SCHEDULING STATUS:
S4

PROPRIETARY NAMES AND DOSAGE FORM:
BIO-AMOKSIKLAV 625 (film coated tablets)
BIO-AMOKSIKLAV 1000 (film coated tablets)

COMPOSITION:
Bio-Amoksiklav 625: Each tablet contains amoxicillin trihydrate equivalent to 500 mg amoxicillin and potassium clavulanate equivalent to 125 mg clavulanic acid.
Bio-Amoksiklav 1000: Each tablet contains amoxicillin trihydrate equivalent to 875 mg amoxicillin and potassium clavulanate equivalent to 125 mg clavulanic acid.
The excipients are:
Core tablet: colloidal anhydrous silica, crospovidone, croscarmellose sodium, magnesium stearate, microcrystalline cellulose, talc.
Coating: ethylcellulose, hydroxypropyl cellulose, polysorbate 80, talc, triethyl citrate, titanium dioxide.
Sugar free.

PHARMACOLOGICAL CLASSIFICATION:
A.20.1.2 Penicillins

PHARMACOLOGICAL ACTION:
Pharmacodynamic properties
Bio-Amoksiklav 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-lactamases, 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* spesies, *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.
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 is 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.

INDICATIONS:
Bio-Amoksiklav formulations are indicated for the treatment of infections caused by amoxicillin resistant organisms producing beta-lactamases sensitive to clavulanic acid:
Upper respiratory tract infections, such as sinusitis, recurrent otitis media, tonsillitis. Lower respiratory tract infections, such as bronchitis and bronchopneumonia. Genito-urinary tract infections, such as cystitis, urethritis, pyelonephritis. Skin and soft tissue infections.
Bio-Amoksiklav 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.
In the treatment of infections caused by *Pseudomonas aeruginosa*, an aminoglycoside should be administered concomitantly.

CONTRAINDICATIONS:
Hypersensitivity to any of the ingredients, including the excipients, penicillin or to cephalosporins. Cross-sensitivity between penicillins and cephalosporins is well documented. Bio-Amoksiklav is contraindicated in patients with a previous history of amoxicillin/ clavulanic-associated jaundice/hepatic dysfunction.

WARNINGS AND SPECIAL PRECAUTIONS:
Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy. Before initiating therapy with Bio-Amoksiklav, 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 penicillins. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and/or a history 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, Bio-Amoksiklav should be discontinued and the appropriate therapy instituted. Serious anaphylactic reactions may require immediate treatment with adrenaline. Oxygen, intravenous steroids and airway management, including intubation may also be required.
Bio-Amoksiklav 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. Since Bio-Amoksiklav 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 rash if amoxicillin is used. Bio-Amoksiklav 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. Pseudomembranous enterocolitis has been reported. Prolongation of prothrombin time has been reported rarely in patients receiving Bio-Amoksiklav. 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.
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.
The use of lignocaine or benzyl alcohol together with amoxicillin must be used only when administering an intramuscular injection, and not given intravenously. The possibility of superinfections with mycotic or bacterial pathogens should be kept in mind during therapy. 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 Bio-Amoksiklav. Transient hepatitis and cholestatic jaundice has been reported. It should be used with care in patients with evidence of hepatic dysfunction.
Impaired renal function:
In patients with moderate or severe renal impairment Bio-Amoksiklav dosage should be adjusted (see DOSAGE AND DIRECTIONS FOR USE).
Bio-Amoksiklav 1000 should not be used in patients with a glomerular filtration rate of less than 30 ml/minute.
Use in lactation:
Amoxicillin is excreted in the milk; there is no data on the excretion of clavulanic acid in human milk.
Therefore, caution should be exercise when Bio-Amoksiklav is administered to a nursing woman.
The use of Bio-Amoksiklav 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.

INTERACTIONS:
Probenecid decreases the renal tubular secretion of amoxicillin, but does not affect clavulanic acid excretion. Concurrent use with Bio-Amoksiklav tablets may result in increased and prolonged blood levels of amoxicillin, but not of clavulanic acid. Bio-Amoksiklav 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 skin rashes in patients receiving both agents 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.
Interaction with Laboratory tests:
It is recommended that when testing for the presence of glucose in urine during Bio-Amoksiklav treatment, enzymatic glucose oxidase methods should be used. Due to the high urinary concentrations of amoxicillin, false positive readings are common with chemical methods.

PREGNANCY AND LACTATION:
Use in pregnancy:
The safety of Bio-Amoksiklav in pregnancy has not been established.
Use in lactation:
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.

DOSAGE AND DIRECTIONS FOR USE:
Tablets should be taken immediately before a meal.
Dosages:
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:
The adult dose for severe infections and infection of the respiratory tract, should be one Bio-Amoksiklav 625 tablet every eight hours at the start of a meal, or one Bio-Amoksiklav 1000 tablet every 12 hours at the start of a meal.
Since Bio-Amoksiklav 625 and 1000 tablets contain the same amount of clavulanic acid (125 mg as the potassium salt) two Bio-Amoksiklav 625 tablets are not equivalent to one Bio-Amoksiklav 1000. Therefore, two Bio-Amoksiklav 625 should not be substituted for one Bio-Amoksiklav 1000 tablet for the treatment of severe infections.
Impaired renal function:
Both amoxicillin and clavulanic acid are excreted by the kidneys and the serum half-life of each increases in patients with renal failure. Therefore, the dose may need to be reduced or the interval extended. Dosage adjustments are based on the maximum recommended level of amoxicillin.
The following schedule is proposed:
Bio-Amoksiklav 625:
Mild impairment (creatinine clearance greater than 30 ml/minute): no change in dosage.
Moderate impairment (creatinine clearance 10 to 30 ml/minute): 1 tablet every 12 hours.
Severe impairment (creatinine clearance less than 10 ml/minute): half a tablet every twelve hours.
Bio-Amoksiklav 1000 should not be used in patients with glomerular filtration rate of less than 30 ml/minutes.
Haemodialysis decreases serum concentrations of both amoxicillin and clavulanic acid and an additional dose should be administered at the end of dialysis.
Dosage Guide:
Amoxicillin sensitive organisms (Adults):

	Upper respiratory tract infections	Lower respiratory tract infections	Urinary tract infections	Skin and soft tissue infections
Bio-Amoksiklav 625	1 tablet 8 hourly	1 tablet 8 hourly	1 tablet 8 hourly	1 tablet 8 hourly
Bio-Amoksiklav 1000	1 tablet 12 hourly	1 tablet 12 hourly	1 tablet 12 hourly	1 tablet 12 hourly

Amoxicillin resistant organisms (Adults)

	Upper respiratory tract infections (OTITIS MEDIA)	Lower respiratory tract infections (BRONCHITIS)	Urinary tract infections	Skin and soft tissue infections
Bio-Amoksiklav 625	1 tablet 8 hourly	1 tablet 8 hourly	1 tablet 8 hourly	1 tablet 8 hourly
Bio-Amoksiklav 1000	1 tablet 12 hourly	1 tablet 12 hourly	1 tablet 12 hourly	1 tablet 12 hourly

SIDE 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 Bio-Amoksiklav at the start of a meal. In addition, as these symptoms are especially related to the potassium clavulanate component, where these gastro-intestinal 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 Bio-Amoksiklav:
Immune system disorders
Frequent: Skin rashes, pruritis and urticaria, serum sickness-like syndrome, erythema multiforme.
Less frequent: Cases of Stevens-Johnson syndrome, hypersensitivity vasculitis, interstitial nephritis and less frequently bullous exfoliative dermatitis and toxic epidermal necrolysis have been reported.
Whenever such reactions occur, Bio-Amoksiklav should be discontinued. Serious and occasional fatal hypersensitivity (anaphylactic) reactions and angioneurotic oedema can occur with oral penicillin (see WARNINGS AND SPECIAL PRECAUTIONS).
Interstitial nephritis can occur rarely.
Gastrointestinal disorders
Frequent: Nausea, vomiting, diarrhoea, gastritis, indigestion, abdominal pain, stomatitis, glossitis, black'hairy' tongue, enterocolitis, mucocutaneous candidiasis and antibiotic-associated colitis (including pseudomembranous colitis and haemorrhagic colitis).
If gastrointestinal reactions are evident, they may be reduced by taking Bio-Amoksiklav at the start of a meal.
Hepato-billiary disorders
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 effects 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 raise in Aspartate transaminase (AST) and/or Alanine transaminase (ALT) has been noted in patients treated with Bio-Amoksiklav, but the significance of these findings is unknown.
Renal and urinary disorders
Less frequent: Crystalluria has been reported.
Blood and lymphatic system disorders
Less frequent: Haemolytic anaemia, reversible thrombocytopenia, thrombocytopenic purpura, eosinophilia, reversible leucopoenia and agranulocytosis have been reported. These reactions are usually reversible on discontinuation of therapy and are believed to be hypersensitivity phenomena. A slight thrombocytosis was noted in less than 1 % of the patients treated with Bio-Amoksiklav. Prolongation of bleeding time and prothrombin time has also been reported less frequently. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly.
Nervous system disorders
Frequent: Headache, dizziness, tiredness and hot flushes.
Less frequent: CNS effects have been seen rarely. These include reversible hyperactivity, dizziness, headache and convulsions. Convulsions may occur with impaired renal function or in those receiving high doses; abnormal taste.
General disorders and administrative site conditions
Less frequent: Superficial tooth discolouration has been reported especially with the suspension and chewable tablet formulations. It can usually be removed by brushing.

KNOWN SYMPTOMS OF OVER DOSAGE AND PARTICULARS OF ITS TREATMENT:
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.

IDENTIFICATION:
BIO-AMOKSIKLAV 625: White to almost white oval biconvex film-coated tablet.
BIO-AMOKSIKLAV 1000: White to almost white oblong film-coated tablet with bevelled edges, scored and debossed with 875/125 on one side and AMC on other side.

PRESENTATION:
BIO-AMOKSIKLAV 625: Glass bottles containing 15 tablets or aluminium blister strip containing 5 tablets. Three blister strips are packed in an outer carton.
BIO-AMOKSIKLAV 1000: Aluminium blister strip containing 5 tablets. Two blister strips are packed in an outer carton.

STORAGE INSTRUCTIONS:
Dispense tablets in their original containers or in moisture proof containers. Store at or below 25 °C. Protect from light and moisture.
KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS:
BIO-AMOKSIKLAV 625: 31/20.1.2/0682
BIO-AMOKSIKLAV 1000: A40/20.1.2/0500

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE REGISTRATION CERTIFICATE:
Biotech Laboratories (Pty) Ltd
Ground Floor, Block K West, Central Park,
400 16th Road, Randjespark, Midrand, 1685, South Africa

DATE OF PUBLICATION OF THIS PACKAGE INSERT:
Bio-Amoksiklav 625: 23 August 1999
Bio-Amoksiklav 1000: 2 March 2007
Date of latest revision of the text as approved by Council: 11 March 2010
Date of notification with regard to amended Reg. 9 and 10: 06 February 2015

Bio-Amoksiklav 625	
Zimbabwe: 97/7.1.2/3267	PP

PI400500/310682-3

SKEDULERINGSTATUS:
S4

EIENDOMSNAAM EN DOSEERVORMS:
BIO-AMOKSIKLAV 625 MG (filmbedekte tablette)
BIO-AMOKSIKLAV 1000 MG (filmbedekte tablette)

SAMESTELLING:
Bio-Amoksiklav 625 mg: Elke tablet bevat amoksisillientrihidraat gelykstaande aan 500 mg amoksisillien en kaliumklavulanaat gelykstaande aan 125 mg klavulaansuur.
Bio-Amoksiklav 1000 mg: Elke tablet bevat amoksisillientrihidraat gelykstaande aan 875 mg amoksisillien en kaliumklavulanaat gelykstaande aan 125 mg klavulaansuur.
Die hulpstowwe is:
Kern tablet: Kolloïdale anhidriese silika, krospovidone, kroskarmellose natrium, magnesiumstearaat, mikrokristalliene sellulose, poeier.
Buitenste laag: Etielsellulose, hidroksipropiel sellulose, polysorbaat 80, poeier, trietiel sitraat titaandioksied.
trietiel
Suikervry.

FARMAKOLOGIESE KLASSIFIKASIE:
A.20.1.2 Penisilliene

FARMAKOLOGIESE WERKING:
Farmakodinamiese eienskappe
BIO-AMOKSIKLAV is 'n kombinasie van amoksisillien en klavulaansuur. Amoksisillien is 'n semi-sintetiese beta-laktamase sensitiewe penisillien, wat *in vitro* bakteriedodende aktiwiteit het teen 'n breë spektrum van nie-beta-laktamase produserende Gram positief en Gram negatiewe organismes. Die spektrum van aktiwiteit sluit nie daardie organismes in wat beta-laktamase produseer nie, naamlik weerstandige stafilokokke en alle stamme van *Pseudomonas, Klebsiella* en Enterobacter. Klavulaansuur het *in vitro* getoon dat dit 'n onomkeerbare inhibeerder is van beta-laktamase geproduseer deur *Staphylococcus aureus*, *Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Proteus vulgaris, Haemophilus influenzae, Neisseria gonorrhoea* en *Bacteroides fragilis*. Klavulaansuur inaktiveer nie die chromosoombeheerde (Sykes Tipe 1 Kefalosporinase) beta-laktamase wat deur *Acinetobacter* spesies, *Citrobacter* spesies, *Enterobacter*, indool positiewe *Proteus, Providencia* spesies en *Serratia marcescens* geproduseer word nie. *In vitro* het die formulering 'n sinergistiese werking teenoor amoksisillienweerstandige organismes getoon met geen bewyse van weerstand nie, en die aktiwiteit is nie deur die teenwoordigheid van serum verminder nie. (*In vitro* aktiwiteit impliseer nie noodwendig *in vivo* doeltreffendheid nie.) Die klavulaansuur het baie min bakteriedodende werking.
Farmakokinetiese eienskappe
Absorpsie:
Amoksisillien is stabiel in die teenwoordigheid van gastriese suur sekresie. Piek bloedvlakke word 1-2 ure na toediening bereik. Daar is 'n liniêre dosisreaksie tydens piek serumvlakke. Die farmakokinetika van amoksisillien en klavulaansuur is nou verwant en nie een word deur die teenwoordigheid van voedsel in die maag nadelig beïnvloed nie.
Verspreiding:
Ongeveer 18 % van die totale plasma amoksisillien inhoud is proteïengebonde. Amoksisillien versprei geredelik in die meeste liggaamsweefsels met die uitsondering van die brein en spinale vloeistof. In die algemeen verhoog inflammasie die deurdringbaarheid van die meninges vir penisillien en dit kan ook van toepassing wees op amoksisillien.
Uitskeiding:
Die eliminerings halfleeftyd van amoksisillien is ongeveer 1 uur. Gelyktydige toeding van probenesied het baie min uitwerking op die uitskeiding van die klavulaansuurbestanddeel van die formulering. Klein hoeveelhede amoksisillien word ook deur die feses en gal uitgeskei.

INDIKASIES:
BIO-AMOKSIKLAV is geskik vir die behandeling van bakteriële infeksies veroorsaak deur amoksisillienweerstandige mikro-organismes wat beta-laktamases produseer en wat gevoelig is vir klavulaansuur:
Boonste lugweginfeksies: soos sinusitis, terugkerende otitis media, tonsillitis. Onderste lugweginfeksies: soos brongitis en brongopneumonie.
Genito-urienweg infeksies: soos sistitis, uretritis, piëlonefritis. Vel- en sagteweefselinfeksies.
Bio-Amoksiklav kan ook gebruik word vir infeksies veroorsaak deur amoksisillien-sensitiewe mikro-organismes teen die paslike amoksisillien dosis, omdat die klavulaansuur komponent in hierdie situasie nie tot die terapeutiese werking bydra nie.

KONTRA-INDIKASIES:
Hypersensitiwiteit teen penisilliene of kefalosporiene. Kruissensitiwiteit tussen penisilliene en kefalosporiene is goed gedokumenteerd.
Bio-Amoksiklav is gekontra-indikeerd in pasiënte wat 'n vorige geskiedenis van amoksisillien/klavulaansuur geassosieerde geelsug of hepatiese disfunksie het.

WAARSKUWINGS EN SPESIALE VOORSORGMAATREELS:
Ernstige en soms noodlottige hipersensitiwiteits (anafilaktiese) reaksies is aangemeld by pasiënte wat penisillienterapie ondergaan. Voordat terapie met Bio-Amoksiklav begin word moet deeglike navraag aangaande vorige hipersensitiwiteitsreaksies teenoor penisillien, kefalosporiene of ander allergene gedoen word. Alhoewel anafilakse meer dikwels voorkom na parenterale terapie, het dit al voorgekom by pasiënte op orale penisillien terapie. Hierdie reaksies is meer geneig om voor te kom by individue met 'n geskiedenis van penisillienhipersensitiwiteit en/of 'n geskiedenis van sensitiwiteit teenoor meervoudige allergene. Gevalle van individue met 'n geskiedenis van penisillien-hipersensitiwiteit, wat ernstige reaksies ervaar het na hulle met kefalosporiene behandel was, is al aangemeld. Indien 'n allergiese reaksie plaasvind behoort Bio-Amoksiklav gestaak te word en moet daar met die geskikte terapie begin word. Ernstige anafilaktiese reaksies mag onmiddelike noodbehandeling met adrenalien vereis. Suurstof, intraveneuse steroïede en lugwegbeheer, insluitende intubasie mag nodig wees. Bio-Amoksiklav behoort vermy te word as infektiewe mononukleose vermoed word, aangesien die voorkoms van 'n maselagtige uitslag geassosieer word met die toestand nadat amoksisillien gebruik was. Aangesien Bio-Amoksiklav amoksisillien bevat, n aminopenisilien, is dit nie die behandeling van keuse in pasiënte wat met seer keel or faringitis presenteer nie, omdat die onderliggende oorsaak moontlik weens infektiewe mononukleose mag wees, in welke geval daar n hoë voorkoms van veluitstlag is, indien amoksisillien gebruik word. Bio-Amoksiklav moet met omsigtigheid gebruik word in pasiënte wat aan limfatiese leukemie ly, aangesien hul veral geneig is tot veluitslag. Langdurige gebruik kan tot oorgroei van nie-gevoelige organismes lei. Pseudomembraam enterocolitis is al aangemeld. Verlenging van protrombientyd word baie selde gerapporteer by pasiënte wat Bio-Amoksiklav ontvang. Toepaslike monitering behoort onderneem te word indien antikoagulante gesamentlik voorgeskryf word. Periodieke evaluering van orgaanfunksie, insluitende nier, lewer en hematopoëtiese funksies, word aanbeveel gedurende langdurige terapie. Bio-Amoksiclav moet met omsigtigheid toegedien word in pasiënte met sifilis, omdat die Jarisch-Herxheimer reaksie mag voorkom in hierdie pasiënte. Wanneer hoë doserings toegedien word, moet genoegsame vloeistof inname en urinere uitskeiding gehandhaaf word. Die natrium inhoud moet in ag geneem word in pasiënte op 'n natrium-beheerde dieët indien administrasie van hoë dosisse nodig is.
Die gesamentlike gebruik van lignocaïne of bensiel alkohol met amoksisillien mag slegs as intramuskulêre inspuiting gedoen word, en nie intraveneus nie. Die moontlikheid van superinfeksies met mikotiese of bakteriële patogene moet in gedagte gehou word tydens die terapie. As superinfeksies voorkom (gewoonlik is Aerobacter, Pseudomonas of Candida teenwoordig), moet die middel gestaak word en/of begin word met die geskikte terapie.
Belemmerde hepatiese funksie:
Veranderinge in lewerfunksie toetse is waargeneem by sommige pasiënte wat BIO-AMOKSIKLAV ontvang het. Verbygaande hepatitis en cholestatiese geelsug is aangemeld. Bio-Amoksiklav behoort met versigtigheid gebruik te word by pasiënte met bewys van hepatiese disfunksie.
Belemmerde renale werking:
By pasiënte met matige of ernstige renale belemmering moet die BIO-AMOKSIKLAV dosis aangepas word (sien DOSIS EN GEBRUIKSAANWYSINGS).
Bio-Amoksiklav 1000 behoort nie gebruik te word by pasiënte met 'n glomulêre filtrasietempo van minder as 30 ml/minuut nie.
Gebruik tydens laktasie:
Amoksisillien word in borsmelk uitgeskei; daar bestaan geen data oor die uitskeiding van klavulaansuur in borsmelk nie.
BIO-AMOKSIKLAV moet daarom met versigtigheid aan 'n vrou wat borsvoed gegee word. Die gebruik van BIO-AMOKSIKLAV mag lei tot die seleksie van weerstandige stamme van organismes en sensitiwiteitstoetse behoort daarom gedoen te word, wanneer moontlik, om die paslikheid van die terapie te verseker.

INTERAKSIES:
Probenesied verlaag die renale tubulêre sekresie van amoksisillien, maar affekteer nie klavulaansuur uitskeiding nie. Gelyktydige toediening saam met Bio-Amoksiklav tablette mag verhoogde en verlengde bloedvlakke van amoksisillien tot gevolg hê, maar nie van klavulaansuur nie. Bio-Amoksiklav kan die doeltreffendheid van orale kontraseptiewe middels verminder en pasiënte moet dienooreenkomstig gewaarsku word. Die gelyktydige toediening van allopurinol en ampisillien verhoog die voorkoms van veluitslag aansienlik by pasiënte wat albei middels ontvang, in vergelyking met pasiënte wat ampisillien alleen ontvang. Dit is nie bekend of hierdie verergering van ampisillien uitslag plaasvind weens allopurinol of die hiperuresemie wat teenwoordig is by hierdie pasiënte nie. Tetrasikliene en ander bakteriostatiese geneesmiddels mag inmeng met die bakteriosidese effekte van amoksisillien.
Interaksies met Laboratorium toetse:
Dit word aanbeveel dat wanneer daar getoets word vir die teenwoordigheid van glukose in uriene tydens Bio-Amoksiklav behandeling, die ensiematiese glukose oksidasie metode gebruik moet word. As gevolg van die hoë konsentrasies amoksisillien in die uriene, is vals positiewe lesings algemeen met chemiese metodes.

SWANGERSKAP EN LAKTASIE:
Gebruik tydens swangerskap:
Die veiligheid van BIO-AMOKSIKLAV in swangerskap is nog nie vasgestel nie.
Gebruik tydens laktasie:
Amoksisillin word in borsmelk uitgeskei. Alhoewel beduidenswaardige probleme in mense nog nie gedokumenteer is nie, kan die gebruik van amoksisillien by moeders wat borsvoed lei tot sensitisering, diarree, kandidiase en veluitslag by die baba.

DOSIS EN GEBRUIKSAANWYSINGS:
Tablette moet onmiddelik voor 'n maaltyd geneem word.
Doserings:
Algemene inligting: Vir infeksies wat deur die amoksisillien-sensitiewe organismes veroorsaak word, is die dosis die soos vir amoksisillien goedgekeur, omdat klavulaansuur nie tot die terapeutiese werking bydra nie.
Volwassenes:
Die volwasse dosis vir meer ernstige infeksies en infeksies van die asemhalingskanaal is een BIO-AMOKSIKLAV 625 tablet elke agt ure met die aanvang van 'n maaltyd of een BIO-AMOKSIKLAV 1000 tablet elke 12 ure met die aanvang van 'n maaltyd.
Siende dat BIO-AMOKSIKLAV 625 and 1000 tablette dieselfde hoeveelheid klavulaansuur bevat (125 mg as die kaliumsout) is twee BIO-AMOKSIKLAV 625 tablette nie ekwivalent aan een BIO-AMOKSIKLAV 1000 nie. Dus twee BIO-AMOKSIKLAV 625 moet nie vervang word vir een BIO-AMOKSIKLAV 1000 tablet vir die behandeling van meer ernstige infeksies nie.
Belemmerde nierwerking:
Beide amoksisillien en klavulaansuur word uitgeskei deur die niere en die serumhalfleeftyd van elk neem toe by pasiënte met nierversaking. Dus kan dit nodig wees om die dosis te verminder of die interval te verleng. Dosis aanpassing is gebaseer op die maksimum aanbevole dosering vir amoksisillien. Die volgende skedule word voorgestel:
BIO-AMOKSIKLAV 625:
Geringe belemmering (kreatinienopruiming groter as 30 ml/minuut): geen verandering in dosis.
Gemiddelde belemmering (kreatinienopruiming 10 tot 30 ml/minuut): 1 tablet elke 12 uur.
Ernstige belemmering (kreatinienoopruiming minder as 10 ml/minuut): 'n halwe tablet elke twaalf uur.
BIO-AMOKSIKLAV 1000 moet nie gebruik word by pasiënte met 'n glomulêre filtrasietempo van minder as 30 ml/minuut nie.
Hemodialise verminder serumkonsentrasies van beide amoksisillien en klavulaansuur en 'n bykomende dosis moet aan die einde van dialise toegedien word.
Doseringsgids:
Amoksisillien sensitiewe organismes (Volwassenes):

	Boonste lugweginfeksies	Onderste lugweginfeksies	Urienweginfeksies	Vel- en sagteweefselinfeksies
Bio-Amoksiklav 625	1 tablet 8 uurliks	1 tablet 8 uurliks	1 tablet 8 uurliks	1 tablet 8 uurliks
Bio-Amoksiklav 1000	1 tablet 12 uurliks	1 tablet 12 uurliks	1 tablet 12 uurliks	1 tablet 12 uurliks

Amoksisillien weerstandige organismes (Volwassenes):

	Boonste lugweginfeksies (OTITIS MEDIA)	Onderste lugweginfeksies (BRONGITIS)	Urienweginfeksies	Vel- en sagteweefselinfeksies
Bio-Amoksiklav 625	1 tablet 8 uurliks	1 tablet 8 uurliks	1 tablet 8 uurliks	1 tablet 8 uurliks
Bio-Amoksiklav 1000	1 tablet 12 uurliks	1 tablet 12 uurliks	1 tablet 12 uurliks	1 tablet 12 uurliks

NEWE-EFFEKTE:
Die ongewensde effekte wat die meeste aangemeld word is diarree, naarheid, braking, slegte spysvertering, abdominale pyn, veluitslag, urtikaria en veelvuldige eriteem, vaginitis, abnormale smaak, hoofpyn, duiseligheid, moegheid en warm gloede.
Die voorkoms en erns van nadelige newe-effekte, veral naarheid en diarree, het toegeneem met die hoër aanbevole dosis en kan beperk word deur BIO-AMOKSIKLAV toe te dien aan die begin van 'n maaltyd. Daarbenewens, aangesien hierdie simptome veral verband hou met die kaliumklavulanaat komponent, waar hierdie gastroïntestinale simptome voorkom en 'n hoër konsentrasie amoksisillien nodig is, moet oorweging daaraan geskenk word om die bykomende amoksisillien afsonderlik toe te dien.
Die volgende newe-effekte is gerapporteer en mag voorkom met BIO-AMOKSIKLAV:
Hipersensitiwiteits reaksies
Dikwels: Veluitslag, pruritus en urtikaria, serumsiekte-gelyksoortige sindroom, veelvuldige eriteem.
Minder dikwels: Seldsame gevalle van Stevens-Johnson sindroom, hypersensitiwiteits vaskulitis, interstisiële nefritis en minder algemeen, bulleuse eksfoliatiewe dermatitis en toksiese epidermale nekrolise, is aangemeld.
Wanneer sulke reaksies plaasvind, moet BIO-AMOKSIKLAV gestaak word. Ernstige en soms noodlottige hipersensitiwiteits (anafilaktiese) reaksies en angioneurotiese edeem kan plaasvind met mondelinge penisillien (sien WAARSKUWINGS).
Interstisiële nefritis kom selde voor.
Gastroïntestinale reaksies
Dikwels: Naarheid, braking, diarree, gastritis, indigestie, abdominale pyn, stomatitis, glossitis, swart 'harige' tong, enterokolitis, mukokutaneuse kandidiase en antibiotikum-geassosieërde kolitis (insluitende pseudomembraneuse kolitis en hemoragiese kolitis).
Indien gastroïntestinale reaksies voorkom kan dit verminder word deur BIO-AMOKSIKLAV aan die begin van 'n maaltyd te neem.
Hepatiese effekte
Minder dikwels: Hepatitis en cholestatiese geelsug is aangemeld. Die voorvalle kan ernstig wees en kom hoofsaaklik by volwasse of bejaarde pasiënte voor. Tekens en simptome vind gewoonlik plaas gedurende of kort na behandeling, maar in sommige gevalle kan dit eers voorkom verskeie weke na behandeling.
Die hepatiese effekte is gewoonlik omkeerbaar. Alhoewel, in uiters seldsame gevalle is sterftes aangemeld. Die voorvalle was byna altyd geassosieër met ernstige onderliggende siekte of meegaande medikasie.
'n Matige styging in Aspartaattransaminase (AST) en/of Alanientransaminase (ALT) is waargeneem by pasiënte wat met BIO-AMOKSIKLAV behandel is, maar die betekenis van die bevindings is onbekend.
Renale effekte
Voorkoms minder dikwels: Kristallurie is aangemeld.
Hematologiese effekte
Minder dikwels: Hemolitiese anemie, omkeerbare trombositopenie, trombositopeniese purpura, eosinofilie, omkeerbare leukopenie en agranulositose is aangemeld. Hierdie reaksies kan gewoonlik omgekeer word deur staking van die terapie en is waarskynlik 'n hipersensitiwiteits verskynsel. 'n Geringe trombositose is opgemerk by minder as 1% van die pasiënte wat met BIO-AMOKSIKLAV behandel is. Verlengde bloedingstyd en protrombientyd is ook minder gereeld aangemeld.
Toepaslike monitering moet onderneem word wanneer antikoagulante gelyktydig voorgeskryf word.
Senuwee Stelsel Effekte
Dikwels: Hoofpyn, duiseligheid, moegheid en warm gloede.
Minder dikwels: SSS effekte kom selde voor. Dit sluit in, omkeerbare hiperaktiwiteit, duiseligheid, hoofpyn en konvulsies. Konvulsies kan voorkom by ontoereikende nierfunksie of waar hoë dossise toegedien word. Abnormale smaak.
Algemene versteurings en toedienings area toestande
Minder dikwels: Oppervlakkige tandverkleuring is aangemeld, veral met die suspensie en koubare tablet formulerings. Dit kan gewoonlik verwyder word deur te borsel.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN:
Oordosering met amoksisillien is gewoonlik asimptomaties. Nietemin kan gastroïntestinale newe-effekte soos naarheid, braking en diarree voorkom en simptome van water en elektroliet wanbalans moet simptomaties behandel word.
Voldoende vloeistofinname en urienlating moet gehandhaaf word om die moontlikheid van kristallurie te verminder.
Amoksisillien kan uit die bloedsomloopstelsel verwyder word deur hemodialise. Die molekulêre gewig, mate van proteïenbinding en farmakokinetiese profiel van klavulaansuur saam met die inligting van 'n enkele pasiënt met renale ontoereikendheid dui alles daarop dat hierdie verbinding ook deur hemodialise verwyder kan word.

IDENTIFIKASIE:
BIO-AMOKSIKLAV 625: Wit tot amper wit, ovaalvormige, bikonvekse filmbedekte tablet.
BIO-AMOKSIKLAV 1000: Wit tot amper wit langwerpige filmbedekte tablet met skuins kante, breeklyn en 875/125 inskrywing op een kant en AMC op die ander kant.

AANBIEDING:
BIO-AMOKSIKLAV 625: Glas bottels met 15 tablette of aluminium stulpstroke wat 5 tablette bevat. Drie stulpstroke word in 'n buitenste karton verpak.
BIO-AMOKSIKLAV 1000: Aluminium stulpverpakking met 5 tablette. Twee stulpverpakkings per kartonhouer.

BERGINGSINSTRUKSIES:
Resepteer tablette in hul oorspronklike houers of in vogdigte houers.
Bewaar teen of benede 25 °C. Beskerm teen lig en vog.
HOU BUITE BEREIK VAN KINDERS.

REGISTRASIENOMMERS:
BIO-AMOKSIKLAV 625 (tablette): 31/20.1.2/0682
BIO-AMOKSIKLAV 1000 (tablette): A40/20.1.2/0500

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE SERTIFIKAAT VAN REGISTRASIE:
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DATUM VAN PUBLIKASIE VAN HIERDIE VOUBILJET:
Bio-Amoksiklav 625: 23 Augustus 1999
Bio-Amoksiklav 1000: 2 Maart 2007
Datum van die jonsgte hersiening van die teks; soos deur die Raad goedgekeur: 11 Maart 2010
Datum van kennisgewing met betrekking tot gewysige Regulasie 9 en 10: 06 Februarie 2015

Bio-Amoksiklav 625	
Zimbabwe 97/7.1.2/3267	PP

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