Co-Amoxiclav

Augmentin®

50mg/12.5mg per mL Powder for Suspension (Infant Drops)

PRODUCT DESCRIPTION

Co-amoxiclav *(Augmentin®)* 50mg/12.5mg per mL Powder for Suspension (Infant Drops): Bottle of Dry powder for reconstitution in water, at time of dispensing, to form an oral sugar-free suspension.
Each mL of the reconstituted suspension contains 50mg amoxicillin as trihydrate and 12.5mg clavulanic acid as potassium salt.

PHARMACOLOGIC PROPERTIES

Pharmacodynamics

Resistance to many antibiotics is caused by bacterial enzymes which destroy the antibiotic before it can act on the pathogen. The clavulanate in Co-amoxiclav *(Augmentin®)* infant drops anticipates this defence mechanism by blocking the β-lactamase enzymes, thus rendering the organisms susceptible to amoxicillin's rapid bactericidal effect at concentrations readily attainable in the body.
Clavulanate by itself has little antibacterial activity; however, in association with amoxicillin as Co-amoxiclav*(Augmentin®)* it produces an antibiotic agent of broad spectrum with wide application in hospital and general practice.
Co-amoxiclav *(Augmentin®)* is bactericidal to a wide range of organisms including:
Gram-positive
Aerobes: *Enterococcus faecalis, Streptococcus pneumoniae, Streptococcus pyogenes, Streptococcus viridans, *Staphylococcus aureus,* *coagulase negative *staphylococci* (including *Staphylococcus epidermidis*), *Corynebacterium* species, *Bacillus anthracis, Listeria monocytogenes.*
Anaerobes: *Clostridium* species, *Peptococcus* species, *Peptostreptococcus*.
Gram-negative
Aerobes: **Haemophilus influenzae, *Escherichia coli, *Proteus mirabilis, *Proteus vulgaris, *Klebsiella* species, **Moraxella catarrhalis, *Salmonella* species, **Shigella* species, *Bordetella pertussis, Brucella* species, **Neisseria gonorrhoeae, Neisseria meningitidis, Vibrio cholerae, Pasteurella multocida.*
Anaerobes: **Bacteroides* spp. including *B. fragilis*.
* Some members of these species of bacteria produce β-lactamase, rendering them insensitive to amoxicillin alone.

Pharmacokinetics

The pharmacokinetics of the two components of Co-amoxiclav *(Augmentin®)* are closely matched. Peak serum levels of both occur about 1 hour after oral administration. Absorption of Co-amoxiclav *(Augmentin®)* is optimised at the start of a meal.
Doubling the dosage of Co-amoxiclav *(Augmentin®)* approximately doubles the serum levels achieved.
Both clavulanate and amoxicillin have low levels of serum binding; about 70% remains free in the serum.

Pre-clinical Safety Data

No further information of relevance.

INDICATIONS

Co-amoxiclav *(Augmentin®)* infant drops are indicated for short-term treatment of bacterial infections at the following sites:
Upper respiratory tract infections (including ENT) e.g. recurrent tonsillitis, sinusitis, otitis media.
Lower respiratory tract infections e.g. acute exacerbation of chronic bronchitis, lobar and bronchopneumonia.
Genito-urinary tract infections e.g. cystitis, urethritis, pyelonephritis.
Skin and soft tissue infections, e.g. boils, abscesses, cellulitis, wound infections.
Bone and joint infections e.g. osteomyelitis.
Other infections e.g. intra-abdominal sepsis.
A comprehensive list of susceptible organisms is provided in the Pharmacodynamics section.
Infections caused by amoxicillin-susceptible organisms are amenable to Co-amoxiclav *(Augmentin®)* treatment due to its amoxicillin content. Mixed infections caused by amoxicillin-susceptible organisms in conjunction with Co-amoxiclav *(Augmentin®)*-susceptible β-lactamase producing organisms may therefore be treated with Co-amoxiclav *(Augmentin®)*.

DOSAGE AND ADMINISTRATION

The usual recommended daily dosage is 25 mg/kg/day* in divided doses every eight hours.
In more serious infections the dosage may be increased up to 50 mg/kg/day in divided doses every eight hours.
***** Each 25 mg Co-amoxiclav *(Augmentin®)* provides 20 mg amoxicillin and 5 mg clavulanate.

Co-amoxiclav *(Augmentin®)* infant drops should be administered using the supplied syringe doser. The syringe doser has markings which correspond to the weight of the child. For example, for a child weighing 7 kg, the syringe piston should be withdrawn until the 7 kg marking is level with the top of the body of the syringe. The dose (equivalent to 0.93 mL) should then be orally administered to the child. A similar dose should be administered once every eight hours.
For information, the volumes of Co-amoxiclav *(Augmentin®)* infant drops which correspond to the weight markings are shown below:

Weight of child (kg)	**Volume (ml) of Co-amoxiclav *(Augmentin®)* infant drops ****

1	0.13
1.5	0.20
2	0.27
2.5	0.33
3	0.40
3.5	0.47
4	0.53
4.5	0.60
5	0.67
5.5	0.73
6	0.80
6.5	0.87
7	0.93
7.5	1.00
8	1.07
8.5	1.14
9	1.20
9.5	1.27
10	1.34

** These doses may be doubled in cases of severe infection.

Dosage in renal impairment

Mild impairment (Creatinine clearance >30 ml/min)	Moderate impairment (Creatinine clearance 10-30 ml/min)	Severe impairment (Creatinine clearance <10 ml/min)
No change in dosage, ie The recommended dose given three times daily[#]	The recommended dose given twice daily instead of three times per day[#]	The recommended dose given once daily instead of three times per day[#]

[#] In more serious cases this dose may be doubled.

Dosage in hepatic impairment
Dose with caution; monitor hepatic function at regular intervals.

Administration
To minimise potential gastrointestinal intolerance, administer at the start of a meal. The absorption of Co-amoxiclav *(Augmentin®)* is optimised when taken at the start of a meal.
Duration of therapy should be appropriate to the indication and should not be extended beyond 14 days without review.

CONTRAINDICATIONS
Co-amoxiclav *(Augmentin®)* is contraindicated in patients with a history of hypersensitivity to beta-lactams, e.g. penicillins and cephalosporins.
Co-amoxiclav *(Augmentin®)* is contraindicated in patients with a previous history of Co-amoxiclav *(Augmentin®)*-associated jaundice/hepatic dysfunction.

WARNINGS AND PRECAUTIONS
Before initiating therapy with Co-amoxiclav *(Augmentin®)*, 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 (see *Contraindications*).
Co-amoxiclav *(Augmentin®)* 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.
Prolongation of prothrombin time has been reported rarely in patients receiving Co-amoxiclav *(Augmentin®)*. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly.
Changes in liver function tests have been observed in some patients receiving Co-amoxiclav *(Augmentin®)*. The clinical significance of these changes is uncertain but Co-amoxiclav *(Augmentin®)* should be used with caution in patients with evidence of hepatic dysfunction.
Cholestatic jaundice, which may be severe, but is usually reversible, has been reported rarely. Signs and symptoms may not become apparent for up to six weeks after treatment has ceased.
In patients with renal impairment Co-amoxiclav *(Augmentin®)* dosage should be adjusted as recommended in the *Dosage and Administration* section.
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 *Overdose).*
Co-amoxiclav *(Augmentin®)* suspensions contain 2.5 mg aspartame per 1 mL, which is a source of phenylalanine, and therefore should be used with caution in patients with phenylketonuria.
Effects on Ability to Drive and Use Machines
Adverse effects on the ability to drive or operate machinery have not been observed.

DRUG INTERACTIONS
Concomitant use of probenecid is not recommended. Probenecid decreases the renal tubular secretion of amoxicillin.
Concomitant use with Co-amoxiclav *(Augmentin®)* may result in increased and prolonged blood levels of amoxicillin but not of clavulanate.
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 Co-amoxiclav *(Augmentin®)* and allopurinol.
In common with other broad spectrum antibiotics, Co-amoxiclav *(Augmentin®)* may reduce the efficacy of oral contraceptives and patients should be warned accordingly.

PREGNANCY AND LACTATION
Reproduction studies in animals (mice and rats) with orally and parenterally administered Co-amoxiclav *(Augmentin®)* 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 Co-amoxiclav *(Augmentin®)* may be associated with an increased risk of necrotising enterocolitis in neonates. As with all medicines, use should be avoided in pregnancy, especially during the first trimester, unless considered essential by the physician.
Co-amoxiclav *(Augmentin®)* may be administered during the period of lactation. With the exception of the risk of sensitisation, associated with the excretion of trace quantities in breast milk, there are no detrimental effects for the infant.

ADVERSE EFFECTS

Data from large clinical trials were 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 (see *Warnings and Precautions*)

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

Common: Diarrhoea, nausea, vomiting

Nausea is more often associated with higher oral dosages. If gastrointestinal reactions are evident, they may be reduced by taking Co-amoxiclav *(Augmentin®)* at the start of a meal.

Uncommon: Indigestion
Very Rare: Antibiotic-associated colitis (including pseudomembranous colitis and haemorrhagic colitis). 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. These events have been very rarely reported in children.

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 *(*see *Overdose)*

OVERDOSAGE AND TREATMENT

Gastrointestinal symptoms and disturbance of the fluid and electrolyte balances may be evident. Gastrointestinal symptoms may be treated symptomatically with attention to the water electrolyte balance.
Amoxicillin crystalluria, in some cases leading to renal failure, has been observed (see *Warnings and Precautions*).
Co-amoxiclav *(Augmentin®)* may be removed from the circulation by haemodialysis.

STORAGE CONDITION

Before reconstitution, the dry powder should be stored in unopened container in a dry place. Store below 25°C.
Reconstituted suspension should be stored in a refrigerator (2-8°C) and used within seven days.

INSTRUCTIONS FOR USE AND HANDLING

First shake the bottle to loosen the powder. Water should be added until the fill line on the bottle label, and then shake the bottle well. Then top up with water until the level of the fill line is reached and shake again. When first reconstituted, allow to stand for 5 minutes to ensure full dispersion.

The device is used to dose patients under 2 years according to the schedule in the *Dosage and Administration* section.

					
Shake bottle before use	Insert pipette into adaptor, ensure firmly located	Invert bottle and withdraw required dose	Place bottle upright and remove pipette from adaptor.	Rinse pipette in clean water	Replace bottle cap

AVAILABILITY

Co-amoxiclav *(Augmentin®)* 50mg/12.5mg per mL Powder for Suspension (Infant Drops): Type III clear glass bottle with an aluminium roll on pilfer-proof cap x 20mL (net content) + plastic syringe dosing device. Box of 1's.

CAUTION

Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.
Keep all medicines out of reach of children.

Version number: GDS15/IPI05 Revision date: 21 April 2005

GlaxoSmithKline

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