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Augmentin™ 1 g

Amoxicillin + clavulanate potassium

QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Augmentin 1 g tablet contains 875 mg amoxycillin as amoxycillin trihydrate Ph. Eur. and 125 mg clavulanic acid as clavulanate potassium Ph. Eur.

PHARMACEUTICAL FORM

White, film coated, oval-shaped tablets engraved A C.

THERAPEUTIC INDICATIONS

Augmentin is an antibiotic agent with a notably broad spectrum of activity against the commonly occurring bacterial pathogens in general practice and hospital. The ß-lactamase inhibitory action of clavulanate extends the spectrum of amoxicillin to embrace a wider range of organisms, including many resistant to other ß-lactam antibiotics.

Augmentin oral preparations are indicated for short term treatment of bacterial infections at the following sites when amoxicillin resistant beta-lactamase producing strains are suspected as the cause. In other situations, amoxicillin alone should be considered.

- *Upper Respiratory Tract Infections (including ENT)* in particular sinusitis, otitis media, recurrent tonsillitis. These infections are often caused by *Streptococcus pneumoniae, Haemophilus influenzae*, Moraxella catarrhalis** and *Streptococcus pyogenes.*
- *Lower Respiratory Tract Infections* in particular acute exacerbations of chronic bronchitis (especially if considered severe), bronchopneumonia. These infections are often caused by *Streptococcus pneumoniae, Haemophilus influenzae** and *Moraxella catarrhalis**.
- *Genito-urinary Tract and Abdominal Infections* in particular cystitis (especially when recurrent or complicated - excluding prostatitis), septic abortion, pelvic or puerperal sepsis and intra-abdominal sepsis. These infections are often caused by *Enterobacteriaceae** (mainly *Escherichia coli**), *Staphylococcus saprophyticus, Enterococcus* species.*
- *Skin and Soft Tissue Infections* in particular cellulitis, animal bites and severe dental abscess with spreading cellulitis. These infections are often caused by *Staphylococcus aureus*, Streptococcus pyogenes* and *Bacteroides species**.

* Some members of these species of bacteria produce beta-lactamase, rendering them insensitive to amoxicillin alone. Mixed infections caused by amoxicillin-susceptible organisms in conjunction with Augmentin-susceptible beta-lactamase-producing organisms may be treated with Augmentin. These infections should not require the addition of another antibiotic resistant to beta-lactamases.

POSOLOGY AND METHOD OF ADMINISTRATION

Dosage: Adults and children over 12 years

Severe Infections (including chronic and recurrent urinary tract infections and those of the lower respiratory tract): One Augmentin 1 g Tablet given bid.
Therapy can be started parenterally and continued with an oral preparation.
Duration of therapy should be appropriate to the indication and should not exceed 14 days without review.

Elderly

No adjustment needed; as for adults, unless there is evidence of renal impairment (see below).

Dosage in Renal Impairment

The 1 g presentation should only be used in patients with a glomerular filtration rate of >30 ml/min.
Mild impairment (creatinine clearance > 30ml/min) - no change in dosage necessary.

Dosage in hepatic impairment

Dose with caution; monitor hepatic function at regular intervals.
There are, as yet, insufficient data on which to base a dosage recommendation.

Method of Administration: Oral.

Tablets should be swallowed whole without chewing. If required, tablets may be broken in half and swallowed without chewing. To minimise potential gastrointestinal intolerance, administer at the start of a meal. The absorption of Augmentin is optimised when taken at the start of a meal.

CONTRAINDICATIONS

Penicillin hypersensitivity. Attention should be paid to possible cross-sensitivity with other ß-lactam antibiotics, e.g. cephalosporins.
A previous history of co-amoxiclav or penicillin-associated jaundice/hepatic dysfunction.

WARNINGS AND PRECAUTIONS

Before initiating therapy with amoxicillin-clavulanate, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other allergens.
Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity. If an allergic reaction occurs, amoxicillin-clavulanate therapy should be discontinued and appropriate alternative therapy instituted. Serious anaphylactoid reactions require immediate emergency treatment with adrenaline. Oxygen, i.v. steroids and airway management, including intubation may also be required.

Amoxicillin-clavulanate 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.
Prolonged use may also occasionally result in overgrowth of non-susceptible organisms.
In general amoxicillin-clavulanate is well tolerated and possesses the characteristic low toxicity of the penicillin group of antibiotics. Periodic assessment of organ system functions, including renal, hepatic and haematopoietic function is advisable during prolonged therapy.
Abnormal prolongation of prothrombin time (increased INR) has been reported rarely in patients receiving amoxicillin-clavulanate and oral anticoagulants. Appropriate monitoring should be undertaken when anticoagulants are prescribed concurrently. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation.
Amoxicillin-clavulanate should be used with caution in patients with evidence of hepatic dysfunction.
In patients with renal impairment, dosage should be adjusted according to the degree of impairment (see Dosage and Administration – Renal Impairment).
In patients with reduced urine output, crystalluria has been observed very rarely, predominantly with parenteral therapy. During the administration of high doses of amoxicillin, it is advisable to maintain adequate fluid intake and urinary output in order to reduce the possibility of amoxicillin crystalluria (see Overdosage).
Amoxicillin-clavulanate Suspensions/Sachets/Chewable Tablets (where applicable), contain aspartame, which is a source of phenylalanine and so should be used with caution in patients with phenylketonuria.

INTERACTIONS

Concomitant use of probenecid is not recommended. Probenecid decreases the renal tubular secretion of amoxicillin.
Concomitant use with amoxicillin-clavulanate may result in increased and prolonged blood levels of amoxicillin, but not of clavulanic acid.
Concomitant use of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions.
There are no data on the concomitant use of amoxicillin-clavulanate and allopurinol.
In common with other antibiotics, amoxicillin-clavulanate may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral contraceptives.
In the literature there are rare cases of increased international normalised ratio in patients maintained on acenocoumarol or warfarin and prescribed a course of amoxicillin. If co-administration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of amoxicillin.

PREGNANCY AND LACTATION

Pregnancy

Reproduction studies in animals (mice and rats at doses up to 10 times the human dose) with orally and parenterally administered amoxicillin-clavulanate have shown no teratogenic effects. In a single study in women with preterm, premature rupture of the foetal membrane (pPROM), it was reported that prophylactic treatment with amoxicillin-clavulanate may be associated with an increased risk of necrotising enterocolitis in neonates. As with all medicines, use should be avoided in pregnancy, unless considered essential by the physician.

Lactation

Amoxicillin-clavulanate may be administered during the period of lactation. With the exception of the risk of sensitization, associated with the excretion of trace quantities in breast milk, there are no known detrimental effects for the breast-fed infant.

ADVERSE REACTIONS

Data from large clinical trials was used to determine the frequency of very common to rare undesirable effects. The frequencies assigned to all other undesirable effects (i.e., those occurring at <1/10,000) were mainly determined using post-marketing data and refer to a reporting rate rather than a true frequency.
The following convention has been used for the classification of frequency:

very common: >1/10
common: >1/100 and <1/10
uncommon: >1/1000 and <1/100
rare : >1/10,000 and <1/1000
very rare: <1/10,000.

Infections and infestations
Common: Mucocutaneous candidiasis
Blood and lymphatic system disorders
Rare: Reversible leucopenia (including neutropenia) and thrombocytopenia
Very rare: Reversible agranulocytosis and haemolytic anaemia. Prolongation of bleeding time and prothrombin time
Immune system disorders
Very rare: Angioneurotic oedema, anaphylaxis, serum sickness-like syndrome, hypersensitivity vasculitis
Nervous system disorders
Uncommon: Dizziness, headache
Very rare: Reversible hyperactivity and convulsions. Convulsions may occur in patients with impaired renal function or in those receiving high doses.
Gastrointestinal disorders
Very common: Diarrhoea
Common: Nausea, vomiting
Nausea is more often associated with higher oral dosages. If gastrointestinal reactions are evident, they may be reduced by taking amoxicillin-clavulanate at the start of a meal.
Uncommon: Indigestion
Very rare: Antibiotic-associated colitis (including pseudomembranous colitis and haemorrhagic colitis).
Black hairy tongue
Superficial tooth discolouration has been reported very rarely in children. Good oral hygiene may help to prevent tooth discolouration as it can usually be removed by brushing.

Hepatobiliary disorders
Uncommon: A moderate rise in AST and/or ALT has been noted in patients treated with beta-lactam class antibiotics, but the significance of these findings is unknown.
Very rare: Hepatitis and cholestatic jaundice. These events have been noted with other penicillins and cephalosporins.
Hepatic events have been reported predominantly in males and elderly patients and may be associated with prolonged treatment.
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 extremely rare 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.
These events have been very rarely reported in children.
Skin and subcutaneous tissue disorders
Uncommon: Skin rash, pruritus, urticaria
Rare: Erythema multiforme
Very rare: Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous exfoliative-dermatitis, acute generalised exanthemous pustulosis (AGEP)
If any hypersensitivity dermatitis reaction occurs, treatment should be discontinued.
Renal and urinary disorders
Very rare: Interstitial nephritis, crystalluria

OVERDOSAGE

Symptoms and Signs

Gastrointestinal symptoms and disturbance of the fluid and electrolyte balances may be evident.
Amoxicillin crystalluria, in some cases leading to renal failure, has been observed.

Treatment

GI symptoms may be treated symptomatically, with attention to the water/electrolyte balance.
Amoxicillin-clavulanate can be removed from the circulation by haemodialysis

List of Excipients

Colloidal silicon dioxide, sodium starch glycollate, magnesium stearate (E572), microcrystalline cellulose, titanium dioxide (E171), hydroxypropyl methylcellulose, polyethylene glycol, dimethicone (silicon oil).

Shelf Life

As indicated on the outer packaging

Special Precautions for Storage

Augmentin 1 g Tablets should be stored in un-opened, well sealed original packs in a dry place at or below 30°C. Keep out of reach of children.

Nature and Contents of Container

Only moisture-proof containers should be used. Augmentin 1 g Tablets supplied in PVC/PVdC blisters in dessicated pouch pack, containing 14 tablets.

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Manufactured by

SmithKline Beecham plc*
Worthing, UK
*Member of the GlaxoSmithKline group of companies
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THIS IS A MEDICAMENT
Medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.

Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.

- The doctor and the pharmacist are the experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.
- Keep all medicaments out of the reach of children.

Council of Arab Health Ministers, Union of Arab Pharmacists.

GlaxoSmithKline