1.5.5 Proposed Professional Information for Medicines for Human Use

SCHEDULING STATUS

S4

1.NAME OF MEDICINE

ALLMOX S powder for oral suspension

ALLMOX SF powder for oral suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ALLMOX S 125 mg/5ml

Each 5 ml of reconstituted suspension contains amoxycillin trihydrate equivalent to 125 mg amoxycillin.

Contains sugar: sorbitol 12 mg per 5 ml

ALLMOX SF 250 mg/5ml

Each 5 ml of reconstituted suspension contains amoxycillin trihydrate equivalent to 250 mg amoxycillin.

Contains sugar: sorbitol 12 mg per 5 ml

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Powder for oral suspension

ALLMOX is a white to off-white powder forming an orange suspension on constitution with water. The resulting suspension has a characteristic flavour.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Infections due to susceptible non-penicillinase producing organisms including (see sections 4.4 and 5.1):

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 gastroenteritis 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

Children under 12 years

• The normal dose for children 6 months to 10 years of age is equivalent of 125 mg (i.e. 5 ml of 125 mg/5 ml) three times a day.

• 0 – 6 months: 62,5 mg three times a day.

Adults and children over 12 years

• **ALLMOX S** 125 mg/5 ml every 8 hours (three times a day).

• Severe infections: **ALLMOX SF** 250 mg/ 5 ml every 8 hours (three times a day).

• Gonorrhoea: 3 g amoxicillin 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.

Method of administration

ALLMOX oral suspension is for oral use. For instructions on reconstitution of the medicine before administration, see section 6.6.

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 agent (e.g. a cephalosporin, carbapenem or monobactam).

ALLMOX should not be given to patients with infectious mononucleosis, since they are especially susceptible to amoxycillin-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

Before initiating therapy with **ALLMOX**, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other beta-lactam medicines (see sections 4.3 and 4.8). 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)

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

Non-susceptible microorganisms

ALLMOX 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 **ALLMOX** (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 **ALLMOX** discontinuation and contraindicates any subsequent administration. **ALLMOX** 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.

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 **ALLMOX**. 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, **ALLMOX** should immediately be discontinued, a medical practitioner consulted and an appropriate therapy initiated. Antiperistaltic medicines are contraindicated in this situation.

Prolonged therapy

Periodic assessment of organ system functions; including renal, hepatic and haematopoietic 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 **ALLMOX**, 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 **ALLMOX** treatment, enzymatic glucose oxidase methods should be used.

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

ALLMOX contains sorbitol

Sorbitol may cause gastrointestinal discomfort and mild laxative effect.

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

Concomitant use of allopurinol during treatment with **ALLMOX** can increase the likelihood of allergic skin reactions.

Tetracyclines

Tetracyclines and other bacteriostatic medicines may interfere with the bactericidal effects of **ALLMOX**. 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 **ALLMOX**. If co-administration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of **ALLMOX**. Moreover, adjustments in the dose of oral anticoagulants may be necessary (see sections 4.4 and 4.8).

Methotrexate

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

Oral contraceptives

ALLMOX may decrease the efficacy of oestrogen-containing oral contraceptives. **ALLMOX** may affect the absorption of other medicines due to its effect on the gastro-intestinal 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 **ALLMOX** 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 teratogenic effects on fertility.

4.7 Effects on ability to drive and use machines

ALLMOX 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.

4.8 Undesirable effects

a. Summary of the safety profile

The most commonly reported adverse reactions (ADRs) are diarrhoea, nausea and skin rash.

b. Tabulated summary of adverse reactions

The ADRs derived from clinical studies and post-marketing surveillance with amoxicillin, presented by MedDRA System Organ Class are listed below:

MedDRA system organ class	**Frequency**	**Adverse reactions**
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)
Cardiac disorders	Frequency unknown	Kounis syndrome (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
	Frequency unknown	IgA disease
	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)
Renal and urinary disorders	Less frequent	Interstitial nephritis, crystalluria (see sections 4.4 and 4.9

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions 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

HOTLINE for reporting of side effects directly to Innovata Pharmaceuticals (Pty) Ltd: 086 999 0912

4.9 Overdose Symptoms

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.

Amoxicillin can be removed from the circulation by hemodialysis.

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 agent 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.
Gram-negative anaerobes: *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

Colloidal anhydrous silica (E551)

Colour Sunset Yellow Supra CI15985 (E110)

Saccharin sodium (E954)

Sodium citrate (E331)

Sorbitol

Tutti Fruitti Flavour AP0551

Xanthan gum (E415)

6.2 Incompatibilities

No data available.

6.3 Shelf life

Dry powder: 2 years.

Reconstituted suspension: 14 days (stored at 2 °C to 8°C in a refrigerator)

6.4 Special precautions for storage

Dry powder: Store at or below 25 °C, protected from moisture. After reconstitution the product must be stored at 2-8 °C in a refrigerator.

KEEP OUT OF REACH OF CHILDREN

6.5 Nature and contents of container

ALLMOX is packed in a 75 ml and 100 ml HDPE bottle with a white polypropylene child resistant closure with an induction sealing liner in an outer carton.

6.6 Special precautions for disposal and other handling

For reconstitution:

• Check cap seal is intact before use.

• Invert and shake bottle to loosen powder.

Add 64 ml and 85 ml water for 75 ml and 100 ml pack respectively in two portions to the dry mixture in the bottle. Shake well after each addition.

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

7. NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

Innovata Pharmaceuticals (Pty) Ltd

Crownwood Office Park

100 Northern Parkway

Ormonde

Johannesburg

2091

South Africa

8. Registration numbers:

Allmox S 125: 36/20.1.2/0117

Allmox SF 250: 36/20.1.2/0118

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

June 2003

10 DATE OF REVISION OF THE TEXT

27 November 2024

1.5.5 Proposed Professional Information for Medicines for Human Use

SKEDULERINGSTATUS

S4

1. NAAM VAN MEDISYNE

ALLMOX S poeier vir orale suspensie

ALLMOX SF poeier vir orale suspensie

2. KWALITATIEWE EN KWANTITATIEWE SAMESTELLING

ALLMOX S 125 mg/5 ml

Elke 5 ml van hersaamgestelde suspensie bevat amoksisillientrihidraat ekwivalent aan 125 mg amoksisillien.

Bevat suiker: sorbitol 12 mg per 5 ml

ALLMOX SF 250 mg/5 ml

Elke 5 ml van hersaamgestelde suspensie bevat amoksisillientrihidraat ekwivalent aan 250 mg amoksisillien.

Bevat suiker: sorbitol 12 mg per 5 ml

Vir volledige lys van eksipiënte, sien afdeling 6.1

3. FARMASEUTIESE VORM

Poeier vir orale suspensie.

ALLMOX is ‘n wit tot naaswit poeier wat ‘n oranje suspensie vorm na samestelling met water. Die gevolglike suspensie het ‘n kenmerkende geur.

4 KLINIESE BESONDERHEDE

4.1 Terapeutiese Indikasies

Infeksies weens gevoelige nie-penisillinase-produserende organismes insluitend: (sien afdelings 4.4 en 5.1):

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

Kinders onder 12 jaar

• Die normale dosis vir kinders 6 maande tot 10 jaar oud is ekwivalent van 125 mg (d.w.s. 5 ml van 125 mg/5 ml) drie keer per dag.

• 0 – 6 maande: 62,5 mg drie keer per dag.

Volwassenes en kinders ouer as 12 jaar

• **ALLMOX S** 125 mg/5 ml elke 8 uur (drie keer per dag).

• Ernstige infeksies: **ALLMOX SF** 250 mg/ 5 ml elke 8 uur (drie keer per dag).

• Gonorree: 3 g amoksisillien as ‘n enkel dosis, gewoonlik gekombineer met 1 g probenesied.

By die behandeling van beta-hemolitiese beta-hemolitiese streptokokkale infeksies, moet ‘n terapeutiese dosering toegedien word vir ten minste 10 dae.

Metode van toediening

ALLMOX orale suspensie is vir orale gebruik. Vir instruksies omtrent hersamestelling van die medisyne voor toediening, sien afdeling 6.6. Absorpsie van **ALLMOX** word onverminderd deur voedsel beïnvloed.

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 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

Voor begin van terapie met **ALLMOX**, moet omsigtige navrae gemaak word aangaande vorige hipersensitiwiteitsreaksies vir penisilliene, kefalosporiene of ander beta-laktam medisynes (sien afdelings 4.3 en 4.8). 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 se sindroom, ‘n ernstige allergiese reaksie wat miokardiale infarksie tot gevolg kan hê (sien afdeling 4.8).

Indien ‘n allergiese reaksie voorkom, staak **ALLMOX**-terapie en begin met ‘n toepaslike alternatiewe terapie.

Nie-gevoelige mikro-organismes

ALLMOX 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 **ALLMOX** (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 **ALLMOX** en word teenaangedui vir enige daaropvolgende toediening.

ALLMOX behoort vermy te word indien aansteeklike mononukleose vermoed word, omdat die voorkoms van ‘n morbillivormige uitslag geassosieer was met hierdie toestand, na die gebruik van amoksisillien.

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 **ALLMOX**.

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 **ALLMOX** onmiddellik gestaak word, ‘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 renale, hepatiese 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 die verlangde vlak van antikoagulasie te handhaaf (sien afdelings 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 **ALLMOX**, 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 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 **ALLMOX-**behandeling, ensiematiese glukose oksidase metodes gebruik moet word.

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

ALLMOX bevat sorbitol

Sorbitol kan gastroïntestinale ongemak veroorsaak en ‘n ligte lakserende effek.

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 **ALLMOX** kan die moontlikheid van allergiese velreaksies laat toeneem.

Tetrasikliene

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

Oral 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 **ALLMOX**. Indien meegaande toediening nodig is, moet die protrombientyd of International Normalised Ratio versigtig gemonitor word met die toevoeging of onttrekking van **ALLMOX**. Aanpassings in die dosering van orale antikoagulante kan egter nodig wees (sien afdelings 4.4 en 4.8).

Metotreksaat

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

Orale voorbehoedmiddels

ALLMOX kan die effektiwiteit van estrogeen-bevattende orale kontraseptiewe middels laat afneem. **ALLMOX** 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 met die gebruik van **ALLMOX** gedurende swangerskap in die mens het nie gedui op ‘n 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 omtrent die effekte van amoksisillien op fertiliteit in die mens nie. Reproduktiewe studies in diere het geen teratogeniese effekte op fertiliteit getoon nie.

4.7 Effekte op vermoë om te bestuur en masjinerie te gebruik

ALLMOX 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.

4.8 Ongewenste effekte

a. Opsomming van die veiligheidsprofiel

Die mees algemene gerapporteerde ongunstige reaksies (ADRs) is diarree, naarheid en veluitslag.

b. Getabuleerde opsomming van ongunstige reaksies

Die ADRs vanuit kliniese studies en na-bemarking waarnemings met amoksisillien, soos gepresenteer deur MedDRA Sisteem Orgaan Klas word hieronder aangedui:

MedDRA sisteem orgaan klas	**Frekwensie**	**Ongunstige reaksies**
Infeksies en infestasies	Minder dikwels	Mukokutaneuse kandidiase
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)
Senuweestelsel-afwykings	Minder dikwels	Hiperkinesie, duiseligheid en konvulsies (sien afdeling 4.4)
Kardiale afwykings	Frekwensie onbekend	Kounis se sindroom (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-bilière afwykings	Minder dikwels	Hepatitis en cholestatiese geelsug, 'n matige toename in AST en/of ALT
Vel- en subkutaneuse weefselafwykings	Dikwels	Veluitslag
	Frekwensie onbekend	IgA siekte
	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)
Renale en urinêre afwykings	Minder dikwels	Interstisiële nefritis, kristallurie (sien afdelings

		4.4 en 4.9)

Repporteer van vermoedelike ongunstige reaksies

Rapporteer van vermoedelike ongunstige reaksies na goedkeuring van die medisyne is belangrik. Dit laat toe vir volgehoue monitering van die voordeel/risiko balans van die medisyne. Gesondheidsorgvoorsieners word versoek om enige vermoedelike ongunstige reaksies te rapporteer aan SAHPRA via die “6.04 Adverse Drug Reactions Reporting Form”, wat aanlyn gevind word onder SAHPRA se publikasies: https://www.sahpra.org.za/Publications/Index/8

HOTLINE vir rapporteer van newe-effekte is direk aan Innovata Pharmaceuticals (Pty) Ltd: 086 999 0912

4.9 Oordosering Simptome

Simptome

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.

Amoksisillien 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

Werkingsmeganisme

Amoksisillien is ‘n penisillinase-gevoelige semisintetiese penisillien (beta-laktam antibiotika). Dit is bakterisideel *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 middel 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.

Inherent weerstandige organismes†
Gram-positiewe aerobes: *Enterococcus faecium*†
Gram-negatiewe aerobes: *Acinetobacter* spp. *Enterobacter* spp. *Klebsiella* spp.

Pseudomonas spp.
Gram-negatiewe anaerobes: *Bacteroides* spp. (baie soorte van *Bacteroides 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.

Distribusie

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 50 - 85 % is 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

Kolloïdale anhidriese silika (E551)

Kleur Sunset Geel Supra CI15985 (E110)

Sakkarien natrium (E954)

Natriumnitraat (E331)

Sorbitol

Tutti Fruitti Geur AP0551

Xanthan gom (E415)

6.2 Onverenigbaarhede

Geen data beskikbaar nie.

6.3 Rakleeftyd

Droë poeier: 2 jaar.

Hersaamgestelde suspensie: 14 dae (bêre by 2 °C tot 8 °C in ‘n koelkas).

6.4 Spesiale voorsorgmaatreëls vir berging

Droë poeier: Berg by of benede 25 °C, beskerm teen vog. Na herkonstitusie moet die produk gebêre word by 2-8 °C in ‘n koelkas.

HOU BUITE DIE BEREIK VAN KINDERS.

6.5 Aard en inhoud van houer

ALLMOX word verpak in ‘n 75 ml en 100 ml HDPE bottel met ‘n wit polipropileen kind-bestande sluiter met ‘n induksie seël voering in ‘n buitenste karton.

6.6 Spesiale voorsorgmaatreëls vir weggooi en ander hantering

Vir hersamestelling:

• Kyk of voering van die doppie intakt is voor gebruik.

• Keer die bottel om en skud om die poeier los te maak.

Voeg 64 ml en 85 ml water vir 75 ml en 100 ml pakke respektiewelik in twee dele by die droë mengsel in die bottel. Skud goed na elke toevoeging.

Enige ongebruikte produk of afvalmateriaal moet weggegooi word volgens die plaaslike vereistes.

7. NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE SERTIFIKAAT VAN REGISTRASIE

Innovata Pharmaceuticals (Pty) Ltd

Crownwood Office Park

100 Northern Parkway

Ormonde

Johannesburg

2091

Suid-Afrika

8. Registrasienommers:

Allmox S 125: 36/20.1.2/0117

Allmox SF 250: 36/20.1.2/0118

9. DATUM VAN EERSTE GOEDKEURING/HERNUWING VAN DIE GOEDKEURING

Junie 2003

10. DATUM VAN REVISIE VAN DIE TEKS

27 November 2024