SCHEDULING STATUS:

S4

1. NAME OF THE MEDICINE:

ALLMOX 250 CAPSULES

ALLMOX 500 CAPSULES

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

ALLMOX 250 contains amoxicillin trihydrate the equivalent of 250 mg amoxicillin per capsule.

ALLMOX 500 contains amoxicillin trihydrate the equivalent of 500 mg amoxicillin per capsule.

3. PHARMACEUTICAL FORM:

ALLMOX 250: Purple/blue hard, size 2, gelatine capsules containing a white granular powder.

ALLMOX 500: Purple/blue hard, size 0, gelatine capsules containing a white granular powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Infections caused by susceptible, non-penicillinase – producing organisms including:

- Respiratory tract infections (upper and lower): sinusitis, pharyngitis, epiglottitis, acute and chronic bronchitis and acute typical pneumonia.

- Otitis media;
- Urinary tract infections;
- Uncomplicated gonococcal infections;
- Meningitis (sensitivity tests must be performed);
- Gastrointestinal infections including salmonella and typhoid;
- Uncomplicated gastro-enteritis and enteric fever;
- Miscellaneous: Skin and soft tissue infections, bacteraemia and as adjunct in the treatment of sepsis caused by gram-negative bacteria.

4.2 Posology and method of administration

Posology

Adults and children over 12 years

- 250 mg to 500 mg every 8 hours depending on the severity of the infection.
- Gonorrhoea: 3 g amoxicillin (e.g. six ALLMOX 500 capsules) as a single dose usually combined with 1 g probenecid.
- In the treatment of beta-haemolytic streptococcal infections, a therapeutic dose should be administered for at least 10 days.

Special Populations

Renal impairment.

Patients with renal insufficiency should have their dosage adapted according to creatinine clearance.

Creatinine clearance dosage of amoxicillin (Allmox)

Creatinine clearance	**Dosage**
> 30 ml / min	Usual dosage

11 – 30 ml / min	2/3 of usual dose
>10 ml / min	1/3 of usual dose

Method of administration

ALLMOX is for oral use.

Swallow with water without opening capsule.

Absorption of ALLMOX is unimpaired by food.

4.3 Contraindications

- Hypersensitivity to amoxicillin, to any of the penicillins or to any of the excipients (see section 6.1)
- History of a severe immediate hypersensitivity reaction (e.g. anaphylaxis) to another beta-lactam medicine (e.g. a cephalosporin, carbapenem or monobactam).
- ALLMOX should not be given to patients with infectious mononucleosis, since they are especially susceptible to amoxicillin-induced skin rashes, patients with lymphatic leukaemia and patients with hyperuricaemia being treated with allopurinol, may be at increased risk of developing skin rashes.

4.4 Special warnings and precautions for use

Hypersensitivity reactions

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 and in atopic individuals.

Hypersensitivity reactions can also progress to Kounis syndrome, a serious allergic reaction that can result in myocardial infarction (see section 4.8). Presenting symptoms of such reactions can include chest pain occurring in association with an allergic reaction to amoxicillin (see section 4.8).

If an allergic reaction occurs, ALLMOX therapy must be discontinued, and appropriate alternative therapy instituted.

Non-susceptible microorganisms

Amoxicillin is not suitable for the treatment of some types of infection unless the pathogen is already documented and known to be susceptible or there is a very high likelihood that the pathogen would be suitable for treatment with amoxicillin (see section 5.1). This particularly applies when considering the treatment of patients with urinary tract infections and severe infections of the ear, nose and throat.

Convulsions

Convulsions may occur in patients with impaired renal function or in those receiving high doses or in patients with predisposing factors (e.g. history of seizures, treated epilepsy or meningeal disorders (see section 4.8).

Renal impairment

In patients with renal impairment, the dose should be adjusted according to the degree of impairment (see section 4.2).

Skin reactions

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 amoxicillin discontinuation and contraindicates any

subsequent administration.

Jarisch-Herxheimer reaction

The Jarisch-Herxheimer reaction has been reported following amoxicillin treatment of syphilis (see section 4.8). Caution should be used when treating syphilis with amoxicillin.

The Jarisch-Herxheimer reaction has been reported following amoxicillin treatment of Lyme disease (see section 4.8). It results directly from the bactericidal activity of amoxicillin on the causative bacteria of Lyme disease, the spirochaete Borrelia burgdorferi. Patients should be reassured that this is a common and usually self-limiting consequence of antibiotic treatment of Lyme disease.

Overgrowth of non-susceptible microorganisms

Prolonged use may result in overgrowth of non-susceptible organisms. Antibiotic-associated colitis has been reported with nearly all antibacterial medicines and may range in severity from mild to life threatening (see section 4.8). Therefore, it is important to consider this diagnosis in patients who present with diarrhoea during, or subsequent to, the administration of any antibiotics. Should antibiotic-associated colitis occur, amoxicillin should immediately be discontinued, a medical practitioner consulted, and an appropriate therapy initiated. Anti-peristaltic medicines are contraindicated in this situation.

Prolonged therapy

Periodic assessment of organ system functions; including renal, hepatic and hematopoietic function is advisable during prolonged therapy. Elevated liver enzymes and changes in blood counts have been reported (see section 4.8).

Anticoagulants

Prolongation of prothrombin time has been reported in patients receiving amoxicillin. Appropriate monitoring should be undertaken when anticoagulants are prescribed

concomitantly. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation (see section 4.5 and 4.8).

Crystalluria

In patients with reduced urine output, crystalluria has been observed, predominantly with parenteral therapy. During the administration of high doses of amoxicillin, it is advisable to maintain adequate fluid intake and urinary output in order to reduce the possibility of amoxicillin crystalluria. In patients with bladder catheters, a regular check of patency should be maintained (see section 4.8 and 4.9).

Interference with diagnostic tests

Elevated serum and urinary levels of amoxicillin are likely to affect certain laboratory tests. Due to the high urinary concentrations of amoxicillin, false positive readings are common with chemical methods.

It is recommended that when testing for the presence of glucose in urine during amoxicillin treatment, enzymatic glucose oxidase methods should be used.

The presence of amoxicillin may distort assay results for estriol in pregnant women.

4.5 Interaction with other medicines and other forms of interaction

Probenecid

Probenecid decreases the renal tubular secretion of amoxicillin. Concomitant use of probenecid may result in increased and prolonged blood levels of amoxicillin.

Allopurinol

Concurrent use of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions.

Tetracyclines

Tetracyclines and other bacteriostatic medicines may interfere with the bactericidal effects

of amoxicillin.

Oral anticoagulants

Oral anticoagulants and penicillin antibiotics have been widely used in practice without reports of interaction. However, in the literature there are cases of increased international normalised ratio (INR) 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. Moreover, adjustments in the dose of oral anticoagulants may be necessary (see sections 4.4 and 4.8).

Methotrexate

Penicillin may reduce the excretion of methotrexate causing a potential increase in toxicity.

Oral contraceptives

Amoxicillin may decrease the efficacy of oestrogen-containing oral contraceptives.

Amoxicillin may affect the absorption of other medicines, due to its effect on the gastrointestinal flora.

4.6 Fertility, pregnancy and lactation

Pregnancy

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. Limited data on the use of amoxicillin during pregnancy in humans do not indicate an increased risk of congenital malformations.

Breastfeeding

Amoxicillin is excreted into breast milk in small quantities with the possible risk of

sensitisation. Consequently, diarrhoea and fungus infection of the mucous membranes are possible in the breastfed infant, so that breastfeeding might have to be discontinued.

Fertility

There are no data on the effects of amoxicillin on fertility in humans. Reproductive studies in animals have shown no effects on fertility.

4.7 Effects on ability to drive and use machines

Amoxicillin may be associated with allergic reactions, dizziness, and convulsions. Therefore, patients must be cautious when driving or using machines and should be advised not to drive or operate machinery if they experience these symptoms (see section 4.8).

4.8 Undesirable effects

Infections and infestations

Less frequent: Mucocutaneous candidiasis

Blood and lymphatic system disorders

Less frequent: Reversible leukopenia (including severe neutropenia or agranulocytosis), reversible thrombocytopenia and haemolytic anaemia, prolongation of bleeding time and prothrombin time (see section 4.4).

Immune system disorders

Less frequent: Severe allergic reactions, including angioedema, anaphylaxis, serum sickness and hypersensitivity vasculitis (see section 4.4)

Frequency unknown: Jarisch-Herxheimer reaction (see section 4.4)

Nervous system disorders

Less frequent: Hyperkinesia, dizziness and convulsions (see section 4.4)

Gastrointestinal disorders

Frequent: Diarrhoea, nausea

Less frequent: Vomiting, antibiotic associated colitis (including pseudomembraneous colitis and haemorrhagic colitis see section 4.4), black hairy tongue.

Hepato-biliary disorders

Less frequent: Hepatitis and cholestatic jaundice, a moderate rise in AST and/or ALT

Skin and subcutaneous tissue disorders

Frequent: Skin rash

Less frequent: Urticaria, pruritus, skin reactions such as erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous and exfoliative dermatitis, acute generalised exanthematous pustulosis (AGEP) (see section 4.4), drug reaction with eosinophilia and systemic symptoms (DRESS)

Frequency unknown: Linear IgA disease

Cardiac Disorders

Frequency unknown: Kounis syndrome

Renal and urinary disorders

Less frequent: Interstitial nephritis, crystalluria (see sections 4.4 and 4.9)

Reporting side effects

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Contact Innovata Pharmaceuticals: regulatory@innovata.co.za

4.9 Overdose

Symptoms

Gastrointestinal symptoms (such as nausea, vomiting and diarrhoea) and disturbance of the fluid and electrolyte balances may be evident. Amoxicillin crystalluria, in some cases leading to renal failure, has been observed. Convulsions may occur in patients with impaired renal function or in those receiving high doses (see sections 4.4 and 4.8).

Treatment

Gastrointestinal symptoms may be treated symptomatically, with attention to the water/electrolyte balance.

ALLMOX can be removed from the circulation by haemodialysis (see section 4.2).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: penicillins with extended spectrum.

ATC code: J01CA04

Mechanism of action

Amoxicillin is a penicillinase-susceptible semisynthetic penicillin (beta-lactam antibiotic). It is bactericidal in vitro against a broad spectrum of gram-positive and

gram-negative pathogens that inhibit one or more enzymes (often referred to as penicillin-binding proteins, PBPs) in the biosynthetic pathway of bacterial peptidoglycan, which is an integral structural component of the bacterial cell wall.

Inhibition of peptidoglycan synthesis leads to weakening of the cell wall, which is usually followed by cell lysis and death.

Amoxicillin is susceptible to degradation by beta-lactamases produced by resistant bacteria and therefore the spectrum of activity of amoxicillin alone does not include organisms which produce these enzymes.

Pharmacokinetic/pharmacodynamic relationship

The time above the minimum inhibitory concentration (T > MIC) is considered to be the major determinant of efficacy for amoxicillin.

Mechanisms of resistance

The main mechanisms of resistance to amoxicillin are:

• Inactivation by bacterial beta-lactamases.

• Alteration of PBPs, which reduce the affinity of the antibacterial medicine for the target.

Impermeability of bacteria or efflux pump mechanisms may cause or contribute to bacterial resistance, particularly in Gram-negative bacteria.

Inherently resistant organisms†
Gram-positive aerobes: *Enterococcus faecium†*
Gram-negative aerobes: *Acinetobacter spp.*

Enterobacter spp. *Klebsiella spp.* *Pseudomonas spp.* *Bacteroides spp.* (many strains of Bacteroides fragilis are resistant).
Others: *Chlamydia spp.* *Mycoplasma spp.* *Legionella spp.*
† Natural intermediate susceptibility in the absence of acquired mechanism of resistance

5.2 Pharmacokinetic properties

Absorption

Amoxicillin fully dissociates in aqueous solution at physiological pH. It is rapidly and well absorbed by the oral route of administration. Following oral administration, amoxicillin is approximately 70 % bioavailable. The time to peak plasma concentration (Tmax) is approximately one hour.

The absorption is not influenced by simultaneous food intake.

Distribution

About 18 % of total plasma amoxicillin is bound to protein and the apparent volume of distribution is around 0,3 to 0,4 l/kg.

Following intravenous administration, amoxicillin has been found in gall bladder, abdominal tissue, skin, fat, muscle tissues, synovial and peritoneal fluids, bile and pus. Amoxicillin does not adequately distribute into the cerebrospinal fluid.

Amoxicillin can be detected in breast milk (see section 4.6).

Amoxicillin has been shown to cross the placental barrier (see section 4.6

Biotransformation

Amoxicillin is partly excreted in the urine as the inactive penicilloic acid in quantities equivalent to up to 10 to 25 % of the initial dose.

Elimination

The major route of elimination for amoxicillin is via the kidney.

Amoxicillin has a mean elimination half-life of approximately one hour and a mean total clearance of approximately 25 l/hour in healthy subjects. Approximately 60 to 70 % of the amoxicillin is excreted unchanged in urine during the first 6 hours after administration of a single 250 mg or 500 mg dose of amoxicillin. Various studies have found the urinary excretion to be 50 - 85 % for amoxicillin over a 24-hour period.

Concomitant use of probenecid delays amoxicillin excretion (see section 4.5).

Haemodialysis can be used for elimination of amoxicillin (see section 4.2).

Special populations

Age

The elimination half-life of amoxicillin is similar for children aged around 3 months to 2 years and older children and adults. For very young children (including preterm newborns) in the first week of life the interval of administration should not exceed twice daily administration due to immaturity of the renal pathway of elimination. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Renal impairment

The total serum clearance of amoxicillin decreases proportionately with decreasing renal function (see sections 4.2 and 4.4).

Hepatic impairment

Hepatic impaired patients should be dosed with caution and hepatic function monitored at regular intervals (see section 4.2).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule content:

Magnesium stearate

Capsule shell:

Purple Indigo Carmine,

Erythrosine ,

Blue Indigo Carmine

Gelatine

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25°C in a dry place.

KEEP OUT OF REACH OF CHILDREN

6.5 Nature and contents of container

ALLMOX is packed in:

15's: HDPE containers and in LDPE patient ready packs

100's: HDPE containers with screw caps

500's HDPE containers with screw caps

1000's HDPE containers with screw caps

6.6 Special precautions for disposal

No special requirements for destruction

7. HOLDER OF CERTIFICATE OF REGISTRATION

Innovata Pharmaceuticals

Crownwood Office Park

100 Northern Parkway

Ormonde

Johannesburg

2091

South Africa

8.REGISTRATION NUMBERS

Allmox 250: Y/20.1.2/161

Allmox 500: Y/20.1.2/162

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Date of registration: 22 October 1991

10.Date of revision of the text

31/03/2025

SKEDULERINGSTATUS:

S4

1. NAAM VAN DIE MEDISYNE:

ALLMOX 250 KAPSULES

ALLMOX 500 KAPSULES

2. KWALITATIEWE EN KWANTITATIEWE SAMESTELLING:

ALLMOX 250 bevat amoksisillientrihidraat die ekwivalent van 250 mg amoksisillien per kapsule.

ALLMOX 500 bevat amoksisillientrihidraat die ekwivalent van 500 mg amoksisillien per kapsule.

3. FARMASEUTIESE VORM:

ALLMOX 250: Pers/blou harde, grootte 2, gelatien kapsules wat ‘n wit granulêre poeier bevat.

ALLMOX 500: Pers/blou harde, grootte 0, gelatien kapsules wat ‘n wit granulêre poeier bevat.

4. KLINIESE BESONDERHEDE

4.1 Terapeutiese indikasies

Infeksies veroorsaak deur gevoelige, nie-penisillinase-produserende organismes insluitend:

- Lugweg-infeksies (boonste en onderste): sinusitis, faringitis, epiglottitis, akute en chroniese brongitis en akute tipiese pneumonie.
- Otitis media;
- Urienweg-infeksies;
- Ongekompliseerde gonokokkale infeksies;
- Meningitis (sensitiwiteitstoetse moet gedoen word);
- Gastroïntestinale infeksies insluitend salmonella en tifoïed;
- Ongekompliseerde gastroënteritis en enteriese koors;
- Verskillend: Vel- en sagte weefselinfeksies, bakteremie en as ‘n adjunk by die behandeling van sepsis veroorsaak deur gram-negatiewe bakterie.

4.2 Posologie en metode van toediening

Posologie

Volwassenes en kinders ouer as 12 jaar

- 250 mg tot 500 mg elke 8 uur afhangende van die erns van die infeksie.
- Gonorree: 3 g amoksisillien (bv. ses ALLMOX 500 kapsules) as ‘n enkel dosis gewoonlik gekombineer met 1 g probenesied.
- By die behandeling van beta-hemolitiese streptokokkale infeksies, ‘n terapeutiese

dosering moet toegedien word vir ten minste 10 dae.

Spesiale Bevolkings

Renale inkorting.

Pasiënte met renale ontoereikendheid moet hulle dosering aanpas volgens die kreatinien-opruiming.

Kreatinien-opruiming dosering van amoksisillien (Allmox)

Kreatinien-opruiming	**Dosering**
> 30 ml / min	Gewone dosering
11 – 30 ml / min	2/3 van gewone dosering
>10 ml / min	1/3 van gewone dosering

Metode van toediening

ALLMOX is vir orale gebruik.

Sluk in met water sonder om die kapsule oop te maak.

Absorpsie van ALLMOX word nie beïnvloed deur voedsel nie.

4.3 Kontra-indikasies

- Hipersensitiwiteit vir amoksisillien, vir enige van die penisilliene, of vir enige van die eksipiënte (sien afdeling 6.1).

- Geskiedenis van ‘n ernstige onmiddellike hipersensitiwiteitsreaksie (bv, anafilakse) of ‘n ander beta-laktam medisyne (bv. ‘n kefalosporien, karbapenem of monobaktam).
- ALLMOX moet nie toegedien word aan pasiënte met ‘n infektiewe mononukleose nie, omdat hulle veral gevoelig is vir amoksisillien-geïnduseerde veluitslag, pasiënte met limfatiese leukemie en pasiënte met hiperurisemie wat behandel word met allopurinol, kan ‘n verhoogde risiko hê vir die ontwikkeling van veluitslag.

4.4 Spesiale waarskuwings en voorsorgmaatreëls vir gebruik

Hipersensitiwiteitsreaksies

Ernstige en soms noodlottige hipersensitiwiteitsreaksies (insluitend anafilaktoïede en ernstige kutaneuse ongunstige reaksies) is gerapporteer by pasiënte op penisillien-terapie. Hierdie reaksies sal meer waarskynlik voorkom by individue met ‘n geskiedenis van penisillien hipersensitiwiteit en by atopiese individue. Hipersensitiwiteitsreaksies kan ook ontwikkel tot die Kounis sindroom, ‘n ernstige allergiese reaksie wat miokardiale infarksie tot gevolg kan hê (sien afdeling 4.8). Simptome wat presenteer met sulke reaksies kan borspyn insluit, wat voorkom in assosiasie met ‘n allergiese reaksie tot amoksisillien (sien afdeling 4.8). Indien ‘n allergiese reaksie voorkom, staak ALLMOX-terapie en begin met alternatiewe terapie.

Hipersensitiwiteitsreaksies kan ook tot Kounis se sindroom vorder, 'n ernstige allergiese reaksie wat tot miokardiale infarksie kan lei (sien afdeling 4.8). Die teenwoordigheid van

simptome van sulke reaksies kan borspyn insluit wat voorkom in verband met 'n allergiese reaksie op amoksisillien (sien afdeling 4.8).

Indien 'n allergiese reaksie voorkom, moet ALLMOX-terapie gestaak word en toepaslike alternatiewe terapie ingestel word.

Nie-gevoelige mikro-organismes

Amoksisillien is nie geskik vir die behandeling van sommige tipes van infeksie nie, tensy die patogene alreeds gedokumenteer is en bekend is om gevoelig te wees of indien daar ‘n baie hoë waarskynlikheid is dat die patogene geskik sal wees vir behandeling met amoksisillien (sien afdeling 5.1). Dit is veral van toepassing wanneer die behandeling by pasiënte met urienweginfeksies oorweeg word en ernstige infeksies van die ore, neus en keel.

Konvulsies

Konvulsies kan voorkom by pasiënte met ingekorte renale funksie en by die wat hoë doserings ontvang of by pasiënte met ontvanklikheidsfaktore (bv. geskiedenis van siekte-aanvalle, behandelde epilepsie of meningeale afwykings (sien afdeling 4.8).

Renale inkorting

By pasiënte met renale inkorting moet die dosering aangepas word volgens die graad van inkorting (sien afdeling 4.2).

Velreaksies

Die voorkoms aan die begin van behandeling van ‘n koorsagtige algemene eriteem geassosieer met pustule kan ‘n simptoom wees van akute algemene eksantemeuse pustulose (AGEP, sien afdeling 4.8). Hierdie reaksie vereis die onttrekking van

amoksisillien en word teenaangedui vir enige daaropvolgende toediening.

Jarisch-Herxheimer reaksie

Die Jarisch-Herxheimer reaksie is gerapporteer na amoksisillien-behandeling van sifillis (sien afdeling 4.8). Omsigtigheid is nodig wanneer sifillis behandel word met amoksisillien.

Die Jarisch-Herxheimer reaksie is gerapporteer na amoksisillien-behandeling van Lyme se siekte (sien afdeling 4.8). Dit is as gevolg van die bakterisidele aktiwiteit van amoksisillien op die oorsaaklike bakterie van Lyme se siekte, die spirocheet Borrelia burgdorferi. Pasiënte moet gerus gestel word dat dit ‘n algemene en gewoonlik self-beperkende gevolg is van die antibiotika behandeling van Lyme se siekte.

Oorgroei van nie-gevoelige mikro-organismes

Verlengde gebruik kan tot gevolg hê in oorgroei van nie-gevoelige organismes. Antibiotika-geassosieerde kolitis is gerapporteer met amper alle antibakteriële medisynes en kan wissel in erns van lig tot lewensgevaarlik (sien afdeling 4.8). Dit is dus belangrik om hierdie diagnose te oorweeg by pasiënte wat presenteer met diarree gedurende, of na die toediening van enige antibiotika. Indien antibiotika-geassosieerde kolitis voorkom, moet amoksisillien gestaak en ‘n mediese praktisyn geraadpleeg, en ‘n toepaslike terapie ingestel word. Anti-peristaltiese medisynes is teenaangedui in hierdie situasie.

Verlengde terapie

Periodieke beraming van orgaan-sisteem funksies; insluitend renaal, hepaties en hematopoïese funksie word aanbeveel gedurende verlengde terapie. Verhoogde

lewerensieme en veranderinge in bloedtellings is gerapporteer (sien afdeling 4.8).

Antikoagulante

Verlenging van protrombientyd is gerapporteer by pasiënte wat amoksisillien ontvang. Toepaslike monitering moet gedoen word wanneer antikoagulante tegelykertyd voorgeskryf word. Aanpassings in die dosering van orale antikoagulante kan nodig wees om the verlangde vlak van antikoagulasie te handhaaf (sien afdeling 4.5 en 4.8).

Kristallurie

By pasiënte met verminderde urienuitsetting was kristallurie waargeneem, hoofsaaklik met parenterale terapie. Gedurende die toediening van hoë doserings van amoksisillien, word dit aanbeveel om voldoende vloeistof inname en urinêre uitset te handhaaf om die moontlikheid van amoksisillien kristallurie te verminder. By pasiënte met blaas-kateters, moet ‘n gereëlde nagaan van deurganklikheid gehandhaaf word (sien afdelings 4.8 en 4.9).

Inmeng met diagnostiese toetse

Verhoogde serum- en urinêre vlakke van amoksisillien mag moontlik sekere laboratoriumtoetse beïnvloed. Weens die hoë urinêre konsentrasies van amoksisillien, is vals positiewe lesings meer algemeen met chemiese metodes.

Dit word aanbeveel dat wanneer daar getoets word vir die teenwoordigheid van glukose in uriene gedurende amoksisillien behandeling, ensiematiese glukose oksidase metodes gebruik moet word.

Die teenwoordigheid van amoksisillien kan toetsresultate versteur vir estriol by swanger vrouens.

4.5 Interaksie met ander medisynes en ander vorms van interaksie

Probenesied

Probenesied verminder die renale tubulêre sekresie van amoxisillien. Meegaande gebruik van probenesied kan tot gevolg hê in verhoogde en verlengde bloedvlakke van amoksisillien.

Allopurinol

Meegaande gebruik van allopurinol gedurende behandeling met amoksisillien kan die moontlikheid van allergiese velreaksies laat toeneem.

Tetrasikliene

Tetrasikliene en ander bakteriostatiese medisynes kan inmeng met die bakterisidele effekte van amoksisillien.

Orale antikoagulante

Orale antikoagulante en penisillien antibiotika word wyd gebruik in praktyk sonder verslae van interaksie. In die literatuur was daar egter gevalle van verhoogde International Normalised Ratio (INR) by pasiënte gehandhaaf op asenokumarol of warfarien en ‘n kursus van amoksisillien. Indien meegaande toediening nodig is, moet die protrombientyd van International Normalised Ratio versigtig gemonitor word met die toevoeging of onttrekking van amoksisillien. Aanpassings in die dosering van orale antikoagulante kan egter nodig wees (sien afdelings 4.4 en 4.8).

Metotreksaat

Penisillien kan die ekskresie laat afneem van metotreksaat wat ‘n potensiële toename in toksisiteit kan veroorsaak.

Orale kontraseptiewe

Amoksisillien kan die effektiwiteit van estrogeen-bevattende orale kontraseptiewe middels laat afneem. Amoksisillien kan die absorpsie van ander medisynes beïnvloed, weens sy effek op die gastroïntestinale flora.

4.6 Fertiliteit, swangerskap en laktasie

Swangerskap

Diere studies dui nie op direkte of nie-direkte skadelike effekte met respek tot reproduktiewe toksisiteit nie. Beperkte data op die gebruik van amoksisillien gedurende swangerskap in die mens het nie gedui op verhooge risiko van kongetinale misvormings nie.

Borsvoeding

Amoksisillien word uitgeskei in borsmelk in klein hoeveelhede met die moontlike risiko van sensitisasie. Gevolglik is diarree en fungusinfeksie van die mukeuse membrane moontlik in die kleuter wat borsvoeding ontvang, sodat borsvoeding onttrek kan word.

Fertiliteit

Daar is geen data op die effekte van amoksisillien op fertiliteit in die mens nie. Reproduktiewe studies in diere het geen effekte op fertiliteit getoon nie.

4.7 Effekte op vermoë om te bestuur en gebruik van masjinerie

Amoksisillien kan geassosieer word met allergiese reaksies, duiseligheid en konvulsies. Dus moet pasiënte versigtig wees wanneer hulle bestuur of masjinerie gebruik en moet aangeraai word om nie te bestuur of masjinerie te gebruik indien hulle hierdie simptome

ondervind nie (sien afdeling 4.8).

4.8 Ongewenste effekte

Infeksies en infestasies

Minder dikwels: Mukokutaneuse kandidiasis

Bloed- en limfatiese stelselafwykings

Minder dikwels: Omkeerbare leukopenie (insluitend ernstige neutropenie of agranulositose), omkeerbare trombositopenie en hemolitiese anemie, verlenging van bloedingstyd en protrombientyd (sien afdeling 4.4).

Immuunstelselafwykings

Minder dikwels: Ernstige allergiese reaksies, insluitend angio-edeem, anafilakse, serum-siekte en hipersensitiwiteit vaskulitis (sien afdeling 4.4).

Frekwensie onbekend: Jarisch-Herxheimer reaksie (sien afdeling 4.4).

Senuweestelselafwykings

Minder dikwels: Hiperkinesie, duiseligheid en konvulsies (sien afdeling 4.4).

Gastroïntestinale afwykings

Dikwels: Diarree, naarheid.

Minder dikwels: Braking, antibiotika-geassosieerde kolitis (insluitend pseudomembraneuse kolitis en hemorragiese kolitis (sien afdeling 4.4), swart harige tong.

Hepato-biliêre afwykings

Minder dikwels: Hepatitis en cholestatiese geelsug, 'n matige toename in AST en/of ALT.

Vel- en subkutaneuse weefselafwykings

Dikwels: Veluitslag

Minder dikwels: Urtikarie, pruritus, velreaksies soos veelvuldige eriteem. Stevens-Johnson se sindroom, toksiese epidermale nekrolise, bulleuse en eksfoliatiewe dermatitis, akute algemene eksanteem pustulose (AGEP) (sien afdeling 4.4), medisyne-reaksie met esinofilie en sistemiese simptome (DRESS).

Frekwensie onbekend: Lineêre IgA siekte

Kardiale afwykings

Frekwensie onbekend: Kounis se sindroom

Renale en urinêre afwykings

Minder dikwels: Interstisiele nefritis, kristallurie (sien afdelings 4.4 en 4.9)

Aanmelding van newe-effekte

Indien jy newe-effekte ervaar, praat met jou dokter of apteker of verpleegster. Jy kan ook newe-effekte aan SAHPRA rapporteer via die Med Safety APP (Medsafety X SAHPRA) en die eReporting-platform (who-umc.org) op die SAHPRA webwerf. Deur newe-effekte aan te meld, kan jy help om meer inligting rakende die veiligheid van ALLMOX te verskaf.

Kontak Innovata Pharmaceuticals:regulatory@innovata.co.za

4.9 Oordosering Symptoms

Gastroïntestinale simptome (soos naarheid, braking en diarree) en versteuring van die vloeistof- en elektrolietbalanse kan waargeneem word. Amoksisillien kristallurie, in sommige gevalle met gevolglike nierversaking, is waargeneem. Konvulsies kan voorkom by pasiënte met ingekorte nierfunksie en by die wat hoë doserings ontvang (sien afdelings 4.4 en 4.8).

Behandeling

Gastroïntestinale simptome kan simptomaties behandel word, met aandag aan die water/elektroliet balans.

ALLMOX kan verwyder word vanuit die sirkulasie deur hemodialise (sien afdeling 4.2).

5 FARMAKOLOGIESE EIENSKAPPE

5.1 Farmakodinamiese eienskappe

Farmakoterapeutiese groep: penisilliene met uitgebreide spektrum.

ATC kode: J01CA04

Meganisme van werking

Amoksisillien is ‘n penisillinase-gevoelige semisintetiese penisillien (beta-laktam antibiotika). Dit is bakterisidaal *in vitro* teen ‘n breë spektrum van gram-positiewe en gram-negatiewe patogene wat een of meer ensieme inhibeer (word dikwels na verwys

as penisillien-binding proteïene, PBPs) in die biosintetiese baan van bakteriële peptidoglikan, wat 'n integrale strukturele komponent is van die bakteriële selwand.

Inhibisie van peptidoglikan sintese het tot gevolg verswakking van die selwand, wat gewoonlik gevolg word deur sel-lise en afsterwe.

Amoksisillien is gevoelig vir degradasie deur beta-laktamase geproduseer deur weerstandige bakterie en dus sluit die spektrum van aktiwiteit van amoksisillien alleen nie die organismes in wat hierdie ensieme produseer nie.

Farmakokinetiese/farmakodinamiese verwantskap

Die tyd oor die minimum inhiberende konsentrasie (T > MIC) word oorweeg om die hoof bepaling te wees van effektiwiteit vir amoksisillien.

Meganismes van weerstand

Die hoof meganismes van weerstand vir amoksisillien is:

• Inaktivering van bakteriële beta-laktamase.

• Verandering van PBPs, wat die affiniteit verminder van die antibakteriële medisyne vir die teiken.

Ondeurdringbaarheid van bakterie of effluks pomp meganismes wat die oorsaak kan wees of bydraend tot bakteriële weerstand, veral in Gram-negatiewe bakterie.

Inherente weerstandige organismes†

Gram-positiewe aerobes: *Enterococcus faecium*†
Gram-negatiewe aerobes: *Acinetobacter spp.* *Enterobacter spp.* *Klebsiella spp.* *Pseudomonas spp.* *Bacteroides spp.* (baie soorte van Bacteroïdes fragilis is weerstandig).
Ander: *Chlamydia spp.* *Mycoplasma spp.* *Legionella spp.*
† Natuurlike intermediêre gevoeligheid in die afwesigheid van verworwe meganisme van weerstand.

5.2 Farmakokinetiese eienskappe

Absorpsie

Amoksisillien dissosieer ten volle in waterige oplossing by fisiologiese pH. Dit word vinnig en goed geabsorbeer deur die orale roete van toediening. Na orale toediening is amoksisillien ongeveer 70 % biobeskikbaar. Die tyd tot piek plasma-konsentrasie (T_{maks}) is ongeveer een uur.

Die absorpsie word nie beïnvloed deur gelyktydige inname van voedsel nie.

Distribusisie

Ongeveer 18 % van totale plasma-amoksisillien is gebonde aan proteïene en die klaarblyklike volume van distribusie is ongeveer 0,3 to 0,4 l/kg.
Na intraveneuse toediening was amoksisillien gevind in die galblaas, abdominale weefsel, vel, vet, spierweefsels, sinoviale en peritoneale vloeistowwe, gal en sug.
Amoksisillien versprei nie voldoende in die serebrospinale vloeistof nie.
Amoksisillien kan waargeneem word in borsmelk (sien afdeling 4.6).
Amoksisillien het gewys om die plasentale skans te kruis (sien afdeling 4.6

Biotransformasie

Amoksisillien word gedeeltelik uitgeskei in die uriene as die onaktiewe penisilloïed-suur in hoeveelhede ekwivalent aan 10 tot 25 % van die aanvanklike dosis.

Eliminasie

Die hoof roete van eliminasie vir amoksisillien is deur die niere.
Amoksisillien het ‘n gemiddelde eliminasie halfleeftyd van ongeveer een uur en ‘n gemiddelde totale opruiming van ongeveer 25 l/uur in gesonde persone. Ongeveer 60

tot 70 % van die amoksisillien word onveranderd uitgeskei in uriene gedurende die eerste 6 uur na toediening van ‘n enkel 250 mg of 500 mg dosis van amoksisillien. Verskillende studies het gevind dat die urinêre ekskresie is 50 - 85 % vir amoksisillien oor ‘n 24-uur periode.

Meegaande gebruik van probenesied vertraag amoksisillien ekskresie (sien afdeling 4.5).

Hemodialise kan gebruik word vir eliminasie van amoksisillien (sien afdeling 4.2).

Spesiale bevolkings

Ouderdom

Die eliminasie half-leeftyd van amoksisillien is soortgelyk vir kinders van ongeveer 3 maande tot 2 jaar sowel as ouer kinders en volwassenes. Vir baie jong kinders (insluitend preterm pasgeborenes) in die eerste week van lewe moet die interval en toediening nie twee keer per dag toediening oorskry nie, weens die onvolwassenheid van die renale deurweg van eliminasie. Omdat bejaarde pasiënte meer geneig kan wees tot ‘n afname in nierfunksie, is omsigtigheid nodig in dosering-seleksie en dit kan nuttig wees om nierfunksie te monitor.

Renale inkorting

Die totale serum-opruiming van amoksisillien verminder proporsioneel met afname in nierfunksie (sien afdelings 4.2 en 4.4).

Hepatiese inkorting

Hepatiese ingekorte pasiënte moet versigtig gedoseer word en hepatiese funksie moet gemonitor word met gereëlde intervalle (sien afdeling 4.2).

6 FARMASEUTIESE BESONDERHEDE

6.1 Lys van eksipiënte

Kapsule inhoud:

Magnesiumstearaat

Kapsule shell:

Pers-pers indigo karmyn

Eritrosien

Blou-pers indigo karmyn

Gelatien

6.2 Onverenigbaarhede

Nie van toepassing nie

6.3 Rakleeftyd

24 maande

6.4 Spesiale voorsorgmaatreëls vir berging

Berg by of benede 25°C in ‘n droë plek.

HOU BUITE DIE BEREIK VAN KINDERS

6.5 Aard en inhoud van houer

ALLMOX word verpak in:

15’s: HDPE houers en in LDPE pasiënt-gereed pakkies

100’s: HDPE houers met skroefdoppies

500’s HDPE houers met skroefdoppies

1000’s HDPE houers met skroefdoppies

6.6 Spesiale voorsorgmaatreëls vir weggooi

Geen spesiale maatreëls vir vernietiging nie

7. HOUER VAN SERTIFIKAAT VAN REGISTRASIE

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2091

South Africa

8.REGISTRASIENOMMERS

Allmox 250: Y/20.1.2/161

Allmox 500: Y/20.1.2/162

9. DATUM VAN EERSTE GOEDKEURING/HERNUWING VAN DIE GOEDKEURING

Datum van registrasie: 22 Oktober 1991

10.Datum van revisie van die teks

31/03/2025