AUGMENTIN TABLETS

SCHEDULING STATUS:

S4

PROPRIETARY NAMES AND DOSAGE FORM:

AUGMENTIN BD tablets

AUGMENTIN SR tablets

COMPOSITION:

AUGMENTIN BD:

White/off-white, capsule-shaped, scored, film-coated tablets containing amoxicillin trihydrate equivalent to 875 mg amoxicillin and potassium clavulanate equivalent to 125 mg clavulanic acid.

Excipients:

The tablet core contains colloidal anhydrous silica, magnesium stearate, microcrystalline cellulose and sodium starch glycollate.

The film-coat contains titanium dioxide (E171), hydroxypropyl methylcellulose, polyethylene glycol and silicone oil.

Sugar-free.

AUGMENTIN SR:

White, capsule-shaped, film-coated, bilayered tablets. Amoxicillin trihydrate equivalent to 562,5 mg amoxicillin and potassium clavulanate equivalent to 62,5 mg clavulanic acid are contained in the "Immediate Release" layer. Amoxicillin sodium equivalent to 437,5 mg amoxicillin is contained in the "Sustained Release" (SR) layer. The tablet strength is 1000 mg/62,5 mg, based on the overall amoxicillin/clavulanate content.

Excipients:

The tablet core contains citric acid, colloidal anhydrous silica, magnesium stearate, microcrystalline cellulose, sodium starch glycollate and xanthan gum.

The film-coat contains titanium dioxide (E171), hydroxypropyl methylcellulose and polyethylene glycol.

Sugar-free.

PHARMACOLOGICAL CLASSIFICATION:

A 20.1.2 Penicillins

PHARMACOLOGICAL ACTION:

(a) Bacteriology:

(i) Spectrum - AUGMENTIN is the group name for formulations containing 7 and 16 parts of a broad spectrum penicillin, amoxicillin and 1 part of potassium clavulanate. Potassium clavulanate has been shown *in vitro* to be an irreversible inhibitor of beta-lactamases produced by *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Proteus vulgaris*, *Haemophilus influenzae*, *Neisseria gonorrhoeae* and *Bacteroides fragilis*. 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 exert a bactericidal action against many strains of 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.

AUGMENTIN SR is a sustained release tablet that provides an extended amoxicillin pharmacokinetic profile.

(b) Absorption:

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 2 parts amoxicillin and 1 part clavulanic acid, 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.

(c) Excretion:

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.

INDICATIONS:

AUGMENTIN formulations are indicated for the treatment of infections caused by amoxicillin-resistant organisms producing β-lactamases sensitive to clavulanic acid:

Upper respiratory tract infections, such as sinusitis, recurrent otitis media, tonsillitis.

Lower respiratory tract infections, such as bronchitis and bronchopneumonia.

Genito-urinary tract infections, such as cystitis, urethritis, pyelonephritis.

Skin and soft tissue infections.

AUGMENTIN 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.

AUGMENTIN SR is indicated for the treatment of respiratory tract infections, e.g. community-acquired pneumonia, acute exacerbations of chronic bronchitis and acute bacterial sinusitis, typically caused by *Streptococcus pneumoniae.*

CONTRA-INDICATIONS:

Hypersensitivity to penicillins or to cephalosporins. Cross-sensitivity between penicillins and cephalosporins is well documented.

AUGMENTIN is contra-indicated in patients with a previous history of amoxicillin/clavulanic-associated jaundice/hepatic dysfunction.

WARNINGS AND SPECIAL PRECAUTIONS:

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy. Before initiating therapy with AUGMENTIN, 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, AUGMENTIN 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.

Since AUGMENTIN contains amoxicillin, an aminopenicillin, it is not the treatment of choice in patients presenting with sore throat or pharyngitis because of the possibility that the underlying cause is infectious mononucleosis, in the presence of which there is

a high incidence of morbilliform rash if amoxicillin is used. AUGMENTIN should be avoided if infectious mononucleosis is suspected.

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.

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

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

Impaired hepatic function: Changes in liver function tests have been observed in some patients receiving AUGMENTIN. Transient hepatitis and cholestatic jaundice has been reported. AUGMENTIN should be used with caution in patients with evidence of hepatic dysfunction.

Impaired renal function: In patients with moderate or severe renal impairment AUGMENTIN dosage should be adjusted (see DOSAGE AND DIRECTIONS FOR USE). AUGMENTIN BD should not be used in patients with a glomerular filtration rate of less than 30 ml/minute. AUGMENTIN SR is not recommended in patients with creatinine clearance <30 ml/minute and in haemodialysis patients.

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.

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

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 AUGMENTIN is administered to a nursing woman.

The use of AUGMENTIN may lead to the selection of resistant strains of organisms and sensitivity testing should, therefore, be carried out whenever possible, to demonstrate the appropriateness of therapy.

INTERACTIONS:

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

AUGMENTIN may reduce the efficacy of oral contraceptives and patients should be warned accordingly.

The concomitant administration of allopurinol and amoxicillin substantially increases the incidence of skin rashes in patients receiving both agents as compared to patients

receiving amoxicillin alone. It is not known whether this potentiation of amoxicillin 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.

Interaction with laboratory tests:

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

PREGNANCY AND LACTATION:

Use in pregnancy: The safety of AUGMENTIN in pregnancy has not been established.

Use in lactation: Amoxicillin is distributed into breast milk. Although significant problems in humans have not been documented, the use of amoxicillin by nursing mothers may lead to sensitisation, diarrhoea, candidiasis and skin rash in the infant.

DOSAGE AND DIRECTIONS FOR USE:

Tablets should be taken immediately before a meal.

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.

Dosages:

General Information: For infections caused by amoxicillin-sensitive organisms the dosage is that approved for amoxicillin as the clavulanic acid component does not contribute to the therapeutic effect.

Adult:

For severe infections and infection of the respiratory tract, the dose should be one AUGMENTIN BD tablet every 12 hours at the start of a meal.

AUGMENTIN SR is only indicated for use in adults, aged 16 or over. Two tablets of AUGMENTIN SR are to be taken orally twice a day.

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.

AUGMENTIN BD 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.

AUGMENTIN SR:

No adjustment in dosage is required in patients with creatinine clearance ≥30 ml/minute. AUGMENTIN SR is not recommended in patients with creatinine clearance <30 ml/minute. AUGMENTIN SR is not recommended in haemodialysis patients.

Dosage Guide:

AMOXICILLIN-SENSITIVE ORGANISMS

PRODUCT	**UPPER RESPIRATORY TRACT INFECTIONS**	**LOWER RESPIRATORY TRACT INFECTIONS**	**URINARY TRACT INFECTIONS**	**SKIN & SOFT TISSUE INFECTIONS**
ADULTS:				
AUGMENTIN BD	1 tablet 12-hourly	1 tablet 12-hourly	1 tablet 12-hourly	1 tablet 12-hourly

AMOXICILLIN-RESISTANT ORGANISMS

PRODUCT	**UPPER RESPIRATORY TRACT INFECTIONS (otitis media)** ***H. influenzae, H. parainfluenzae***	**LOWER RESPIRATORY TRACT INFECTIONS (bronchitis)** ***H. influenzae, H. parainfluenzae***	**URINARY TRACT INFECTIONS** ***E. coli, Klebsiella pneumoniae***	**SKIN & SOFT TISSUE INFECTIONS** ***Staphylococcus aureus***
ADULTS:				
AUGMENTIN BD	1 tablet 12-hourly	1 tablet 12-hourly	1 tablet 12-hourly	1 tablet 12- hourly

AUGMENTIN SR:

Community acquired pneumonia	2 tablets 12-hourly for 7 to 10 days
Acute exacerbations of chronic bronchitis	2 tablets 12-hourly for 7 days
Acute bacterial sinusitis	2 tablets 12-hourly for 10 days

SIDE EFFECTS:

The most frequently reported adverse effects 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 AUGMENTIN at the start of a meal. In addition, as these symptoms are especially related to the potassium clavulanate component, where these gastrointestinal symptoms occur and a higher concentration of amoxicillin is required, consideration should be given to administering the additional amoxicillin separately.

The following adverse reactions have been reported and may occur with AUGMENTIN**:**

Hypersensitivity reactions: Skin rashes, pruritus and urticaria, serum sickness-like syndrome, erythema multiforme, rare cases of Stevens-Johnson syndrome, hypersensitivity vasculitis and less frequently bullous exfoliative dermatitis, acute generalised exanthematous pustulosis (AGEP) and toxic epidermal necrolysis have been reported. Whenever such reactions occur, AUGMENTIN should be discontinued. Serious and occasional fatal hypersensitivity (anaphylactic) reactions and angioneurotic oedema can occur with oral penicillin (see WARNINGS AND SPECIAL PRECAUTIONS).

Interstitial nephritis can occur rarely.

Gastrointestinal reactions: Nausea, vomiting, diarrhoea, gastritis, stomatitis, glossitis, black 'hairy' tongue, enterocolitis, mucocutaneous candidiasis and antibiotic-associated colitis (including pseudomembranous colitis and haemorrhagic colitis). If gastrointestinal reactions are evident, they may be reduced by taking AUGMENTIN at the start of a meal.

Hepatic effects: Hepatitis and cholestatic jaundice have been reported. The events may be severe and occur predominantly in adult or elderly patients. Signs and symptoms usually occur during or shortly after treatment, but in some cases may not become apparent until several weeks after treatment has ceased. The hepatic events are usually reversible. However, in extremely rare circumstances, death has been reported. These have almost always been cases associated with serious underlying disease or concomitant medication.

A moderate rise in aspartate transaminase (AST) and/or alanine transaminase (ALT) has been noted in patients treated with AUGMENTIN, but the significance of these findings is unknown.

Renal effects: Crystalluria has been reported.

Haematological effects: Haemolytic anaemia, reversible thrombocytopenia, thrombocytopenic purpura, eosinophilia, reversible leucopenia (including neutropenia)

and agranulocytosis have been reported. These reactions are usually reversible on discontinuation of therapy and are believed to be hypersensitivity phenomena. A slight thrombocytosis was noted in less than 1 % of the patients treated with AUGMENTIN. Prolongation of bleeding time and prothrombin time have also been reported less frequently. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly.

CNS effects: CNS effects have been seen rarely. These include reversible hyperactivity, dizziness, headache and convulsions. Convulsions may occur with impaired renal function or in those receiving high doses.

Miscellaneous: Superficial tooth discolouration has been reported. It can usually be removed by brushing.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Overdosage with amoxicillin is usually asymptomatic. However, gastrointestinal effects such as nausea, vomiting and diarrhoea may be evident and symptoms of water and electrolyte imbalance should be treated symptomatically.

Adequate fluid intake and urinary output must be maintained to minimise the possibility of crystalluria.

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

IDENTIFICATION:

AUGMENTIN BD:	White to off-white capsule-shaped, film-coated tablets, monogrammed with a breakline on one side.
AUGMENTIN SR:	White capsule-shaped, film-coated tablets, debossed with ‘AC 1000/62.5’ on one side and a bisect breakline on the other side.

PRESENTATION:

AUGMENTIN BD: The 10's pack consists of one aluminium pouch, containing a desiccant and a blister strip of 10 tablets packed into an outer carton. The blister is composed of a transparent PVC/PVdC laminate and grey aluminium foil.

AUGMENTIN SR: Aluminium/aluminium blister strips with one or two film-coated tablets per blister pocket packed into an outer carton.

STORAGE INSTRUCTIONS:

AUGMENTIN BD:

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

DO NOT REMOVE DESICCANT.

Keep out of reach of children.

AUGMENTIN SR:

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

Keep out of reach of children.

REGISTRATION NUMBER:

AUGMENTIN BD tablets: 32/20.1.2/0239

AUGMENTIN SR tablets: 36/20.1.2/0288

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

GlaxoSmithKline South Africa (Pty) Ltd

39 Hawkins Avenue

Epping Industria 1, 7460

DATE OF PUBLICATION OF THIS PACKAGE INSERT:

Date of registration:

Augmentin BD: 07 April 1999

Augmentin SR: 28 May 2004

Date of last revision: 27 February 2004

Date compliant with Regulation 11: 02 February 2016

MDS7

MANUFACTURER:

Augmentin BD:

SmithKline Beecham Pharmaceuticals, Clarendon Road, Worthing, West Sussex BN14 8QH, UK

Augmentin SR:

Glaxo Wellcome Production, ZI de la Peyennière, 53100 Mayenne, France

Botswana:

Augmentin BD tablets - Reg No. BOT0400723 S2

Augmentin SR tablets - Reg No. BOT0701010 S2

Namibia:

Augmentin BD tablets - Reg No. 04/20.1.2/0897 NS2

Augmentin SR tablets - Reg No. 04/20.1.2/1734 NS2

Zambia:

Augmentin BD tablets – Reg No. 179/037 POM

Zimbabwe:

Augmentin BD tablets - Reg No. 2001/7.1.2/3960 PP

Augmentin SR tablets – Reg No. 2014/7.1.2/4931 PP

SKEDULERINGSTATUS:

S4

EIENDOMSNAAM EN DOSEERVORM:

AUGMENTIN BD tablette

AUGMENTIN SR tablette

SAMESTELLING:

AUGMENTIN BD:

Wit/naaswit, kapsuulvormige, gekeepte, filmbedekte tablette wat amoksisillientrihidraat gelykstaande aan 875 mg amoksisillien en kaliumklavulanaat gelykstaande aan 125 mg klavulaansuur bevat.

Mengmiddels:

Die pit van die tablet bevat kolloïdale anhidriese silika, magnesiumstearaat, mikrokristallyne sellulose en natriumstyselglikolaat.

Die filmbedekking bevat titaandioksied (E171), hidroksipropielmetiel-sellulose, poliëtileenglikol en silikoonolie.

Suikervry.

AUGMENTIN SR:

Wit, kapsuulvormige, filmbedekte, twee-laag tablette. Die “Vinnige Vrystelling” laag bevat amoksisillientrihidraat gelykstaande aan 562,5 mg amoksisillien en kaliumklavulanaat gelykstaande aan 62,5 mg klavulaansuur. Die “Volgehoue Vrystelling” (“Sustained Release” (SR)) laag bevat natriumamoksisillien gelykstaande aan 437,5 mg amoksisillien. Die sterkte van die tablette is 1000 mg/62,5 mg gegrond op die algehele amoksisillien/klavulaansuur inhoud.

Mengmiddels:

Die pit van die tablet bevat sitroensuur, kolloïdale anhidriese silika, magnesiumstearaat, mikrokristallyne sellulose, natriumstyselglikolaat en xantaangom.

Die filmbedekking bevat titaandioksied (E171), hidroksipropielmetiel-sellulose en poliëtileenglikol.

Suikervry.

FARMAKOLOGIESE KLASSIFIKASIE:

A 20.1.2 Penisilliene

FARMAKOLOGIESE WERKING:

(a) Bakteriologie:

(i) Spektrum - AUGMENTIN is die groepnaam vir formulerings wat 7 en 16 dele van 'n breëspektrumpenisillien, amoksisillien, en 1 deel kaliumklavulanaat bevat. Kaliumklavulanaat het *in vitro* getoon dat dit 'n onomkeerbare inhibeerder is van beta-laktamases, geproduseer deur *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Proteus vulgaris*, *Haemophilus influenzae*, *Neisseria gonorrhoeae* en *Bacteroides fragilis*. Kaliumklavulanaat 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 met geen bewyse van antagonisme nie en die uitwerking is nie deur die teenwoordigheid van serum verminder nie. (*In vitro*-aktiwiteit impliseer nie noodwending *in vivo*-doeltreffendheid nie).

(ii) Bakterisidiese werking - 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.

AUGMENTIN SR is ’n tablet met volgehoue vrystelling wat ’n uitgebreide amoksisillien farmakokinetiese profiel verskaf.

(b) Absorpsie:

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 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 dosis verdubbel feitlik die piek serumvlak.

(c) Uitskeiding:

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.

INDIKASIES:

AUGMENTIN formulerings word aangedui vir die behandeling van infeksies, veroorsaak deur amoksisillien-weerstandige organismes wat β-laktamases produseer wat gevoelig is vir klavulaansuur:

Boonste lugweginfeksies, soos sinusitis, terugkerende otitis media, tonsillitis.

Onderste lugweginfeksies, soos brongitis en bronchopneumonie.

Genito-urienweginfeksies, soos sistitis, uretritis, piëlonefritis.

Vel- en sagteweefselinfeksies.

AUGMENTIN 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.

AUGMENTIN SR word aangedui vir die behandeling van infeksies van die respiratoriese stelsel, bv. gemeenskapsverworwe pneumonie, akute verergerings van chroniese brongitis en akute bakteriële sinusitis, wat tipies deur *Streptococcus pneumoniae* veroorsaak word.

KONTRA-INDIKASIES:

Hipersensitiwiteit teenoor penisilliene en kefalosporiene. Kruis-sensitiwiteit tussen penisilliene en kefalosporiene is goed gedokumenteer.

AUGMENTIN word teenaangedui by pasiënte met 'n vorige geskiedenis van amoksisillien/klavulaniese-verbandhoudende geelsug/hepatiese disfunksie.

WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS:

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 AUGMENTIN 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 penisillien-hipersensitiwiteit, wat ernstige reaksies ervaar het as hulle met kefalosporiene behandel is. As 'n allergiese reaksie plaasvind, moet AUGMENTIN 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.

Aangesien AUGMENTIN amoksisillien, 'n aminopenisillien bevat, is dit nie die behandeling van keuse by pasiënte wat presenteer met keelseer of faringitis nie weens die moontlikheid dat die onderliggende oorsaak infektiewe mononukleose kan wees, in die teenwoordigheid

waarvan daar ’n hoë voorkoms van maselagtige uitslag is as amoksisillien gebruik word. AUGMENTIN moet vermy word indien infektiewe mononukleose vermoed word.

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.

Verlenging van protrombien-tyd is selde gerapporteer in pasiënte wat AUGMENTIN ontvang. Toepaslike monitering behoort onderneem te word wanneer antikoagulante gesamentlik voorgeskryf 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 AUGMENTIN ontvang het. Verbygaande hepatitis en cholestatiese geelsug is aangemeld. AUGMENTIN moet met sorg gebruik word by pasiënte met bewys van hepatiese disfunksie.

Ingekorte nierfunksie: By pasiënte met matige of ernstige renale inkorting moet die dosis AUGMENTIN aangepas word (sien DOSIS EN GEBRUIKSAANWYSINGS). AUGMENTIN BD moet nie gebruik word by pasiënte met ’n glomerulêre filtrasie tempo van minder as 30 ml/minuut nie. AUGMENTIN SR word nie in pasiënte met kreatienopruiming <30 ml/minuut en in hemodialise pasiënte aanbeveel nie.

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 vloeistof inname en urinêre uitskeiding gehandhaaf word.

Die natriuminhoud moet in ag geneem word in pasiënte wat op ’n natrium-beperkte dieet is as die toediening van hoë dosisse noodsaaklik is.

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

Gebruik tydens laktasie: Amoksisillien word in borsmelk uitgeskei; daar bestaan geen data oor die uitskeiding van klavulaansuur in borsmelk nie. Daarom behoort versigtigheid aan die dag gelê te word wanneer AUGMENTIN toegedien word aan ’n borsvoedende vrou.

Die gebruik van AUGMENTIN 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.

INTERAKSIES:

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.

AUGMENTIN 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 amoksisillien-uitslag 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.

Interaksie met laboratorium toetse:

Dit word aanbeveel dat wanneer daar getoets word vir die aanwesigheid van glukose in urien gedurende AUGMENTIN behandeling, ensiematiese glukose oksidase metodes gebruik behoort te word. As gevolg van die hoë urinêre konsentrasies van amoksisillien is vals positiewe lesings met chemiese metodes algemeen.

SWANGERSKAP EN LAKTASIE:

Gebruik gedurende swangerskap: Die veiligheid van AUGMENTIN gedurende swangerskap is nie vasgestel nie.

Gebruik gedurende laktasie: Amoksisillien word in borsmelk versprei. Alhoewel betekenisvolle probleme in die mens nie gedokumenteer is nie, mag die gebruik van amoksisillien deur borsvoedende moeders lei tot sensitisasie, diarree, kandidiase en veluitslag in die baba.

DOSIS EN GEBRUIKSAANWYSINGS:

Tablette moet onmiddellik voor ’n maaltyd geneem word.

Tydens die toediening van amoksisillien is dit raadsaam om toereikende vloeistofinname en urinêre uitskeiding te onderhou om die moontlikheid van amoksisillien-kristalurie te vermy.

Doserings:

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

Volwassenes:

Vir ernstige infeksies en infeksie van die respiratoriese kanaal, is die dosis een AUGMENTIN BD tablet elke 12 uur by die aanvang van 'n maaltyd.

AUGMENTIN SR word slegs vir gebruik in volwassenes van 16 jaar of ouer aangedui. Twee tablette AUGMENTIN SR moet twee keer per dag mondeliks geneem word.

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.

AUGMENTIN BD 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.

AUGMENTIN SR:

Geen dosisaanpassing word in pasiënte met kreatienopruiming ≥30 ml/minuut benodig nie.

AUGMENTIN SR word nie in pasiënte met kreatienopruiming <30 ml/minuut aanbeveel nie.

AUGMENTIN SR word nie in hemodialise pasiënte aanbeveel nie.

Doseringsgids:

AMOKSISILLIEN-SENSITIEWE ORGANISMES

PRODUK	**BOONSTE LUGWEG-INFEKSIES**	**ONDERSTE LUGWEG-INFEKSIES**	**URIENWEG-INFEKSIES**	**VEL- EN SAGTE-WEEFSELINFEKSIES**
VOLWASSENES:				
AUGMENTIN BD	1 tablet 12-uurliks	1 tablet 12-uurliks	1 tablet 12-uurliks	1 tablet 12-uurliks

AMOKSISILLIEN-WEERSTANDIGE ORGANISMES

PRODUK	BOONSTE LUGWEG-INFEKSIES (otitis media) *H. influenzae, H. parainfluenzae*	ONDERSTE LUGWEG-INFEKSIES (brongitis) *H. influenzae, H. parainfluenzae*	URIENWEG-INFEKSIES *E. coli, Klebsiella pneumoniae*	VEL- EN SAGTE-WEEFSELINFEKSIES *Staphylococcus aureus*
VOLWASSENES:				
AUGMENTIN BD	1 tablet 12-uurliks	1 tablet 12-uurliks	1 tablet 12-uurliks	1 tablet 12-uurliks

AUGMENTIN SR:

Gemeenskapsverworwe pneumonie	2 tablette elke 12 uur vir 7 tot 10 dae
Akute verergerings van chroniese brongitis	2 tablette elke 12 uur vir 7 dae
Akute bakteriële sinusitis	2 tablette elke 12 uur vir 10 dae

NEWE-EFFEKTE:

Die nadelige uitwerkings wat die meeste aangemeld word, is diarree, naarheid, braking, indigestie, abdominale pyn, veluitslae, urtikaria en erythema multiforme, vaginitis, genitale moniliase, 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.

Die volgende nadelige reaksies is aangemeld en kan voorkom met AUGMENTIN:

Hipersensitiwiteitsreaksies: Veluitslag, pruritus en urtikarie, 'n sindroom wat soortgelyk is aan serumsiekte, erythema multiforme, seldsame gevalle van Stevens-Johnson-sindroom, hipersensitiwiteitsvaskulitis en minder dikwels bulleuse eksfoliatiewe dermatitis, akute

veralgemeende eksantemateuse pustulose en toksiese epidermale nekrolise is gerapporteer. Wanneer sulke reaksies plaasvind moet AUGMENTIN gestaak word. Ernstige en soms noodlottige hipersensitiwiteitsreaksies (anafilaktiese reaksies) en angioneurotiese edeem kan plaasvind met mondelikse penisillien (sien WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS).

Interstisiële nefritis kan selde voorkom.

Gastroïntestinale reaksies: Naarheid, braking, diarree, gastritis, stomatitis, glossitis, swart 'harige' tong, enterokolitis, mukokutaneuse kandidiase en antibiotikum-geassosiëerde kolitis (insluitende pseudomembraneuse kolitis en hemoragiese kolitis). As gastroïntestinale reaksies plaasvind, kan hulle verminder word deur AUGMENTIN aan die begin van 'n maaltyd te neem.

Hepatiese effekte: Hepatitis en cholestatiese geelsug is aangemeld. Die voorvalle mag ernstig wees en kom hoofsaaklik in volwasse of bejaarde pasiente voor. Tekens en simptome vind gewoonlik plaas gedurende of kort na behandeling, maar in sommige gevalle kan dit eers aan die lig kom verskeie weke na behandeling gestaak is. Die hepatiese voorvalle is gewoonlik omkeerbaar. In uiters seldsame omstandighede, is sterftes egter aangemeld. Hierdie gevalle is amper altyd geassosieer met ernstige onderliggende siektes of medikasie wat gelyktydig geneem is.

'n Matige styging in aspartaattransaminase (AST) en/of alanientransaminase (ALT) is waargeneem by pasiënte wat met AUGMENTIN behandel is, maar die betekenis daarvan is nie bekend nie.

Renale effekte: Kristalurie is aangemeld.

Hematologiese effekte: Hemolitiese anemie, omkeerbare trombositopenie, trombositopeniese purpura, eosinofilie, omkeerbare leukopenie (insluitend neutropenie) en agranulositose is gerapporteer. Hierdie reaksies kan gewoonlik omgekeer word met staking van terapie en daar word geglo dat dit hipersensitiwiteitsverskynsels is. 'n Geringe trombositose is opgemerk by minder as 1 % van die pasiënte wat met AUGMENTIN behandel is. Verlengde bloedingstydperk en protrombientydperk is ook minder dikwels

aangemeld. Toepaslike monitering moet toegepas word wanneer antikoagulante gelyktydig voorgeskryf word.

Sentrale senuweestelsel effekte: Sentrale senuweestelsel effekte kom selde voor. Dit sluit in, omkeerbare hiperaktiwiteit, duiseligheid, hoofpyn en konvulsies. Konvulsies kan voorkom by ingekorte nierfunksie of waar hoë dossise toegedien word.

Allerlei: Oppervlakkige tandverkleuring is al aangemeld. Dit kan gewoonlik verwyder word deur te borsel.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN:

Gevalle van 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.

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.

IDENTIFIKASIE:

AUGMENTIN BD: Wit tot naaswit kapsuulvormige, filmbedekte tablette gemerk met ’n breeklyn op een kant.

AUGMENTIN SR Wit kapsuulvormige, filmbedekte tablette gedebosseleer met ‘AC 1000/62.5’ op een kant en ’n halveringsbreeklyn op die anderkant.

AANBIEDING:

AUGMENTIN BD: Die 10's pak bestaan uit 'n aluminiumpakkie, wat 'n droogmiddel en 'n stolpverpakkingstrokie met 10 tablette bevat, verpak in 'n buitenste karton. Die stolpverpakking bestaan uit 'n deursigtige PVC/PVdC laminaat en grys aluminiumfoelie.

AUGMENTIN SR: Aluminium/aluminium stolpverpakkingstrokie met een of twee film-bedekte tablette per stolp, verpak in 'n buitenste karton.

BERGINGSAANWYSINGS:

AUGMENTIN BD:

Bewaar in 'n droë plek by of benede 25 °C.

MOET NIE DROOGMIDDEL VERWYDER NIE.

Hou buite bereik van kinders.

AUGMENTIN SR:

Bewaar in 'n droë plek by of benede 25 °C.

Hou buite bereik van kinders.

REGISTRASIENOMMER:

AUGMENTIN BD tablette: 32/20.1.2/0239

AUGMENTIN SR tablette: 36/20.1.2/0288

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT:

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