SCHEDULING STATUS: S4

1. NAME OF THE MEDICINAL PRODUCT

AUGSPEC 1 g (Film-coated tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains amoxicillin trihydrate equivalent to 875 mg amoxicillin and potassium clavulanate equivalent to 125 mg clavulanic acid.
For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Film-coated tablets.
White to off white 22 mm by 10 mm oblong film-coated tablets with score line.
The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

AUGSPEC 1 g is indicated in adults for the treatment of the following infections caused by amoxicillin-resistant organisms producing β-lactamases sensitive to clavulanic acid (see section 4.2, section 4.4 and section 5.1)

- 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.

AUGSPEC 1 g formulations will also be effective in the treatment of infections caused by amoxicillin-sensitive organisms at the appropriate amoxicillin dosage since in this situation the clavulanic acid component does not contribute to the therapeutic effect.

4.2. Posology and method of administration

Posology

During the administration of amoxicillin, it is advisable to maintain adequate fluid intake and urinary output in order to prevent any possibility of amoxicillin crystalluria.

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.

Adults:
For severe infections, one AUGSPEC 1 g tablet every 12 hours at the start of a meal.

Special populations

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.
AUGSPEC 1 g should not be used in patients with a glomerular filtration rate of less than 30 ml/minute.
Haemodialysis decreases serum concentrations of both amoxicillin and clavulanic acid and an additional dose should be administered at the end of dialysis.

Elderly:
No dose adjustment is considered necessary.

Hepatic impairment:
Dose with caution and monitor hepatic function at regular intervals (see section 4.3 and section 4.4).

Method of administration

AUGSPEC 1 g is for oral use.
Tablets should be taken immediately before a meal.

Dosage Guide:

Amoxicillin-Sensitive Organisms			
Upper respiratory tract infections	Lower respiratory tract infections	Urinary tract infections	Skin and soft tissue infections
Adults:			
1 tablet 12-hourly	1 tablet 12-hourly	1 tablet 12-hourly	1 tablet 12-hourly

Amoxicillin-Resistant Organisms:			
Upper respiratory tract infections (Otitis media) *H. influenzae, H. parainfluenzae*	Lower respiratory tract infections (Otitis media) *H. influenzae, H. parainfluenzae*	Urinary tract infections *E. coli, Klebsiella pneumoniae*	Skin and soft tissue infections *Methicillin sensitive Staphylococcus aureus*
Adults:			
1 tablet 12-hourly	1 tablet 12-hourly	1 tablet 12-hourly	1 tablet 12-hourly

4.3. Contraindications

AUGSPEC 1 g is contraindicated in:

- Hypersensitivity to the active substances amoxicillin or clavulanic acid or to any of the excipients (see section 6.1).
- Hypersensitivity to penicillins or to cephalosporins. Cross-sensitivity between penicillins and cephalosporins is well documented.
- AUGSPEC 1 g is contraindicated in patients with a previous history of amoxicillin/clavulanic-associated jaundice/hepatic dysfunction (see section 4.8).

4.4. Special warnings and precautions for use

Prescribers must adhere to the principles of antibiotic stewardship. Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy. Before initiating therapy with AUGSPEC 1 g, 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 of sensitivity to multiple allergens. There have been reports of individuals with a history of penicillin hypersensitivity, who have experienced severe reactions when treated with cephalosporins. If an allergic reaction occurs, AUGSPEC 1 g should be discontinued and the appropriate therapy instituted. Serious anaphylactic reactions may require immediate emergency treatment with adrenaline. Oxygen, intravenous steroids and airway management, including intubation may also be required.

Severe cutaneous adverse reactions (SCAR), such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalised exanthematous pustulosis (AGEP) have been reported in patients taking beta-lactam antibiotics. When SCAR is suspected, beta-lactam antibiotics should be discontinued.

In the case that an infection is proven to be due to an amoxicillin-susceptible organism(s) then consideration should be given to switching from amoxicillin/clavulanic acid to amoxicillin.

AUGSPEC 1 g is not suitable for use when there is a high risk that the presumptive pathogens have resistance to beta-lactam agents that is not mediated by beta-lactamases susceptible to inhibition by clavulanic acid. AUGSPEC 1 g should not be used to treat penicillin-resistant *S. pneumoniae*.

AUGSPEC 1 g 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.

Convulsions may occur in patients with impaired renal function or in those receiving high doses (see section 4.8)

Prolonged use may result in overgrowth of non-susceptible organisms. Pseudomembranous enterocolitis has been reported.
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.

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 AUGSPEC 1 g discontinuation and contraindicates any subsequent administration of amoxicillin.

Prolongation of prothrombin time has been reported rarely in patients receiving AUGSPEC 1 g.
Appropriate monitoring should be undertaken when anticoagulants are prescribed concurrently.

Antibiotic-associated colitis, (including pseudomembranous colitis, haemorrhagic colitis *Clostridium difficile* associated diarrhoea (CDAD)), has been reported with nearly all antibacterial agents including amoxicillin 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, AUGSPEC 1 g should immediately be discontinued, a medical practitioner be consulted and an appropriate therapy initiated. Anti-peristaltic medicinal products are contraindicated in this situation.

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.

AUGSPEC 1 g should be given with caution to patients with lymphatic leukaemia since they are especially susceptible to amoxicillin-induced skin rashes.

Periodic assessment of organ function, including renal, hepatic and haematopoietic functions, is advisable during prolonged therapy.

Impaired hepatic function: Changes in liver function tests have been observed in some patients receiving AUGSPEC 1 g. Transient hepatitis and cholestatic jaundice have been reported. AUGSPEC 1 g should be used with caution in patients with evidence of hepatic dysfunction. Hepatic events have been reported predominantly in males and elderly patients and may be associated with prolonged treatment. These events have been very seldom reported in children. In all populations, signs and symptoms usually occur during or shortly after treatment but in some cases may not become apparent until several weeks after treatment has ceased. These are usually reversible. Hepatic events may be severe and, in less frequent circumstances, deaths have been reported. These have almost always occurred in patients with serious underlying disease or taking concomitant medications known to have the potential for hepatic effects (see section 4.8).

Impaired renal function: In patients with moderate or severe renal impairment AUGSPEC 1 g dosage should be adjusted (see section 4.2). AUGSPEC 1 g 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 exercised when AUGSPEC 1 g is administered to a nursing woman (see section 4.6).

The use of AUGSPEC 1 g 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.

Interference with serological testing

It is recommended that when testing for the presence of glucose in urine during AUGSPEC 1 g treatment, enzymatic glucose oxidase methods should be used.
Due to the high urinary concentrations of amoxicillin, false positive readings are common with chemical methods.

The presence of clavulanic acid in AUGSPEC 1 g may cause a non-specific binding of IgG and albumin by red cell membranes leading to a false positive Coombs test.

4.5. Interaction with other medicines and other forms of interaction

Probenecid decreases the renal tubular secretion of amoxicillin but does not affect clavulanic acid excretion. Concurrent use with AUGSPEC 1 g may result in increased and prolonged blood levels of amoxicillin but not of clavulanic acid.

AUGSPEC 1 g 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 drugs may interfere with the bactericidal effects of amoxicillin.

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 in patients maintained on acenocoumarol or warfarin and prescribed a course of amoxicillin. If coadministration 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.

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

In patients receiving mycophenolate mofetil, reduction in pre-dose concentration of the active metabolite mycophenolic acid (MPA) of approximately 50 % has been reported following commencement of oral amoxicillin plus clavulanic acid. The change in pre-dose level may not accurately represent changes in overall MPA exposure. Therefore, a change in the dose of mycophenolate mofetil should not normally be necessary in the absence of clinical evidence of graft dysfunction. However, close clinical monitoring should be performed during the combination and shortly after antibiotic treatment.

There have been reports of positive test results using an Aspergillus EIA test in patients receiving amoxicillin/clavulanic acid who were subsequently found to be free of Aspergillus infection. Cross-reactions with non-Aspergillus polysaccharides and polyfuranoses have been reported. Therefore, positive test Aspergillus results in patients receiving amoxicillin/clavulanic acid should be interpreted cautiously and confirmed by other diagnostic methods.

4.6. Fertility, pregnancy and lactation

Women of childbearing potential/Contraception in males and females.

Concurrent use of AUGSPEC 1 g and oral contraceptives decreases the efficacy of oral contraceptives. Patients should be strongly advised to use an alternative or additional method of contraception while taking this medicine (see section 4.5).

Pregnancy

The safety of AUGSPEC 1 g during pregnancy has not been established (see section 4.3, section 4.4 and/or section 4.8)

Breastfeeding

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.

Fertility

No fertility data is available.

4.7. Effects on ability to drive and use machines

AUGSPEC 1 g has no or negligible influence on the ability to drive and use machines. However, undesirable effects may occur (e.g. allergic reaction, dizziness, convulsions), which may influence the ability to drive and use machines (see section 4.8).

4.8. Undesirable effects

a. Summary of the safety profile

The most commonly reported adverse drug reactions (ADRs) are diarrhoea, nausea, vomiting, indigestion, abdominal pain, skin rashes, urticaria and erythema multiforme, vaginitis, genital moniliasis, 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 AUGSPEC 1 g at the start of a meal. In addition, as these symptoms are especially related to the potassium clavulanate component, where these gastrointestinal symptoms occur and a higher concentration of amoxicillin is required, consideration should be given to administering the additional amoxicillin separately.

b. Tabulated summary of adverse reactions

System Organ Class	Frequency	Undesirable effect
Infections and Infestations	Frequent	Mucocutaneous candidiasis
	Frequency unknown	Overgrowth of non-susceptible organisms Clostridium difficile
Blood and the lymphatic system disorders	Less frequent	Haemolytic anaemia, reversible thrombocytopenia, thrombocytopenic purpura, eosinophilia, reversible leukopenia (including neutropenia) and agranulocytosis.
	Frequency unknown	Prolongation of bleeding time and prothrombin time.
Immune system disorders	Less frequent	Hypersensitivity reactions (Skin rashes, pruritus and urticaria, serum sickness-like syndrome, angioedema, erythema multiforme, Stevens-Johnson syndrome, hypersensitivity vasculitis and less frequently bullous exfoliative dermatitis, acute generalised exanthematous pustulosis (AGEP) and toxic epidermal necrolysis have been reported).
	Frequency unknown	Hypersensitivity interstitial nephritis, angioneurotic oedema, serum sickness-like syndrome, hypersensitivity vasculitis.
Nervous system disorders	Frequent	Dysgeusia, tiredness, fever, chills.
	Less frequent	Hyperactivity, convulsions, dizziness, headache, CNS toxicity.
	Frequency unknown	Aseptic meningitis
Gastrointestinal disorders	Frequent	Diarrhoea, nausea, vomiting, indigestion, abdominal pain.
	Less frequent	Gastritis, stomatitis, glossitis, enterocolitis, mucocutaneous candidiasis, antibiotic-associated colitis (including pseudomembranous colitis and haemorrhagic colitis)
	Frequency unknown	Superficial tooth discolouration, black hairy tongue
Hepato-biliary disorders	Less frequent	Rises in AST and/or ALT
	Frequency unknown	Hepatitis and cholestatic jaundice.
Skin and subcutaneous tissue disorders	Less frequent	Skin rashes, pruritis, urticaria and erythema multiforme.
	Frequency unknown	Purpura, diaphoresis, flushing, petechiae, Stevens-Johnson syndrome, Toxic epidermal necrolysis, Bullous exfoliative-dermatitis, acute generalised exanthemous pustulosis (AGEP), drug reaction with eosinophilia and systemic syndrome (DRESS)
Renal and urinary disorders	Less frequent	Crystalluria
	Frequency unknown	Nephropathy and interstitial nephritis

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. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9. Overdose

Symptoms: 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. 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.

Treatment: Adequate fluid intake and urinary output must be maintained to minimize the possibility of crystalluria.

Amoxicillin may be removed from the circulation by haemodialysis. The molecular weight, degree of protein binding and pharmacokinetic profile of clavulanic acid together with information from a single patient with renal insufficiency all suggest that this compound may also be removed by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

A 20.1.2 Penicillins
Amoxicillin/Clavulanic acid tablets contain 7 parts (875 mg) of a broad-spectrum penicillin, amoxicillin and 1 part (125 mg) of potassium clavulanate.

(i) Mechanism of Action

Amoxicillin is a semisynthetic penicillin (beta-lactam antibiotic) that inhibits one or more penicillin-binding proteins in the biosynthetic pathway of bacterial peptidoglycan, leading 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. Clavulanic acid is a beta-lactam structurally related to penicillin. It inactivates some beta-lactamase enzymes thereby preventing inactivation of amoxicillin.

Potassium clavulanate has been shown *in vitro* to be an irreversible inhibitor of beta-lactamases.

Potassium clavulanate does not inactivate the chromosomally mediated (Sykes Type 1 Cephalosporinase) β-lactamases produced by *Acinetobacter* species, *Citrobacter* species, *Enterobacter*, indole positive *Proteus*, *Providencia* species and *Serratia marcescens*. *In vitro* the formulation showed synergism against amoxicillin-resistant organisms, with no evidence of antagonism and the activity was not reduced in the presence of serum. (*In vitro* activity does not necessarily imply *in vivo* efficacy).

(ii) Bactericidal Action

The amoxicillin component of the formulations is bactericidal for both Gram-positive and Gram-negative organisms. The clavulanic acid component has very little bactericidal action. It does however, by inactivation of susceptible β-lactamases, protect amoxicillin from degradation by a large number of β-lactamase enzymes produced by penicillin-resistant strains of organisms.

Resistance

The prevalence of resistance may vary geographically and with time for selected species, and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

MRSA (Staphylococcus aureus organisms resistant to methicillin)
Inherently resistant organisms:
Aerobic gram-negative micro-organisms
Acinetobacter sp. Citrobacter freundii Enterobacter sp.
Legionella pneumophila Morganella morganii Providencia spp.
Pseudomonas sp.
Serratia sp.
Stenotrophomonas maltophilia
Other micro-organisms:
Chlamydophila pneumoniae
Chlamydophila psittaci
Coxiella burnetti
Mycoplasma pneumoniae

5.2. Pharmacokinetic properties

Absorption

Amoxicillin and clavulanic acid are fully dissociated in aqueous solution at physiological pH. Both components are rapidly and well absorbed by the oral route of administration. Following oral administration, amoxicillin and clavulanic acid are approximately 70 % bioavailable. The plasma profiles of both components are similar and the time to peak plasma concentration (T_{max}) in each case is approximately one hour. Amoxicillin and clavulanic acid serum concentrations achieved with amoxicillin/clavulanic acid are similar to those produced by the oral administration of equivalent doses of amoxicillin or clavulanic acid alone.

The pharmacokinetics of amoxicillin and clavulanic acid are closely allied, and neither are adversely affected by the presence of food in the stomach. After an oral dose of the 2 parts amoxicillin and 1 part clavulanic acid (Amoxicillin/Clavulanic acid 375 mg), taken at the start of a meal, a mean peak serum level of 5,7 µg amoxicillin and 3,8 µg clavulanic acid per millilitre was achieved within one hour in healthy volunteers. Doubling the dose virtually doubles the peak serum level.

Distribution

About 25 % of total plasma clavulanic acid and 18 % of total plasma amoxicillin is bound to protein. The apparent volume of distribution is around 0,3 – 0,4 l/kg for amoxicillin and around 0,2 l/kg for clavulanic acid.

Following intravenous administration, both amoxicillin and clavulanic acid have 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.

From animal studies there is no evidence for significant tissue retention of drug-derived material for either component. Amoxicillin, like most penicillins, can be detected in breast milk. Trace quantities of clavulanic acid can also be detected in breast milk (see section 4.6).

Biotransformation

The major route of elimination for amoxicillin is via the kidney, whereas for clavulanic acid it is by both renal and non-renal mechanisms. 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. Clavulanic acid is extensively metabolized in man and eliminated in urine and faeces and as carbon dioxide in expired air.

Elimination

64,9 % of amoxicillin and 37,5 % of clavulanic acid are excreted unchanged in the urine in the first 6 hours after an oral dose of 2 to 1 amoxicillin/clavulanic acid tablets. Co-administration of probenecid has little effect on the excretion of the clavulanic acid component of the formulation.

Renal impairment

The total serum clearance of amoxicillin/clavulanic acid decreases proportionately with decreasing renal function. The reduction in drug clearance is more pronounced for amoxicillin than for clavulanic acid, as a higher proportion of amoxicillin is excreted via the renal route. Doses in renal impairment must therefore prevent undue accumulation of amoxicillin while maintaining adequate levels of clavulanic acid (see section 4.2).

Hepatic impairment

Hepatically impaired patients should be dosed with caution and hepatic function monitored at regular intervals.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on studies of safety pharmacology, genotoxicity and toxicity to reproduction. Carcinogenicity studies have not been conducted with amoxicillin/clavulanic acid.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Basic butylated methacrylate copolymer (Eudragit E 12.5)
Croscarmellose sodium (E468)
Crospovidone Type A (E1202)
Macrogol 6000
Magnesium stearate (E470b)
Microcrystalline cellulose (E460)
Silica colloidal anhydrous (E551)
Talc (E553b)
Titanium dioxide (E171)

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

2 years

6.4. Special precautions for storage

Store at or below 25 °C. Protect from light and moisture.
Keep the blisters in the outer carton until required for use.

6.5. Nature and contents of container

Blister Ground foil consisting of OPA/Al/PVC sealed with aluminium lidding foil. Each blister strip contains 5 tablets. Pack size of 10 tablets.

6.6. Special precautions for disposal of a used medicine or waste materials derived from such medicine and other handling of the product

No special requirements

7. HOLDER OF CERTIFICATE OF REGISTRATION

TRINITY PHARMA (PTY) LTD
106 16th Road, Building 2, Midrand, 1686, South Africa

8. REGISTRATION NUMBER(S)

52/20.1.2/0777.776

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 30 March 2021

10. DATE OF REVISION OF TEXT

N.A

TRINITY PHARMA

Tel: 010 594 5610. Email: PV@kahmagroup.co.za

Claudia Law - Approved - 18.06.2021

SKEDULERINGSTATUS: S4

1. NAAM VAN DIE GENEESMIDDEL

AUGSPEC 1 g (Filmbedekte tablette)

2. KWALITATIEWE EN KWANTITATIEWE KOMPOSISIE

Elke filmbedekte tablette bevat amoksisillientrihidraat gelyk aan 875 mg amoksisillien en kaliumklavulaanaat gelyk aan 125 mg klavulaansuur.
Sien afdeling 6.1 vir 'n volledige lys hulpstowwe

3. FARMASEUTIESE VORM

Filmbedekte tablette.
Wit tot afwit 22 mm by 10 mm langwerpige filmbedekte tablette met inkeeplyn.
Die inkeep is slegs om breek te vergemaklik vir die gemak van sluk en nie in gelyke dosisse te verdeel nie.

4. KLINIESE BESONDERHEDE

4.1. Terapeutiese indikasies

AUGSPEC 1 g word aangedui by volwassenes vir die behandeling van die volgende infeksies wat deur amoksisillien-weerstandige organismes veroorsaak word wat β-laktamases produseer wat sensitief is vir klavulaansuur (sien afdeling 4.2, afdeling 4.4 en afdeling 5.1)

- Boonste lugweginfeksies - soos sinusitis, herhalende otitis media, mangelontsteking
- Laer lugweginfeksies - soos brongitis en brongopneumonie
- Genito-urienweginfeksies - soos sistitis, uretritis, piëlonefritis
- Vel- en sagteweefselinfeksies.

AUGSPEC 1 g formulerings sal ook doeltreffend wees by die behandeling van infeksies veroorsaak deur amoksisillien-sensitiewe organismes teen die paslike amoksisilliendosis, omdat klavulaansuur in hierdie situasie nie tot die terapeutiese uitwerking bydra nie.

4.2. Posologie en metode van toediening

Posologie

Tydens toediening van amoksisillien is dit raadsaam om voldoende vloeistofinname en urinêre uitskeiding te onderhou om die moontlikheid van amoksisillienkristallurie te voorkom.

Algemene Inligting: Vir infeksies wat deur amoksisillien-sensitiewe organismes veroorsaak is, is die dosis dié soos vir amoksisillien goedgekeur, aangesien die komponent van klavulaansuur nie bydra tot die terapeutiese effek nie.

Volwassenes:
Vir ernstige infeksies, een AUGSPEC 1 g tablet elke 12 ure voor 'n maaltyd.

Spesiale populasies

Ingekorte nierfunksie:
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. Dosisaanpassings is gebaseer op die maksimum aanbevole vlak vir amoksisillien.
AUGSPEC 1 g moet nie gebruik word by pasiënte met 'n glomerulêre filtrasie tempo 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.

Bejaardes:
Geen dosis verandering word as noodsaaklik beskou.

Hepatiese inkorting:
Doseer met omsigtigheid en monitor die lewerfunksie met gereelde tussenposes (sien afdeling 4.3 en 4.4).

Metode van toediening

AUGSPEC 1 g is vir orale gebruik.
Tablette moet onmiddellik voor ete geneem word.

Doseringsgids:

Amoksisillien-Sensitiewe Organismes			
Boonste lugweg-infeksies	Onderste lugweg-infeksies	Urienweginfeksies	Vel- en sagteweefselinfeksies
Volwassenes:			
1 tablet 12-uurliks	1 tablet 12-uurliks	1 tablet 12-uurliks	1 tablet 12-uurliks

Amoksisillien-Weerstandige Organismes:			
Boonste lugweg-infeksies (Otitis media) *H. influenzae, H. parainfluenzae*	Onderste lugweg-infeksies (Otitis media) *H. influenzae, H. parainfluenzae*	Urienweginfeksies *E. coli, Klebsiella pneumoniae*	Vel- en sagteweefselinfeksies *Metisillien-sensitiewe Staphylococcus aureus*
Volwassenes:			
1 tablet 12-uurliks	1 tablet 12-uurliks	1 tablet 12-uurliks	1 tablet 12-uurliks

4.3. Kontraindikasies

AUGSPEC 1 g is teenaangedui in:

- Hipersensitiwiteit vir die aktiewe stowwe amoksisillien of klavulaansuur of vir enige van die hulpstowwe (sien afdeling 6.1).
- Hipersensitiwiteit vir penisilliene of kefalosporiene. Kruis-sensitiwiteit tussen penisilliene en kefalosporiene is goed gedokumenteer.
- AUGSPEC 1 g is teenaangedui by pasiënte met 'n vorige geskiedenis van amoksisillien/klavulaan-geassosieerde geelsug/hepatiese disfunksie (sien afdeling 4.8).

4.4. Spesiale waarskuwings en voorsorgmaatreëls vir gebruik

Voorskrywers moet die beginsels van antibiotika-rentmeesterskap nakom. Ernstige en soms noodlottige hipersensitiwiteitsreaksies (anafilaktiese reaksies) is aangemeld by pasiënte wat penisillienterapie ondergaan. Deeglike navrae aangaande vorige hipersensitiwiteitsreaksies teenoor penisilliene, kefalosporiene of ander allergene moet gedoen word, alvorens behandeling met AUGSPEC 1 g aanvang neem. Hoewel anafilakse meer dikwels voorkom na parenterale terapie, het dit voorgekom by pasiënte op mondelikse penisilliene. Hierdie reaksies is meer geneig om voor te kom by individue met 'n geskiedenis van penisillien-hipersensitiwiteit en/of 'n geskiedenis van sensitiwiteit teenoor meervoudige allergene. Daar was berigte van individue met 'n geskiedenis van penisillienhipersensitiwiteit, wat ernstige reaksies ervaar het as hulle met kefalosporiene behandel is.
As 'n allergiese reaksie plaasvind, moet AUGSPEC 1 g gestaak word en met die geskikte terapie begin word. Ernstige anafilaktiese reaksies mag onmiddelike noodbehandeling met adrenalien benodig. Suurstof, intraveneuse steroïede en bestuur van die lugweg, insluitend intubasie, mag ook benodig word

Ernstige kutane newe-effekte (SCAR), soos Stevens-Johnson-sindroom (SJS), toksiese epidermale nekrolise (TEN), geneesmiddelreaksie met eosinofilie en sistemiese simptome (DRESS) en akute veralgemeende eksantematiese pustulose (AVEP) is gerapporteer by pasiënte wat met beta-laktaam antibiotika behandel is. As SCAR vermoed word, moet beta-laktaam-antibiotika gestaak word.

In die geval dat dit bewys word dat 'n infeksie te wyte is aan 'n amoksisillien-vatbare organisme(s), moet dit oorweeg word om oorteskakel van amoksisillien/klavulaansuur na amoksisillien toe.

AUGSPEC 1 g is nie geskik vir gebruik as daar 'n groot risiko bestaan dat die veronderstelde patogene weerstandig is teen beta-laktaam-middels wat nie bemiddel word deur beta-laktamases wat vatbaar tot inhibisie deur klavulaansuur is nie. AUGSPEC 1 g moet nie gebruik word vir die behandeling van penisillien-weerstandige *S. pneumoniae* nie.

AUGSPEC 1 g moet vermy word indien aansteeklike mononukleose vermoed word, aangesien die voorkoms van 'n morbillivorme uitslag met die toestand geassosieer is na die gebruik van amoksisillien.

Konvulsies kan voorkom by pasiënte met ingekorte nierfunksie of by die wat hoë dosisse ontvang (sien afdeling 4.8)

Verlengde gebruik mag lei tot oorgroei van nie-gevoelige organismes. Pseudomembraneuse enterokolitis is gerapporteer. Die moontlikheid van superinfeksies met mikotiese of bakteriële patogene moet in gedagte gehou word tydens terapie. Indien superinfeksies voorkom (gewoonlik is *Aerobacter*, *Pseudomonas* of *Candida* teenwoordig), moet die middel gestaak word en/of geskikte terapie begin word

Die voorkoms tydens die aanvang van die behandeling van 'n koorsagtige eriteem wat verband hou met pustula kan 'n simptoom wees van akute veralgemeende-eksantheme pustulose (AGEP) (sien afdeling 4.8). Hierdie reaksie vereis dat AUGSPEC 1 g gestaak word en kontraindikeer die daaropvolgende toediening van amoksisillien.

Verlenging van protrombientyd is selde gerapporteer by pasiënte wat AUGSPEC 1 g ontvang.
Toepaslike monitering behoort onderneem te word wanneer antikoagulante gelyktydig voorgeskryf word.

Antibiotikum-geassosieerde kolitis, (insluitend pseudomembraneuse kolitis, hemorragiese kolitis *Clostridium difficile*-geassosieerde diarree (CDAD)), is aangemeld met byna alle antibakteriële middels, insluitend amoksisillien, en kan in erns wissel van lig tot lewensbedreigend (sien afdeling 4.8). Daarom is dit belangrik om hierdie diagnose te oorweeg by pasiënte met diarree tydens of na die toediening van enige antibiotika. Indien antibiotikum-geassosieerde kolitis voorkom, moet AUGSPEC 1 g onmiddellik gestaak word, 'n dokter geraadpleeg word en toepaslike behandeling geïnisieer word. Anti-peristaltiese middels is in hierdie situasie teenaangedui.

Omsigtigheid moet gebruik word wanneer amoksisillien aan pasiënte met sifilis toegedien word, aangesien die Jarisch-Herxheimer-reaksie in hierdie pasiënte mag voorkom..

Wanneer hoë dosisse toegedien word, moet voldoende vloeistofinname en urinêre uitskeiding gehandhaaf word.

Die natriuminhoud moet in ag geneem word by pasiënte met 'n natrium-beperkte dieet as die toediening van hoë dosisse benodig is.

AUGSPEC 1 g moet met sorg toegedien word aan pasiënte met limfatiese leukemie aangesien hulle veral vatbaar is vir veluitslag wat deur amoksisillien veroorsaak word.

Periodieke evaluasie van orgaanfunksie, insluitend renale-, hepatiese- en hematopoëtiese funksies word aanbeveel gedurende verlengde terapie.

Ingekorte lewerfunksie: Veranderings in lewerfunksietoetse is waargeneem by sommige pasiënte wat AUGSPEC 1 g ontvang het. Verbygaande hepatitis en cholestatiese geelsug is aangemeld. AUGSPEC 1 g moet met sorg gebruik word by pasiënte met bewys van hepatiese disfunksie. Hepatiese gebeure is hoofsaaklik by mans en bejaarde pasiënte gerapporteer en kan met langdurige behandeling geassosieer word. Hierdie gebeure is baie selde by kinders aangemeld. In alle populasies verskyn tekens en simptome gewoonlik tydens of kort na die behandeling, maar in sommige gevalle kan dit eers 'n paar weke nadat die behandeling gestaak is, sigbaar word. Dit is gewoonlik omkeerbaar. Hepatiese gebeure kan ernstig wees en in minder gereelde omstandighede, is sterftes aangemeld. Dit het byna altyd voorgekom by pasiënte met ernstige onderliggende siektes of wat gelyktydige medikasie gebruik wat bekend staan vir die potensiaal om hepatiese effekte te veroorsaak (sien afdeling 4.8).

Ingekorte nierfunksie: By pasiënte met matige of ernstige renale inkorting, moet die dosis AUGSPEC 1 g aangepas word (sien afdeling 4.2). AUGSPEC 1 g moet nie gebruik word by pasiënte met 'n glomerulêre filtrasie tempo van minder as 30 ml/minuut nie.

Gebruik tydens laktasie: Amoksisillien word in borsmelk uitgeskei; daar is geen data oor die uitskeiding van klavulaansuur in borsmelk nie. Wees dus versigtig wanneer AUGSPEC 1 g aan 'n borsvoedende vrou toegedien word (sien afdeling 4.6).

Die gebruik van AUGSPEC 1 g kan lei tot die seleksie van weerstandige stamme van organismes en daarom moet sensitiwiteitstoetse, waar moontlik, uitgevoer word om die toepaslikheid van terapie te verseker

Inmenging met serologiese toetse

Dit word aanbeveel dat ensiematiese glukose-oksidasemetodes gebruik word wanneer daar getoets word vir die teenwoordigheid van glukose in urine tydens die AUGSPEC 1 g behandeling.
As gevolg van die hoë urinêre-konsentrasies van amoksisillien, is vals-positiewe lesings algemeen by chemiese metodes.

Die teenwoordigheid van klavulaansuur in AUGSPEC 1 g kan 'n nie-spesifieke binding van IgG en albumien deur rooibloedselle veroorsaak, wat tot 'n vals positiewe Coombs-toets lei.

4.5 Interaksie met ander medisyne en ander vorme van interaksie

Probenesied verlaag die renale tubulêre sekresie van amoksisillien, maar affekteer nie klavulaansuur uitskeiding nie. Gelyktydige gebruik met AUGMENTIN kan verhoogde en verlengde amoksisillienbloedvlakke tot gevolg hê, maar nie van klavulaansuur nie.

AUGSPEC 1 g kan die doeltreffendheid van mondelikse voorbehoedmiddels verminder en pasiënte moet vervolgens gewaarsku word.

Die gelyktydige toediening van allopurinol en amoksisillien verhoog die voorkoms van veluitslae aansienlik by pasiënte wat albei middels ontvang in vergelyking met pasiënte wat amoksisillien alleen ontvang. Dit is nie bekend of hierdie verergering van amoksisillienuitslag plaasvind weens allopurinol of die hiperurisemie wat teenwoordig is by hierdie pasiënte nie.

Tetrasikliene en ander bakteriostatiese geneesmiddels mag inmeng met die bakterisidiese uitwerking van amoksisillien.

Mondelikse antikoagulante en penisillienantibiotika word in die praktyk wyd gebruik sonder gerapporteerde interaksie. In die literatuur is daar egter gevalle van verhoogde internasionale genormaliseerde verhoudings by pasiënte wat op asenokoumarol of warfarien instand gehou word, en ook 'n voorgeskrewe kursus amoksisillien ontvang. As gesamentlike-toediening nodig is, moet die protrombientyd of internasionale genormaliseerde verhouding noukeurig gemonitor word met die toevoeging of onttrekking van amoksisillien. Verder kan aanpassings in die mondelikse dosis van die antikoagulante nodig wees.

Penisilliene kan die uitskeiding van metotreksaat verminder, wat 'n potensiële toename in toksisiteit kan veroorsaak.

By pasiënte wat mikofenolaatmofetil ontvang, is 'n vermindering van die aktiewe metaboliet mikofenolsuur (MPA) van ongeveer 50 % voor die dosis gerapporteer na die aanvang van mondelikse amoksisillien plus klavulaansuur. Die verandering in die voor-dosis vlak kan die veranderinge in die totale blootstelling aan MPA moontlik nie akkuraat verteenwoordig nie. Daarom moet 'n verandering in die dosis mikofenolaatmofetil normaalweg nie nodig wees nie, aangesien daar geen kliniese bewyse van wanfunksionering van die ent is nie. Noukeurige kliniese monitering moet egter tydens die kombinasie en kort na die behandeling van antibiotika uitgevoer word.

Daar is verslae van positiewe toetsresultate met behulp van 'n Aspergillus OIB-toets by pasiënte wat amoksisillien/klavulaansuur ontvang het, waar dit daarna bevind is dat hulle vry is van Aspergillus-infeksie. Kruisreaksies met nie-Aspergillus polisakkariede en polifuranoses is gerapporteer. Daarom moet die positiewe toets van Aspergillus as gevolg van pasiënte wat amoksisillien/klavulaansuur ontvang, met versigtigheid geïnterpreteer word en met ander diagnostiese metodes bevestig word.

4.6. Vrugbaarheid, swangerskap en laktasie

Vroue in die vrugbare ouderdom/Voorbehoeding by mans en vroue.

Gelyktydige gebruik van AUGSPEC 1 g en mondelikse voorbehoedmiddels verminder die effektiwiteit van mondelikse voorbehoedmiddels. Pasiënte moet sterk aangeraai word om 'n alternatiewe of bykomende voorbehoedmiddel te gebruik tydens die gebruik van hierdie medisyne (sien afdeling 4.5).

Swangerskap

Die veiligheid en effektiwiteit van AUGSPEC 1 g tydens swangerskap is nie vasgestel nie (sien afdeling 4.3, afdeling 4.4 en/of afdeling 4.8).

Laktasie

Amoksisillien word in borsmelk versprei. Alhoewel daar nie ernstige probleme by mense gedokumenteer is nie, kan die gebruik van amoksisillien deur moeders wat borsvoed, lei tot sensitisasie, diarree, kandidiase en veluitslag by die baba.

Vrugbaarheid

Geen data beskikbaar.

4.7. Effekte op die vermoë om te bestuur en masjiene te gebruik

AUGSPEC 1 g het geen of 'm weglaatbare invloed op die vermoë om te bestuur en masjiene te gebruik. Ongewenste effekte kan egter voorkom (bv. allergiese reaksie, duiseligheid, konvulsies), wat die vermoë om te bestuur en masjiene te gebruik kan beïnvloed (sien afdeling 4.8).

4.8. Ongewenste effekte

a. Opsomming van die veiligheidsprofiel

Die algemeenste gerapporteerde newe-effekte (ADR's) is diarree, naarheid, braking, slegte spysvertering, abdominale pyn, veluitslae, urtikaria en eriteem multiforme, vaginitis, genitale moniliasis, abnormale smaak, hoofpyn, duiseligheid, moegheid en warm gloede.

Die voorkoms en erns van nadelige uitwerkings, veral naarheid en diarree, het toegeneem met die hoër aanbevole dosis en kan beperk word deur AUGMENTIN 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.

b. Opsomming van nadelige reaksies in tabelvorm

Stelsel orgaanklas	Frekwensie	Nadelige reaksies
Infeksies en besmettings	Gereeld	Mukokutaneuse kandidiasis
	Frekwensie onbekend	Oorgroei van nie-vatbare organismes Clostridium difficile
Bloed-en limfstelselafwykings	Minder gereeld	Hemolitiese anemie, omkeerbare trombositopenie, trombositopeniese purpura, eosinofilie, omkeerbare leukopenie (insluitend neutropenie) en agranulositose.
	Frekwensie onbekend	Verlenging van bloedingstyd en protrombientyd.
Immuunstelselafwykings	Minder gereeld	Hipersensitiwiteitsreaksies (veluitslag, pruritus en urtikaria, serumsiekte-agtige sindroom, angio-edeem, eriteem multiforme, Stevens-Johnson-sindroom, hipersensitiwiteitsvaskulitis en minder gereeld bulleuse eksfoliatiewe dermatitis, akute veralgemeende eksantematiese pustulose (AGEP) en toksiese epidermale nekrolise is gerapporteer).
	Frekwensie onbekend	Hipersensiteits-interstisiële nefritis, angioneurotiese edeem, serum siek-agtige sindroom, hipersensitiwiteits vaskulitis.
Senuweestelsel afwykings	Gereeld	Disgeusie, moegheid, koors, kouekoors.
	Minder gereeld	Hiperaktiwiteit, konvulsies, duiseligheid, hoofpyn, SSS-toksisiteit.
	Frekwensie onbekend	Aseptiese meningitis
Gastro-intestinale afwykings	Gereeld	Diarree, naarheid, braking, slegte spysvertering, abdominale pyn.
	Minder gereeld	Gastritis, stomatitis, glossitis, enterokolitis, mukokutaneuse kandidiasis, antibiotikum-geassosieerde kolitis (insluitende pseudomembraneuse kolitis en hemoragiese kolitis)
	Frekwensie onbekend	Oppervlakkige tandverkleuring, swart harige tong
Hepatiese-biliêre afwykings	Minder gereeld	Verhogings in AST en/of ALT
	Frekwensie onbekend	Hepatitis en cholestatiese geelsug.
Vel- en subkutane weefsel afwykings	Minder gereeld	Veluitslag, pruritis, urtikaria en eriteem multiforme.
	Frekwensie onbekend	Purpura, diaforese, spoeling, petechiae, Stevens-Johnson-sindroom, toksiese epidermale nekrolise, Bulleuse eksfoliatiewe dermatitis, akute veralgemeende eksantematiese pustulose (AGEP), geneesmiddelreaksie met eosinofilie en sistemiese sindroom (DRESS)
Renale en urinere afwykings	Minder gereeld	Kristallurie
	Frekwensie onbekend	Nefropatie en interstisiële nefritis

Aanmelding van vermoedelike nadelige reaksies

Dit is belangrik om newe-effekte wat vermoed word na die medisyne gemagtig is, te rapporteer.
Dit laat die voortgesette monitering van die voordeel/risiko-balans van die medisyne toe.
Gesondheidsverskaffers word gevra om enige vermoedens van newe-effekte aan te meld by SAHPRA deur die "6.04 Adverse Drug Reaction Reporting Form", wat aanlyn gevind word onder SAHPRA se publikasies: https://www.sahpra.org.za/Publications/Index/8

4.9. Oordosering

Simptome: Oordosering met amoksisillien is gewoonlik asimptomaties. Gastroïntestinale effekte soos naarheid, braking en diarree mag egter voorkom en simptome van water- en elektrolietbalans behoort simptomaties behandel te word. Amoksisillienkristallurie is waargeneem, wat in sommige gevalle tot nierversaking lei.

Konvulsies kan voorkom by pasiënte met ingekorte nierfunksie of by die wat hoë dosisse ontvang.

Genoegsame vloeistof inname en urinêre uitskeiding moet gehandhaaf word om die moontlikheid van kristalurie te minimaliseer.

Amoksisillien kan uit die bloedsomloopstelsel verwyder word deur hemodialise. Die molekulêre gewig, mate van proteïenbinding en farmakokinetiese profiel van klavulaansuur, saam met inligting van 'n enkele pasiënt met renale ontoereikendheid, dui alles daarop dat hierdie verbinding ook deur hemodialise verwyder kan word.

5. FARMAKOLOGIESE EIENDOMME

5.1. Farmakodinamiese eienskappe

A 20.1.2 Penisilliene
Amoksisillien/Klavulaansuur tablette bevat 7 dele (875 mg) van 'n breëspektrum penisillien, amoksisillien en 1 deel (125 mg) van kaliumklavulaanaat.

(i) Meganisme van aksie

Amoksisillien is 'n semisintetiese penisillien (beta-laktaam-antibiotika) wat een of meer penisillienbindende proteïene in die biosintetiese weg van bakteriële peptidoglikaan inhibeer, wat lei tot die verswakking van die selwand, wat gewoonlik gevolg word deur sellisering en dood. Amoksisillien is vatbaar vir afbraak deur beta-laktamases wat deur weerstandbiedende bakterieë geproduseer word, en daarom bevat die spektrum van aktiwiteit van amoksisillien alleen nie organismes wat hierdie ensieme produseer nie. Klavulaansuur is 'n beta-laktaam wat struktureel verwant is aan penisillien. Dit deaktiveer sommige beta-laktamase-ensieme, wat die amoksisillien inaktiveer.

Daar is getoon dat kaliumklavulaanaat *in vitro* 'n onomkeerbare remmer van beta-laktamases is.

Kaliumklavulaanaat inaktiveer nie die chromosoombeheerde (Sykes tipe 1 kefalosporinase) β-laktamases wat deur *Acinetobacter* spesies, *Citrobacter* spesies, *Enterobacter*, indool-positiewe *Proteus*, *Providencia* spesies en *Serratia marcescens* geproduseer word nie. *In vitro* het die formulering sinergisme teen amoksisillien-weerstandige organismes getoon, sonder bewyse van antagonisme, en die aktiwiteit is nie verminder in die teenwoordigheid van serum nie. (*In vitro*-aktiwiteit impliseer nie noodwendig effektiwiteit *in vivo* nie).

(ii) Bakterisidiese aksie

Die amoksisillienkomponent van die formulerings oefen 'n bakteriedodende werking teen baie stamme van Gram-positiewe en Gram-negatiewe organismes uit. Die klavulaansuurkomponent het baie min bakterisidiese werking. Dit beskerm egter amoksisillien, deur gevoelige β-laktamases te inaktiveer, teen afbreking deur 'n groot aantal β-laktamase ensieme wat deur penisillien-weerstandige stamme van organismes geproduseer word.

Weerstand

Die voorkoms van weerstandigheid kan vir geselekteerde spesies geografies en mettertyd wissel, en plaaslike inligting oor weerstand is wenslik, veral wanneer ernstige infeksies behandel word. Indien nodig, moet kundige advies ingewin word wanneer die plaaslike weerstand so groot is dat die nut van die middel in ten minste sommige soorte infeksies bevraagteken kan word.

MRSA (*Staphylococcus aureus*-organismes wat bestand is teen metisillien)
Inherente weerstandbiedende organismes:
Aërobiese gram-negatiewe mikro-organismes
Acinetobacter sp. Citrobacter freundii Enterobacter sp.
Legionella pneumophila Morganella morganii Providencia spp.
Pseudomonas sp.
Serratia sp.
Stenotrophomonas maltophilia
Ander mikro-organismes:
Chlamydophila pneumoniae
Chlamydophila psittaci
Coxiella burnetti
Mycoplasma pneumoniae

5.2. Farmakokinetiese eienskappe

Absorpsie

Amoksisillien en klavulaansuur word volledig gedisosieer in waterige oplossing by fisiologiese pH. Albei komponente word vinnig en goed geabsorbeer deur die mondelikse toedieningsweg. Na mondelikse toediening is amoksisillien en klavulaansuur ongeveer 70 % biobeskikbaar. Die plasmaprofiele van albei komponente is dieselfde en die tyd tot die maksimum plasmakonsentrasie (T_{max}) is in elk geval ongeveer een uur. Amoksisillien- en klavulaansuur-serumkonsentrasies wat met amoksisillien/klavulaansuur bereik word, is soortgelyk aan dié wat deur die orale toediening van gelykstaande dosisse amoksisillien of klavulaansuur alleen geproduseer word.

Die farmakokinetika van amoksisillien en klavulaansuur is nou verwant en nie een word deur die teenwoordigheid van voedsel in die maag nadelig beïnvloed nie. Na 'n mondelikse dosis van 2 dele amoksisillien en 1 deel klavulaansuur (Amoksisillien/klavulaansuur 375 mg), met die aanvang van 'n maal, is 'n gemiddelde piek serumvlak van 5,7 µg amoksisillien en 3,8 µg klavulaansuur per milliliter binne een uur by gesonde vrywilligers bereik. Verdubbeling van die dosis verdubbel feitlik die piek serumvlak.

Verspreiding

Ongeveer 25 % van die totale plasma-klavulaansuur en 18 % van die totale plasma amoksisillien is gebonde aan proteïene. Die skynbare verspreidingsvolume is ongeveer 0,3 – 0,4 l/kg vir amoksisillien en rondom 0,2 l/kg vir klavulaansuur.

Na intraveneuse toediening is beide amoksisillien en klavulaansuur in die galblaas, buikweefsel, vel, vet, spierweefsel, sinoviale- en peritoneale vloeistowwe, gal en etter gevind.

Amoksisillien versprei nie voldoende in die serebrospinale vloeistof nie.

Uit dierstudies is daar geen bewyse vir beduidende weefselretensie van geneesmiddel-afgeleide materiaal vir enige komponent nie. Amoksisillien, soos die meeste penisilliene, kan in borsmelk opgespoor word. Spoorhoeveelhede klavulaansuur kan ook in borsmelk opgespoor word (sien afdeling 4.6).

Biotransformasie

Die hoof roete van eliminasie van amoksisillien is via die niere, terwyl vir klavulaansuur is dit deur middel van renale- en nie-renalemeganismes. Amoksisillien word gedeeltelik in die urine uitgeskei as die onaktiewe penisilloïensuur in hoeveelhede gelykstaande aan 10 tot 25 % van die aanvanklike dosis. Klavulaansuur word op grootskaal by die mens gemetaboliseer en word in urine en ontlasting uitgeskei en as koolstofdioksied in lug wat uitgeasem is.

Eliminasie

64,9 % amoksisillien en 37,5 % klavulaansuur word onveranderd binne die eerste 6 uur na 'n mondelikse dosis van 2 tot 1 amoksisillien/klavulaansuur tablette, in die urien uitgeskei. Gelyktydige toediening van probenesied het min uitwerking op die uitskeiding van die klavulaansuurbestanddeel van die formulering.

Renale inkorting

Die totale serumopreiming van amoksisillien/klavulaansuur neem proporsioneel af met afnemende renale funksie. Die vermindering van geneesmiddelopruiming is meer uitgesproke vir amoksisillien as vir klavulaansuur, aangesien 'n hoër persentasie amoksisillien via die renaleroete uitgeskei word. Dosisse in renale inkorting moet dus onnodige ophoping van amoksisillien voorkom, terwyl voldoende vlakke van klavulaansuur gehandhaaf word. (sien afdeling 4.2).

Hepatiese inkorting

Pasiënte met hepatiese inkorting moet met omsigtigheid gedoseer word en die lewerfunksie moet gereeld gemonitor word.

5.3 Prekliniese veiligheidsdata

Prekliniese data toon geen spesiale gevaar vir mense op grond van konvensionele studies van veiligheidsfarmakologie, genotoksisiteit en toksisiteit vir voortplanting nie. Daar is nie karsinogenisiteitstudies met amoksisillien/klavulaansuur gedoen nie.

6. FARMASEUTIESE BESONDERHEDE

6.1. Lys van hulpstowwe

Basiese butileerde metakrilaatkopolimeer (Eudragit E 12.5)
Natriumkroskarmellose (E468)
Krospovidoon Tipe A (E1202)
Makrogol 6000
Magnesiumstearaat (E470b)
Mikrokristallynesellulose (E460)
Watervrye kolloïdale silika (E551)
Talk (E553b)
Titaandioksied (E171)

6.2. Onverenigbaarede

Nie van toepassing.

6.3. Raklewe

2 jaar

6.4. Spesiale voorsorgmaatreëls vir berging

Bere by of onder 25 °C. Beskerm teen lug en vog.
Hou stulpverpakking in die buitenste karton totdat dit benodig word.

6.5. Aard en inhoud van die houer

Stulpverpakking basis-foelie wat uit OPA/Al/PVC bestaan, wat met aluminiumdekselfolie verseël is.
Elke stulpstrook bevat 5 tablette. Pakgrootte van 10 tablette.

6.6. Spesiale voorsorgmaatreëls vir wegdoening van 'n gebruikte medisyne of afvalstowwe wat van sodanige medisyne verkry word, en ander hantering van die produk

Geen spesiale vereistes nie.

7. HOUER VAN DIE SERTIFIKAAT VAN REGISTRASIE

TRINITY PHARMA (PTY) LTD
106 16de Weg, Gebou 2, Midrand, 1686, Suid-Afrika

8. REGISTRASIE NOMMER(S)

52/20.1.2/0777.776

9. DATUM VAN EERSTE MAGTIGING/HERNUWING VAN DIE MAGTIGING

Datum van eerste magtiging: 30 Maart 2021

10. DATUM VAN HERSIENING VAN DIE TEKS

N.A