently. Adjustments in the dose of Intravenous anticoagulants may be necessary to maintain the desired level of anticoagulation.

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 sosea pf amoxicillin, it is advisable to maintain adequate fluid intake and urinary in order to reduce the possibility of amoxicillin crystalluria (see overdose).

The presence of clavulanic acid in AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM may cause a non specific binding of IgG and albumin by red cell membranes leading to a false positive coombs test.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use of probenecid is not recommended. Probenecid decreases the renal tubular secretion of amoxicillin. Concomitant use with AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM may result in increased and prolonged blood levels of amoxicillin, but not of clavulanate.

Concomitant use of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions. There are no data on the concomitant use of AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM and allopurinol.

In common with other antibiotics, AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral contraceptives.

MODULE-1 ADMINISTRATIVE INFORMATION

The presence of clavulanic acid in AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM may cause a non-specific binding of IgG and albumin by red cell membranes leading to a false positive Coombs test.

In the literature there are rare cases of increased international normalised ratio in patients maintained on acenocoumarol or warfarin and prescribed a course of amoxicillin. If co-administration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM

In patients receiving mycophenolate mofetil, reduction in pre-dose concentration of the active metabolite mycophenolic acid of approximately 50% has been reported following commencement of oral amoxicillin plus clavulanic acid. The change in pre- dose level may not accurately represent changes in overall MPA exposure.

4.6 Fertility, pregnancy and lactation

Use in pregnancy

Reproduction studies in animals (mice and rats) with parentally administered AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM have shown no teratogenic effects. In a single study in women with preterm, premature rupture of the foetal membrane, it was reported that prophylactic treatment with AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM may be associated with an increased risk of necrotising enterocolitis in neonates. As with all medicines, use should be avoided in pregnancy, unless considered essential by the physician.

Use in lactation

AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM may be administered during the period of lactation. With the exception of the risk of sensitisation, associated with the excretion of trace quantities in breast milk, there are no known detrimental effects for the breastfed infant.

4.7 Effects on ability to drive and operate machine

Adverse effects on the ability to drive or operate machinery have not been observed.

MODULE-1 ADMINISTRATIVE INFORMATION

4.8 Undesirable effects

Data from large clinical trials was used to determine the frequency of very common to rare undesirable effects. The frequencies assigned to all other undesirable effects (i.e., those occurring at < 1/10,000) were mainly determined using post-marketing data and refer to a reporting rate rather than a true frequency.

The following convention has been used for the classification of frequency:

very common > 1/10

common > 1/100 and < 1/10

uncommon > 1/1000 and < 1/100

rare > 1/10,000 and < 1/1000

very rare <1/10,000.

Infections and infestations:

Common: Mucocutaneous candidiasis

Blood and lymphatic system disorders:

Rare: Reversible leucopenia (including neutropenia) and thrombocytopenia

Very rare: Reversible agranulocytosis and haemolytic anaemia. Prolongation of bleeding time and prothrombin time

Immune system disorders:

Very rare: Angioneurotic oedema, anaphylaxis, serum sickness-like syndrome, hypersensitivity vasculitis

Nervous system disorders:

Uncommon: Dizziness, headache

Very rare: Reversible hyperactivity and convulsions. Convulsions may occur in patients with impaired renal function or in those receiving high doses.

Vascular disorders:

Rare: Thrombophlebitis at the site of injection

Gastrointestinal disorders:

Common: Diarrhoea

Uncommon: Nausea, vomiting, indigestion

Very rare: Antibiotic-associated colitis (including pseudomembranous colitis and haemorrhagic colitis - Special warnings and precautions) are less likely to occur after parenteral administration.

Hepatobiliary disorders:

Uncommon: A moderate rise in AST and/or ALT has been noted in patients treated with beta-lactam class antibiotics, but the significance of these findings is unknown.

Very rare: Hepatitis and cholestatic jaundice. These events have been noted with other penicillins and cephalosporins.

Heptic events have been reported predominantly in males and elderly patients and may be associated with prolonged treatment.

Signs and symptoms usually occur during or shortly after treatment but in some cases may not become apparent until several weeks after treatment has ceased. These are usually reversible. Hepatic events may be severe and in extremely rare circumstances, deaths have been reported. These have almost always occurred in patients with serious underlying disease or taking concomitant medications known to have the potential for hepatic effects.

Skin and subcutaneous tissue disorders:

Uncommon: Skin rash, pruritus, urticaria

Rare: Erythema multiforme

Very rare: Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous exfoliative-dermatitis, acute generalised exanthemous pustulosis (AGEP), and drug reaction with eosinophilia and systemic symptoms (DRESS)

If any hypersensitivity dermatitis reaction occurs, treatment should be discontinued.

Renal and urinary disorders:

Very rare: Interstitial nephritis, crystalluria

MODULE-1 ADMINISTRATIVE INFORMATION

4.9 Overdose

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

Amoxicillin crystalluria, in some cases leading to renal failure, has been observed (warnings and precautions).

AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM can be removed from the circulation by haemodialysis.

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

BRAND NAME:	MEDNOCLAV
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MODULE-1 ADMINISTRATIVE INFORMATION

5. Pharmacological properties

5.1 Pharmacodynamic property

Pharmacotherapeutic group: Beta-Lactamase Inhibitors

ATC code: J01CR02

Resistance to many antibiotics is caused by bacterial enzymes which destroy the antibiotic before it can act on the pathogen. The clavulanate in AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM anticipates this defence mechanism by blocking the β-lactamase enzymes, thus rendering the organism sensitive to amoxicillin's rapid bactericidal effect at concentration readily attainable in the body.

Clavulanate by itself has little antibacterial activity; however, in association with amoxicillin as AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM, it produces an antibiotic agent of broad spectrum with wide application in hospital and general practice.

5.2 Pharmacokinetic properties

the pharmacokinetics of the two components of AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM are closely matched.

Both clavulanate and amoxicillin have low levels of serum binding; about 70 % remains free in the serum.

Doubling the dosage of AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM approximately doubles the serum levels achieved

5.3 Preclinical safety data

NA

6. Pharmaceutical particulars

6.1 List of excipients

Not applicable

6.2 Incompatibilities

Not applicable

BRAND NAME:	MEDNOCLAV
GENERIC NAME:	AMOXICILLIN AND POTASSIUM CLAVULANATE INJECTION BP 1.2 GM

MODULE-1 ADMINISTRATIVE INFORMATION

6.3 Shelf life

36 month

6.4 Special precautions for storage

Store below 30°C. Protect from light. Keep out of reach of children.

6.5 Nature and contents of container

1340 mg powder filled in glass vial with chlorobutyl rubber stopper sealed with Aluminium flip off seal with one ampoule of 20 ml sterile water for injection packed in monocarton along with package leaflet.

7. Marketing authorisation holder

MEDNORAL PHARMACEUTICAL LTD.

3, OLAIDE BENSON STREET,

MARYLAND LAGOS. NIGERIA.

8. Marketing authorisation number(s)

9. Date of first authorisation/renewal of the authorisation

10. Date of revision of the text