Scheduling status: [S4]
1. Name of medicine
APOCLAV 0,6 g (Powder for Solution for Injection or Infusion)
APOCLAV 1,2 g (Powder for Solution for Injection or Infusion)
2. Qualitative and quantitative composition
Each vial of **APOCLAV 0,6 g** Powder for Solution for Intravenous Injection or Infusion contains 530 mg of amoxicillin sodium equivalent to 500 mg of amoxicillin and potassium clavulanate equivalent to 100 mg clavulanic acid.
Each vial of **APOCLAV 1,2 g** Powder for Solution for Intravenous Injection or Infusion contains 1 060 mg of amoxicillin sodium equivalent to 1000 mg of amoxicillin and potassium clavulanate equivalent to 200 mg clavulanic acid.
For the full list of excipients, see section 6.1.
3. Pharmaceutical form
APOCLAV 0,6 g Powder for Solution for Injection or Infusion:
White to cream powder in vials when reconstituted a clear pale yellow solution which is practically free from particulate matter.
APOCLAV 1,2 g Powder for Solution for Injection or Infusion:
White to cream powder in vials when reconstituted a clear pale yellow solution which is practically free from particulate matter.
4. Clinical particulars
4.1 Therapeutic indications
APOCLAV 0,6 g and APOCLAV 1,2 g are indicated for the treatment of infections caused by amoxicillin resistant organisms producing ß-lactamases sensitive to clavulanic acid:

- Upper respiratory tract, such as sinusitis, recurrent otitis media, tonsillitis
- Lower respiratory tract, such as bronchitis and bronchopneumonia
- Genito-urinary tract infections, such as cystitis, urethritis, pyelonephritis
- Skin and soft tissue infections.

APOCLAV formulations will also be effective in the treatment of infections caused by Amoxicillin sensitive organisms at the appropriate amoxicillin dosage since in this situation the clavulanic acid component does not contribute to the therapeutic effect.
4.2 Posology and method of administration
Posology:
General information:
For infections caused by amoxicillin sensitive organisms the dosage is that approved for amoxicillin, as the clavulanic acid component does not contribute to the therapeutic effect.
Adult (Intravenous):For severe infections of the respiratory tract, urinary tract and skin and soft tissue requiring parenteral therapy initially **APOCLAV 1,2 g** Powder for Solution for Injection or Infusion vial containing the equivalent of 1000 mg amoxicillin and 200 mg clavulanic acid can be administered intravenously 6 to 8 hourly by intravenous injection (2 minutes) or intravenous infusion (30 minutes) until condition settles followed by oral therapy with amoxicillin / clavulanic acid tablets at the recommended dose. If no response has occurred within 48 hours therapy must be reviewed. Intravenous treatment with **APOCLAV** should not extend beyond 10 days without review and the total daily administration of clavulanic acid should not exceed 800 mg. Treatment can be continued with amoxicillin/clavulanic acid tablets orally where appropriate after a satisfactory therapeutic response has been obtained.

DOSAGE GUIDE: AMOXICILLIN - SENSITIVE ORGANISMS

PRODUCT	Upper Respiratory Tract Infections	Lower Respiratory Tract Infections	Urinary Tract Infections	Skin and Soft Tissue Infections
Adults:				
APOCLAV 1,2 g Powder for Solution for Injection or Infusion	1 Vial [†] 6–8 hourly	1 Vial [†] 6 -8 hourly	1 Vial [†] 6 - 8 hourly	1 Vial [†] 6 - 8 hourly
APOCLAV 0,6 g Powder for Solution for Injection or Infusion			2 Vials [†] 6 - 8 hourly	2 Vials [†] 6 -8 hourly

APOCLAV vials should not be reconstituted or mixed with:

- dextrose solution
- sodium bicarbonate solution for injection
- protein hydrolysates or other proteinaceous fluids
- blood or plasma
- intravenous lipids

However, the reconstituted solution may be injected into the drip tubing of infusion fluids containing glucose, bicarbonate and dextran over a period of 3-4 minutes.
6.3 Shelf life
Unopened powder in vials: 3 years
Compatibility and stability;
The period of stability of **APOCLAV** infusion fluids after reconstitution and dilution are as follows:

STRENGTH	INFUSION FLUID	VOLUME OF FLUID INFUSION (ml)		STABILITY(hours)	
		APOCLAV 0,6 g Powder for Solution for Injection or Infusion	**APOCLAV 1,2 g** Powder for Solution for Injection or Infusion	*2-8°C	25°C
APOCLAV 0,6 g Powder for Solution for Injection or Infusion 600 mg reconstituted with 10 ml Water for Injections	Water for Injections	50	100	6	4
	Sodium Chloride Intravenous Infusion (0,9% m/v)	50	100	6	4
	**Sodium Lactate Intravenous Infusion. (M/6)	50	100		4
	**Compound Sodium Chloride Injection. (Ringers Solution)	50	100		3
APOCLAV 1,2 g Powder for Solution for Injection or Infusion 1,2 g reconstituted with 20 ml Water for injections	Compound Sodium Lactate Intravenous Infusion (Hartmann's Solution; Ringer-Lactate Solution)	50	100		3
	Potassium Chloride and Sodium Chloride Intravenous Infusion.	50	100		3

*For storage at 2-8 °C, the reconstituted solutions should be added to a pre-refrigerated bag of infusion fluid. In use, the solution should be allowed to reach room temperature and then administered without delay.
** Data referred from literature.

AMOXICILLIN - RESISTANT ORGANISMS

PRODUCT	Upper Respiratory Tract Infections (Otitis Media)	Lower Respiratory Tract Infections (Bronchitis)	Urinary Tract Infections	Skin and Soft Tissue Infections
Adults:				
APOCLAV 1,2 g Powder for Solution for Injection or Infusion	1 Vial [†] 6–8 hourly	1 Vial [†] 6 -8 hourly	1 Vial [†] 6 - 8 hourly	1 Vial [†] 6 - 8 hourly
APOCLAV 0,6 g Powder for Solution for Injection or Infusion			2 Vials [†] 6 - 8 hourly	2 Vials [†] 6 -8 hourly

†.Intravenous therapy should not be continued for longer than 10 days

Special populations
NOTE:
1. Insufficient evidence exists at present to recommend an intravenous dosage in children.
2. Patients with renal impairment:
Each APOCLAV 0,6 g Powder for Solution for Injection or Infusion vial contains 0,5 mmol of potassium and 1,4 mmol of sodium.
Each APOCLAV 1,2 g Powder for Solution for Injection or Infusion vial contains 1,0 mmol of potassium and 2,8 mmol of sodium.
As both the amoxicillin and clavulanic acid components of APOCLAV are excreted by the kidneys, accumulation of both may occur in patients with renal insufficiency. In these cases monitoring of the serum levels and a reduction in the number of administrations of the suggested dosage may be required. Experience in a limited number of patients with varying degrees of renal insufficiency suggests that the following schedule of dosage based on creatinine clearance of the patient may be used as a guideline:

Creatinine Clearance	Dosage
> 30 mL/min	no dosage adjustment
10-30 mL/min	1,2 g APOCLAV stat and 600 mg 12 hourly
< 10 mL/min	1,2 g APOCLAV stat and 600 mg daily

Method of administration
APOCLAV 0,6 g and APOCLAV 1,2 g are for intravenous use.
APOCLAV 0,6 g and APOCLAV 1,2 g may be administered either by slow intravenous injection over a period of 3 to 4 min directly into a vein or via a drip tube or by infusion over 30 to 40 min. APOCLAV 0,6 g and APOCLAV 1,2 g is not suitable for intramuscular administration.
Children aged less than 3 months should be administered APOCLAV 0,6 g and APOCLAV 1,2 g by infusion only.
Treatment with APOCLAV 0,6 g and APOCLAV 1,2 g may be initiated by the use of an intravenous preparation and completed with an appropriate oral presentation as considered appropriate for the individual patient.
4.3 Contraindications
Hypersensitivity to penicillins or to cephalosporins. Cross-sensitivity between penicillins and cephalosporins is well documented.
APOCLAV formulations is contraindicated in patients with a previous history of amoxicillin/clavulanic-associated jaundice/ hepatic dysfunction. Safety and efficacy in children have not been established with the parenteral forms of APOCLAV 0,6 g and APOCLAV 1,2 g.
4.4 Special warnings and precautions for use
Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy. Before initiating therapy with APOCLAV, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other allergens. Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients on oral penicillin. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and/or a history of sensitivity to multiple allergens. There have been reports of individuals with a history of penicillin hypersensitivity, who have experienced severe reactions when treated with cephalosporins. If an allergic reaction occurs, **APOCLAV** should be discontinued and the appropriate therapy instituted. Serious anaphylactic reactions may require immediate emergency treatment with epinephrine (adrenaline). Oxygen, intravenous steroids and airway management, including intubation may also be required.
Convulsions may occur in patients with impaired renal function or in those receiving high doses (see section 4.8).
The occurrence at the treatment initiation of a feverish generalised erythema associated with pustula may be a symptom of acute generalised exanthemous pustulosis (AGEP) (see section 4.8). This reaction requires APOCLAV discontinuation and contraindicates any subsequent administration of amoxicillin.
Pseudomembranous enterocolitis has been reported. Prolongation of prothrombin time has been reported less frequently in patients receiving **APOCLAV**. Appropriate monitoring should be undertaken when anticoagulants are prescribed concurrently.
Periodic assessment of organ function, including renal, hepatic and haematopoietic functions, is advisable during prolonged therapy. **APOCLAV** IV formulations should not be given intramuscularly or subcutaneously.
Caution is needed when administering amoxicillin to patients with syphilis, as the Jarisch-Herxheimer reaction may occur in these patients. When high doses are administered, adequate fluid intake and urinary output must be maintained. The sodium content must be taken into account in patients on a sodium-restricted diet if the administration of high doses is necessary.
Since APOCLAV contains amoxicillin, an aminopenicillin, it is not the treatment of choice in patients presenting with sore throat or pharyngitis because of the possibility that the underlying cause is infectious mononucleosis, in the presence of which there is a high incidence of erythematous rash if amoxicillin is used. **APOCLAV** should be given with caution to patients with lymphatic leukaemia since they are especially susceptible to amoxicillin induced skin rashes. Prolonged use may result in overgrowth of non-susceptible organisms. If superinfections occur (usually involving *Aerobacter, Pseudomonas* or *Candida*), the agent should be discontinued and/or appropriate therapy instituted.
Impaired hepatic function;
Changes in liver function tests have been observed in some patients receiving **APOCLAV**. It should be used with care in patients with evidence of severe hepatic dysfunction. Transient hepatitis and cholestatic jaundice has been reported.
APOCLAV should be used with caution in patients with evidence of hepatic dysfunction.
Impaired renal function:
In patients with moderate or severe renal impairment **APOCLAV** dosage should be adjusted (See Dosage and administration).
The use of **APOCLAV** may lead to the selection of resistant strains of organisms and sensitivity testing should, therefore, be carried out whenever possible, to demonstrate the appropriateness of therapy.
Intravenous administration can cause local irritation, induration and phlebitis at the injection site.
During treatment with amoxicillin, enzymatic glucose oxidase methods should be used whenever testing for the presence of glucose in urine because false positive results may occur with non-enzymatic methods.
The presence of clavulanic acid in amoxicillin-clavulanate may cause a non-specific binding of IgG and albumin by red cell membranes leading to a false positive Coombs test.
There have been reports of positive test results using the Bio-Rad Laboratories Platelia Aspergillus EIA test in patients receiving amoxicillin/clavulanic acid who were subsequently found to be free of Aspergillus infection. Cross reactions with non-Aspergillus polysaccharides and polyfuranoses with Bio-Rad Laboratories Platelia Aspergillus EIA test have been reported. Therefore, positive test results in patients receiving amoxicillin/clavulanic acid should be interpreted cautiously and confirmed by other diagnostic methods.
4.5 Interaction with other medicinal products and other forms of interaction
Probenecid decreases the renal tubular secretion of amoxicillin, but does not affect clavulanic acid excretion. Concurrent use with **APOCLAV** may result in increased and prolonged blood levels of amoxicillin but not of clavulanic acid.
APOCLAV may reduce the efficacy of oral contraceptives and patients should be warned accordingly.
The concomitant administration of allopurinol and ampicillin substantially increases the incidence of rashes in patients receiving both medicines as compared to patients receiving ampicillin alone. It is not known whether this potentiation of ampicillin rashes is due to allopurinol or the hyperuricaemia present in these patients. Tetracyclines and other bacteriostatic medicines may interfere with the bactericidal effects of amoxicillin.
In patients receiving mycophenolate mofetil, reduction in pre-dose concentration of the active metabolite mycophenolic acid (MPA) 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. Therefore, a change in the dose of mycophenolate mofetil should not normally be necessary in the absence of clinical evidence of graft dysfunction. However, close clinical monitoring should be performed during the combination and shortly after antibiotic treatment.
Interaction with Laboratory tests:
It is recommended that when testing for the presence of glucose in urine during **APOCLAV** treatment, enzymatic glucose oxidase methods should be used. Due to the high urinary concentrations of amoxicillin, false positive readings are common with chemical methods.

ADMINISTRATION:
Note:
APOCLAV IV formulations are not suitable for intramuscular or subcutaneous administration.
The reconstituted vials can be administered intravenously by injection (2 minutes) or slow intravenous infusion (30 minutes). Infusion should be completed within the period of stability of APOCLAV infusions after reconstitution and dilution as reflected in the table under the section "Compatibility and Stability" presented above.
The contents of the vials must be used within 20 minutes and thereafter any unused material discarded.
6.4 Special precautions for storage
Keep out of reach of children.
APOCLAV preparations should be stored in a cool, dry place below 25 °C.
APOCLAV vials should be kept in the outer carton until required for use.
APOCLAV (Injection) vials:
IV Injection: Once reconstituted, vials must be used within 20 minutes.
IV Infusion: Infusions after reconstitution must be used within the time period and storage temperature stipulated under "Compatibility and stability" (Section 6.3).
6.5 Nature and contents of container
APOCLAV 0,6 g Powder for Solution for Injection or Infusion:
10 ml Type II clear glass vial (moulded glass vial) with a grey rubber stopper (Halogenated butyl rubber stopper) containing Powder for solution for injection/infusion in carton of single vial or carton containing 10 vials.
APOCLAV 1,2 g Powder for Solution for Injection or Infusion:
20 ml Type II clear glass vial (moulded glass vial) with a grey rubber stopper (Halogenated butyl rubber stopper) containing Powder for solution for injection/infusion in carton of single vial or carton containing 10 vials.
6.6 Special precautions for disposal and other handling
Directions for use:
APOCLAV 0,6 g Powder for Solution for Injection or Infusion can be reconstituted by dissolving in 10 ml Water for Injections.
APOCLAV 1,2 g Powder for Solution for Injection or Infusion can be reconstituted by dissolving in 20 ml Water for Injections.
When a diluent is added a transient pink colouration or slight opalescence will be observed where after, a pale yellow fluid.
For intravenous infusion, the reconstituted vial should be further diluted with the desired volume of a suitable infusion fluid (see compatibility and stability section 6.3).
For single use only - discard any unused portion of the reconstituted/diluted solution.

7. Marketing authorisation holder
APOTHECON LABS cc
No 72 4TH STREET
BOOYSENS RESERVE
2091

8. Marketing authorisation number(s)
APOCLAV 0,6 g (vials) – 43/20.1.2/0585
APOCLAV 1,2g (vials) – 43/20.1.2/0586

9. Date of first authorisation/renewal of the authorisation
7TH September 2021

10. Date of revision of the text
27 October 2022

4.6 Fertility, pregnancy and lactation:
Pregnancy:
The safety of **APOCLAV** in pregnancy has not been established.
Breast feeding:
Amoxicillin is distributed into breast milk. Although significant problems in humans have not been documented, the use of amoxicillin by nursing mothers may lead to sensitisation, diarrhoea, candidiasis and skin rash in the infant. Amoxicillin is excreted in the milk; there is no data on the excretion of clavulanic acid in human milk. Therefore, caution should be exercised when **APOCLAV** is administered to a breast feeding woman.
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. However, undesirable effects may occur (e.g. allergic reactions, dizziness, convulsions), which may influence the ability to drive and use machines (see section 4.8).
4.8 Undesirable effects
The most frequently reported adverse effects are diarrhoea, nausea, vomiting, indigestion, abdominal pain, skin rashes, urticaria and erythema multiforme, vaginitis, abnormal taste, headache, dizziness, tiredness and hot flushes. The incidence and severity of adverse effects, particularly nausea and diarrhoea, increased with the higher recommended dose and can be minimised by administering APOCLAV at the start of a meal. In addition, as these symptoms are especially related to the potassium clavulanate component, where these gastrointestinal symptoms occur and a higher concentration of amoxicillin is required, consideration should be given to administering the additional amoxicillin separately.
The following adverse reactions have been reported and may occur with **APOCLAV**:
Frequent
Less frequent
Not known (cannot be estimated from the available data)

Infections and infestations:	
Mucocutaneous candidosis	Frequent
Overgrowth of non-susceptible organisms	Not known
Blood and lymphatic system disorders:	
Reversible leucopenia (including neutropenia)	Less frequent
Thrombocytopenia	Less frequent
Reversible agranulocytosis	Not known
Haemolytic anaemia	Not known
Prolongation of bleeding time and prothrombin time (1)	Not known
Immune system disorders (10)	
Angioedema	Not known
Anaphylaxis	Not known
Serum sickness-like syndrome	Not known
Hypersensitivity vasculitis	Not known
Nervous system disorders:	
Dizziness	Less frequent
Haemolytic anaemia	Less frequent
Headache	Less frequent
Convulsions (2)	Not known
Aseptic meningitis	Not known
Vascular disorders:	
Thrombophlebitis (3)	Less frequent
Gastrointestinal disorders	
Diarrhoea	Frequent
Nausea	Less frequent
Vomiting	Less frequent
Indigestion	Less frequent
Antibiotic-associated colitis (4)	Not known
Hepatobiliary disorders	
Increases in AST and/or ALT (5)	Less frequent
Hepatitis (6)	Not known
Cholestatic jaundice (6)	Not known
Skin and subcutaneous tissue disorders(7)	
Skin rash	Less frequent
Pruritus	Less frequent
Urticaria	Less frequent
Erythema multiforme	Less frequent
Stevens-Johnson syndrome	Not known
Toxic epidermal necrolysis	Not known
Bullous exfoliative-dermatitis	Not known
Acute generalised exanthemous pustulosis (AGEP) (9)	Not known
Drug reaction with eosinophilia and systemic symptoms (DRESS)	Not known
Renal and urinary disorders	
Interstitial nephritis	Not known
Crystalluria (8)	Not known

1 See section 4.4
2 See section 4.4
3 At the site of injection
4 Including pseudomembranous colitis and haemorrhagic colitis (see section 4.4)
5 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.
6 These events have been noted with other penicillins and cephalosporins.
7 If any hypersensitivity dermatitis reaction occurs, treatment should be discontinued (see section 4.4).
8 See section 4.9
9 See section 4.4
10 See sections 4.3 and 4.4

Gastrointestinal reactions:
If gastro-intestinal reactions are evident, they may be reduced by administering **APOCLAV** at the start of a meal.
Hepatic effects:
Less frequent: Hepatitis and cholestatic jaundice have been reported. The events may be severe, and occur predominantly in adult or elderly patients. 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. The hepatic events are usually reversible. However, in extremely rare circumstances, death has been reported. These have almost always been cases associated with serious underlying disease or concomitant medication. A moderate increase in aspartate transaminase and/or alanine transaminase has been noted in patients treated with APOCLAV, but the significance of these findings is unknown.

Haematological effects:
Less frequent: Haemolytic anaemia, reversible thrombocytopenia, thrombocytopenic purpura, eosinophilia, reversible leukopenia and agranulocytosis. These reactions are usually reversible on discontinuation of therapy and are believed to be a hypersensitivity phenomena. A slight thrombocytosis was noted in less than 1 % of the patients treated with **APOCLAV**. Prolongation of bleeding time and prothrombin time have also been reported less frequently. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly.

CNS Effects:
Less frequent: CNS effects. These include reversible hyperactivity, dizziness, headache and convulsions. Convulsions may occur with impaired renal function or in those receiving high doses.
4.9 Overdose
(See Section 4.8 and Section 4.4)
Overdosage with amoxicillin is usually asymptomatic. However, gastrointestinal effects such as nausea, vomiting and diarrhoea may be evident and symptoms of water and electrolyte imbalance should be treated symptomatically. Adequate fluid intake and urinary output must be maintained to minimise the possibility of crystalluria. Amoxicillin may be removed from the circulation by haemodialysis. The molecular weight, degree of protein binding and pharmacokinetic profile of clavulanic acid together with information from a single patient with renal insufficiency all suggest that this compound may also be removed by haemodialysis.
5. Pharmacological properties
A 20.1.2 Penicillins
5.1 Pharmacodynamic properties
APOCLAV 0,6 g and 1,2 g is a combination of amoxicillin and clavulanic acid. Amoxicillin is a semisynthetic beta-lactamase-susceptible penicillin, which has in-vitro bactericidal activity against broad spectrum of non beta-lactamase-producing Gram positive, and Gram negative organisms. The spectrum of activity does not include those organisms that produce beta-lactamase, namely resistant staphylococci, and all strains of *Pseudomonas, Klebsiella* and *Enterobacter*. Clavulanic acid has been shown in vitro to be an irreversible inhibitor of beta- lactamases produced by: *Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Proteus vulgaris, Haemophilus influenzae, Neisseria gonorrhoea and Bacteroides fragilis*. Clavulanic acid does not inactivate the chromosomally mediated (Sykes Type 1 Cephalosporinase) beta-lactamases produced by *Acinetobacter species, Citrobacter species, Enterobacter,* Indole positive *Proteus, Providencia species* and *Serratia marcescens*. *In vitro* the formulation showed synergism against amoxicillin-resistant organisms, with no evidence of antagonism and the activity was not reduced in the presence of serum. (*In vitro* activity does not necessarily imply *in vivo* efficacy.) The clavulanic acid component has very little bactericidal action.
Species for which acquired resistance may be a problem:
Aerobic Gram-positive micro-organisms:
Enterococcus faecium
Aerobic Gram-negative micro-organisms:
Escherichia coli, Klebsiella oxytoca , Klebsiella pneumoniae, Proteus mirabilis, Proteus vulgaris
Inherently resistant organisms:
Aerobic Gram-negative micro-organisms:
Acinetobacter sp., Citrobacter freundii, Enterobacter sp., Legionella pneumophila, Morganella morganii, Providencia spp., Pseudomonas sp., Serratia sp., Stenotrophomonas maltophilia
Other micro-organisms:
Chlamydia trachomatis, Chlamydophila pneumoniae, Chlamydophila psittaci, Coxiella burnetti, Mycoplasma pneumoniae
5.2 Pharmacokinetic properties
Absorption
Amoxicillin is stable in the presence of acidic gastric secretions. Peak blood levels are achieved 1 – 2 hours after administration. There is a linear dose response in peak serum levels. The pharmacokinetics of amoxicillin and clavulanic acid are closely allied and neither are adversely affected by the presence of food in the stomach.
Distribution
Approximately 18% of the total plasma amoxicillin content is protein bound. Amoxicillin diffuses readily into most body tissues with the exception of the brain and spinal fluid. Inflammation generally increases the permeability of the meninges to penicillins and this may apply to amoxicillin.
Excretion
The elimination half-life of amoxicillin is approximately 1 hour. Co - administration of probenecid has little effect on the excretion of the clavulanic acid component of the formulation. Small amounts of amoxicillin are also excreted in the faeces and bile.
6. Pharmaceutical particulars
6.1 List of excipients
None.
6.2 Incompatibilities
This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6. **APOCLAV** IV formulations, should not be mixed with aminoglycosides in the same syringe or giving set, as substantial inactivation of the aminoglycosides can result.

SCHEDULING STATUS: [S4]
APOCLAV (Powder for solution for injection/infusion)
Read all of this leaflet carefully before you start taking APOCLAV

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- APOCLAV has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What APOCLAV is and what it is used for
2. What you need to know before you have APOCLAV
3. How APOCLAV is given
4. Possible side effects
5. How to store APOCLAV
6. Contents of the pack and other information

1.What APOCLAV is and what it is used for

APOCLAV is an antibiotic containing amoxicillin and clavulanic acid. Amoxicillin belongs to a class of antibiotics called penicillins and clavulanic acid is a compound that prevents certain bacteria from inactivating amoxicillin. APOCLAV is indicated for the treatment of certain infections:

- Upper respiratory tract, such as infection of the sinuses, recurrent ear infections, infection of the tonsils.
- Lower respiratory tract, such as bronchitis and lung infections
- Genito-urinary tract infections, such as bladder and kidney infections
- Skin and soft tissue infections.

2.WHAT YOU NEED TO KNOW BEFORE RECEIVING APOCLAV
Who should not take this medication
Do not take APOCLAV:

- If you are allergic to penicillins (i.e. a class of medicines that APOCLAV belongs to) or to cephalosporins. Cross-sensitivity between penicillins and cephalosporins is well documented.
- APOCLAV formulations must not be received if there has been a previous history of amoxicillin/clavulanic-associated jaundice (i.e. yellow colour of skin and eyes) /liver abnormalities.
- Safety and effectiveness in children have not been established with the injectable forms of APOCLAV 0,6 g and APOCLAV 1,2 g

Warnings and Precautions
Tell your doctor or health care provider before being given the injection.
Take special care with APOCLAV if you:

- have glandular fever
- are being treated for liver or kidney problems
- are not passing water regularly.

Conditions you need to look out for :
APOCLAV can make some existing conditions worse, or cause serious side effects. These include:

- allergic reactions,
- convulsions (fits) and
- inflammation of the large intestine.

Look out for certain symptoms while you are taking APOCLAV, to reduce the risk of any problems. See 'Conditions you need to look out for' in **section 4**.
Blood and urine tests:
Since APOCLAV can affect the results of blood test (such as red blood cell status tests or liver function tests) or urine tests you should let the doctor or healthcare professional know that you are taking APOCLAV.
Children and adolescents
Safety and effectiveness in children have not been established with the injectable forms of APOCLAV 0,6 g and APOCLAV 1,2 g.

Other medicines and APOCLAV
Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)
The following medications may affect how APOCLAV works or increase the risk of side effects:

- probenecid
- concomitant administration of allopurinol and ampicillin
- tetracyclines

The following medications may be affected by APOCLAV:

- Oral contraceptives
- mycophenolate mofetil (a medicine used to prevent the rejection of transplanted organs).

Pregnancy, breastfeeding and fertility
If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking APOCLAV.

- **Pregnancy:** APOCLAV should not be used during pregnancy.
- **Breast-feeding:** APOCLAV passes into breast milk. The safety of this medication for use while breast feeding has not been established.

Driving and using machines
It is not always possible to predict to what extent APOCLAV side effects and symptoms may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which APOCLAV affects them.
APOCLAV contains sodium and potassium

- APOCLAV 0,6 g contains approximately 1.4 mmol of sodium (the main component of cooking/table salt) per vial, which is equivalent to 1.6% of the recommended maximum daily dietary intake of sodium for an adult. This should be considered if you are on a controlled sodium diet. APOCLAV 0,6 g contains approximately 0.5 mmol of potassium per vial, which at less than 39 mg (1 mmol) is considered essentially 'potassium-free'.
- APOCLAV 1,2 g contains approximately 2.8 mmol of sodium (the main component of cooking/table salt) per vial or bottle, which is equivalent to 3.2% of the recommended maximum daily dietary intake of sodium for an adult. This should be considered if you are on a controlled sodium diet.
- APOCLAV 1,2 g contains approximately 1.0 mmol of potassium per vial or bottle. This should be considered by patients with kidney problems or patients on a controlled potassium diet.

3.How to use APOCLAV 0,6 g and APOCLAV 1,2 g

- Do not share medicines prescribed for you with any other person
- You will not be expected to give yourself APOCLAV. It will be given to you by a person who is qualified to do so.

Adults: Depending on the severity of the infection and the type of infection your doctor will choose the appropriate dose of APOCLAV 1,2 g or APOCLAV 0,6 g (Please Section 6 for any reconstitution instructions). Once the condition settles he may continue treatment with oral amoxicillin / clavulanic acid tablets at the recommended dose.
Since a health care provider will administer APOCLAV, it is unlikely that the dose will be missed.
If you receive more APOCLAV than you should:
If you think you have been given too much APOCLAV, tell your doctor, pharmacist or nurse immediately. Signs may be an upset stomach (feeling sick, being sick or diarrhoea) or convulsions.
In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.
APOCLAV will only be administered in hospital and your attending doctor will treat the over dosage according to appropriate guidelines.
4.Possible side effects
APOCLAV can have side effects
"Not all side-effects reported for APOCLAV are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking APOCLAV, please consult your health care provider for advice."
If any of the following happen, stop taking APOCLAV and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips, mouth, or throat which may cause difficulty in swallowing or breathing,
- skin rashes or itching
- less urine than is normal for you
- yellowing of the skin or eyes

These are all serious side effects. If you have them, you may have had a serious allergic reaction to APOCLAV. You may need immediate medical attention or hospitalization.
Check with your doctor if any of the side - effects listed below become bothersome.
Frequent side effects

- diarrhoea
- Yeast infections (i.e. a cottage cheese – like appearance)
- Abdominal pain

Less Frequent side effects

- skin rash, itching
- Nausea, vomiting, indigestion
- raised itchy rash (hives)
- dizziness, headache.

Less frequent side effects that may show up in your blood tests:

- increase in some substances (enzymes) produced by the liver.
- skin rash, which may blister, and looks like small targets (central dark spots surrounded by a paler area, with a dark ring around the edge - erythema multiforme)

If you notice any of these symptoms contact a doctor urgently

- swelling and redness along a vein which is extremely tender when touched

Frequency not known
Frequency cannot be estimated from the available data.

- Allergic reactions
- Inflammation of the large intestine
- Inflammation of the protective membrane surrounding the brain (aseptic meningitis)
- Serious skin reactions:
  - a widespread rash with blisters and peeling skin, particularly around the mouth, nose, eyes and genitals (Stevens-Johnson syndrome), and a more severe form, causing extensive peeling of the skin (more than 30% of the body surface - toxic epidermal necrolysis)
  - widespread red skin rash with small pus-containing blisters (bullous exfoliative dermatitis) - a red, scaly rash with bumps under the skin and blisters (exanthemous pustulosis).
  - flu-like symptoms with a rash, fever, swollen glands, and abnormal blood test results (including increased white blood cells (eosinophilia) and liver enzymes) (Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)).

Contact a doctor immediately if you get any of these symptoms.

- inflammation of the liver (hepatitis) jaundice, caused by increases in the blood of bilirubin (a substance produced in the liver) which may make your skin and whites of the eyes appear yellow
- inflammation of tubes in the kidney
- blood takes longer to clot
- convulsions (in people taking high doses of APOCLAV or who have kidney problems).

Side effects that may show up in your blood or urine tests:

- severe reduction in the number of white blood cells
- low number of red blood cells (haemolytic anaemia)
- crystals in urine.

Some people may experience side effects other than those listed.
Check with your doctor if you notice any symptom that worries you while you are taking this medication.
If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.
Reporting of side effects
If you get side effects, talk to your doctor. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of **APOCLAV 0,6 g** and **APOCLAV 1,2 g**.

5.How to store APOCLAV
STORE ALL MEDICINES OUT OF REACH OF CHILDREN.
APOCLAV preparations should be stored in a cool, dry place below 25°C. APOCLAV vials should be kept in the outer carton until required for use.
APOCLAV (Injection) vials:

- IV Injection: Once reconstituted, vials must be used within 20 minutes.
- IV Infusion: Infusions after reconstitution must be used within the time period and storage temperature stipulated under "Compatibility and stability".

For single use only - discard any unused portion of the reconstituted/diluted solution.
Return all unused medicine to your pharmacist. Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).
6. Contents of pack and other information
What APOCLAV contains
APOCLAV 1,2 g Powder for solution for injection/infusion:
Each vial contains 1 060 mg of amoxicillin sodium equivalent to 1 000 mg amoxicillin and potassium clavulanate equivalent to 200 mg clavulanic acid.
APOCLAV 0,6 g Powder for solution for injection/infusion:
Each vial contains 530 mg of amoxicillin sodium equivalent to 500 mg amoxicillin and potassium clavulanate equivalent to 100 mg clavulanic acid.
There are no other ingredients. However, see section 2 for further important information about sodium and potassium in APOCLAV.
The doctor, nurse or pharmacist will make up the injection before use using an appropriate fluid (such as Water for Injections or an injection/infusion fluid).
What APOCLAV looks like and contents of the pack
APOCLAV 0,6 g Powder for Solution for Injection or Infusion:
10 ml Type II clear glass vial (moulded glass vial) with a grey rubber stopper containing powder for solution for injection/ infusion in carton of single vial or carton containing 10 vials. The contents is a white to cream powder in vials, when reconstituted forms a clear pale yellow solution which is practically free from particulate matter.
APOCLAV 1,2 g Powder for Solution for Injection or Infusion:
20 ml Type II clear glass vial (moulded glass vial) with a grey rubber stopper containing powder for solution for injection/ infusion in carton of single vial or carton containing 10 vials. The contents is a white to cream powder in vials, when reconstituted forms a clear pale yellow solution which is practically free from particulate matter.

Holder of Certificate of Registration:
APOTHECON LABS cc, No 72 4th Street, Booysens Reserve, 2091
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Access to the corresponding Professional Information
To request a copy of this corresponding PI leaflet, large print or electronically please call, Apothecon Labs cc on tel no 0110220041 or email info@nutrissentials.co.za

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