

Augmentin 1 g

Amoxicillin trihydrate + potassium clavulanate

QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Augmentin 1 g tablet contains 875 mg amoxicillin (as amoxicillin trihydrate) and 125 mg clavulanic acid (as potassium clavulanate). For a full list of excipients, see section 'List of Excipients'.

PHARMACEUTICAL FORM

White to off-white, film-coated tablets debossed with "AC" on both sides and a scoreline on one side. The score line is only to facilitate breaking and ease of swallowing and not to divide into equal doses.

CLINICAL PARTICULARS

Therapeutic Indications

Augmentin is indicated for the treatment of the following infections in adults and children:

- Acute bacterial sinusitis (adequately diagnosed)
- Acute otitis media
- Acute exacerbations of chronic bronchitis (adequately diagnosed)
- Community acquired pneumonia
- Cystitis
- Pyelonephritis
- Skin and soft tissue infections in particular cellulitis, animal bites, severe dental abscess with spreading cellulitis.
- Bone and joint infections, in particular osteomyelitis.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

Posology and Method of Administration

Doses are expressed throughout in terms of amoxicillin/clavulanic acid content except when doses are stated in terms of an individual component.

The dose of Augmentin that is selected to treat an individual infection should take into account:

- The expected pathogens and their likely susceptibility to antibacterial agents
- The severity and the site of the infection
- The age, weight and renal function of the patient as shown below

The use of alternative presentations of Augmentin (e.g. those that provide higher doses of amoxicillin and/or different ratios of amoxicillin to clavulanic acid) should be considered as necessary.

For adults and children ≥ 40 kg, this formulation of Augmentin provides a total daily dose of 1750 mg amoxicillin/250 mg clavulanic acid with twice daily dosing and 2625 mg amoxicillin/375 mg clavulanic acid with three times daily dosing, when administered as recommended below. For children < 40 kg, this formulation of Augmentin provides a maximum daily dose of 1000-2800 mg amoxicillin/143-400 mg clavulanic acid, when administered as recommended below.

If it is considered that a higher daily dose of amoxicillin is required, it is recommended that another preparation of Augmentin is selected in order to avoid administration of unnecessarily high daily doses of clavulanic acid.

The duration of therapy should be determined by the response of the patient.

Some infections (e.g. osteomyelitis) require longer periods of treatment.

Treatment should not be extended beyond 14 days without review.

Adults and children ≥ 40 kg

Recommended doses:

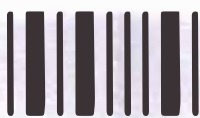
- standard dose: (for all indications) 875 mg/125 mg two times a day;
- higher dose - (particularly for infections such as otitis media, sinusitis, lower respiratory tract infections and urinary tract infections): 875 mg/125 mg three times a day.

Children < 40 kg

Children may be treated with Augmentin tablets, suspensions or paediatric sachets.

Recommended doses:

- 25 mg/3.6 mg/kg/day to 45 mg/6.4 mg/kg/day given as two divided doses;
- up to 70 mg/10 mg/kg/day given as two divided doses may be considered for some infections (such as otitis media, sinusitis and lower respiratory tract infections).



As the tablets cannot be divided, children weighing less than 25 kg must not be treated with Augmentin tablets.

The table below presents the received dose (mg/kg body weight) in children weighing 25 kg to 40 kg upon administering a single 875/125 mg tablet.

| Body weight [kg] | 40 | 35 | 30 | 25 | Single dose recommended [mg/kg body weight] (see above) |
|--|------|------|------|------|---|
| Amoxicillin [mg/kg body weight] per single dose (1 film-coated tablet) | 21.9 | 25.0 | 29.2 | 35.0 | 12.5 – 22.5 (up to 35) |
| Clavulanic acid [mg/kg body weight] per single dose (1 film-coated tablet) | 3.1 | 3.6 | 4.2 | 5.0 | 1.8 – 3.2 (up to 5) |

Children weighing less than 25 kg should preferably be treated with Augmentin suspension or paediatric sachets. No clinical data are available for Augmentin 7:1 formulations regarding doses higher than 45 mg/6.4 mg per kg per day in children under 2 years.

There are no clinical data for Augmentin 7:1 formulations for patients under 2 months of age.

Dosing recommendations in this population therefore cannot be made.

Elderly

No dose adjustment is considered necessary.

Renal impairment

No dose adjustment is required in patients with creatinine clearance (CrCl) greater than 30 ml/min. In patients with creatinine clearance less than 30 ml/min, the use of Augmentin presentations with an amoxicillin to clavulanic acid ratio of 7:1 is not recommended, as no recommendations for dose adjustments are available.

Hepatic impairment

Dose with caution and monitor hepatic function at regular intervals.

Method of administration

Augmentin is for oral use.

Administer at the start of a meal to minimise potential gastrointestinal intolerance and optimise absorption of amoxicillin/clavulanic acid. Therapy can be started parenterally according to the prescribing information of the IV-formulation and continued with an oral preparation.

Contraindications

Amoxicillin-clavulanate is contra-indicated:

- in patients with a history of hypersensitivity to beta-lactams, e.g. penicillins and cephalosporins
- in patients with a previous history of amoxicillin-clavulanate-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.

Pseudomembranous colitis has been reported with the use of antibiotics and may range in severity from mild to life-threatening. Therefore, it is important to consider its diagnosis in patients who develop diarrhoea during or after antibiotic use. If prolonged or significant diarrhoea occurs or the patient experiences abdominal cramps, treatment should be discontinued immediately and the patient investigated further.

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.

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. 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. In patients receiving mycophenolate mofetil, reduction in pre-dose concentration of the active metabolite mycophenolic acid 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.

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 pre-term, 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.

Ability to perform tasks that require judgement, motor or cognitive skills

Adverse effects on the ability to drive or operate machinery have not been observed.

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:

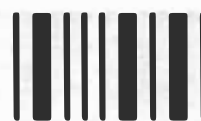
very common $>1/10$

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 infestation

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

Adults:

Very common Diarrhoea

Common Nausea, vomiting

Children:

Common Diarrhoea, nausea, vomiting

All populations:

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*.

*This statement is core safety for the syrup, suspension and chewable tablet formulations.

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.

Children (additional statement):

These events have been very rarely reported in children.

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 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.

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.

Children (additional statement):

A prospective study of 51 paediatric patients at a poison control centre suggested that overdosages of less than 250 mg/kg of amoxicillin are not associated with significant clinical symptoms and do not require gastric emptying.

Drug abuse and dependence

Drug dependency, addiction and recreational abuse have not been reported as a problem with this compound.

PHARMACEUTICAL DATA

List of Excipients

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

Incompatibilities

None known.

Shelf-life

As indicated on the outer packaging.

Special Precautions for Storage

Store in a dry place at or below 30°C.

Store in the original package in order to protect from moisture.

Tablets in desiccated pouch packs should be used within 30 days of opening.

Nature and Contents of Container

Only moisture-proof containers should be used. Augmentin 1g is supplied in a carton containing 14 tablets in blisters inside a desiccated pouch.

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