# AUGMENTIN INFANT DROPS

**Amoxicillin trihydrate - Potassium clavulanate**

## QUALITATIVE AND QUANTITATIVE COMPOSITION

When reconstituted each 1 mL contains 50 mg amoxicillin (as amoxicillin trihydrate) and 12.5 mg clavulanic acid (as potassium clavulanate).

## PHARMACEUTICAL FORM

An off-white dry powder for reconstitution in water to form a fruit flavoured suspension.

## CLINICAL PARTICULARS

### Indications

*AUGMENTIN* should be used in accordance with local official antibiotic-prescribing guidelines and local susceptibility data.

*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.

Susceptibility to *AUGMENTIN* will vary with geography and time (see *Pharamcological Properties, Pharmacodynamics* for further information). Local susceptibility data should be consulted where available, and microbiological sampling and susceptibility testing performed where necessary.

Infections caused by amoxicillin-susceptible organisms are amenable to *AUGMENTIN* treatment due to its amoxicillin content. Mixed infections caused by amoxicillin-susceptible organisms in conjunction with *AUGMENTIN*-susceptible beta-lactamase producing organisms may therefore be treated with *AUGMENTIN*.

## Dosage and Administration

Dosage depends on the weight and renal function of the patient and the severity of the infection.

Dosages are expressed throughout in terms of amoxicillin/clavulanate content except when doses are stated in terms of an individual component.

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.

Treatment should not be extended beyond 14 days without review.

Therapy can be started parenterally and continued with an oral preparation.

*AUGMENTIN* infant drops should be administered orally using the supplied dosing syringe. The syringe is graduated to permit accurate and reproducible volumes to be dispensed (see *Instructions for Use/Handling*).

The usual recommended daily dosage is:

- *Lower dose*: 20/5 mg/kg/day in three divided doses for mild to moderate infections (upper respiratory tract infections e.g. recurrent tonsillitis, lower respiratory infections and skin and soft tissue infections).
- *Higher dose*: 40/10 mg/kg/day in three divided doses for the treatment of more serious infections (upper respiratory tract infections e.g. otitis media and sinusitis, lower respiratory tract infections e.g. bronchopneumonia and urinary tract infections).

For information, the volumes of *AUGMENTIN* infant drops which correspond to the weight of a child are shown below. For more severe infections where a higher dose is required the lower dose recommendations may be doubled.

| Body Weight (kg) | Lower Dose at 20/5 mg/kg/day (mL every 8 hours) |
|---|---|
| 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 |

**Renal Impairment**

Dosage adjustments are based on the maximum recommended level of amoxicillin.

No adjustment in dose is required in patients with creatinine clearance (CrCl) greater than 30 mL/min.

| | |
|---|---|
| CrCl 10-30 mL/min | The recommended dose given every **12 hours** instead of every 8 hours[#] (maximum 10 mL twice daily) |
| CrCl < 10 mL/min | The recommended dose given every **24 hours** instead of every 8 hours[#] (maximum 10 mL) |
| Haemodialysis | The recommended dose given every **24 hours** instead of every 8 hours[#]<br><br>Prior to haemodialysis a single dose should be administered. In order to restore circulating drug levels, an additional dose should be administered after haemodialysis. |

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

**Hepatic Impairment**

Dose with caution; monitor hepatic function at regular intervals.

## Contraindications

*AUGMENTIN* is contraindicated in patients with a history of hypersensitivity to beta-lactams, e.g. penicillins and cephalosporins.

*AUGMENTIN* is contraindicated in patients with a previous history of *AUGMENTIN*-associated jaundice/hepatic dysfunction.

## Warnings and Precautions

Before initiating therapy with *AUGMENTIN*, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other allergens.

Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse 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*). If an allergic reaction occurs, *AUGMENTIN* therapy must be discontinued and appropriate alternative therapy instituted. Serious anaphylactic reactions require immediate emergency treatment with adrenaline. Oxygen, intravenous (i.v.) steroids and airway management (including intubation) may also be required.

*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.

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.

Abnormal prolongation of prothrombin time (increased INR) has been reported rarely in patients receiving *AUGMENTIN* 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.

Changes in liver function tests have been observed in some patients receiving *AUGMENTIN*. The clinical significance of these changes is uncertain but *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 *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).*

*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.

## Interactions

Concomitant use of probenecid is not recommended. Probenecid decreases the renal tubular secretion of amoxicillin. Concomitant use with *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 *AUGMENTIN* and allopurinol.

In common with other antibiotics, *AUGMENTIN* 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 *AUGMENTIN*.

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

Reproduction studies in animals (mice and rats) with orally and parenterally administered *AUGMENTIN* 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 *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.

*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.

## Effects on Ability to Drive and Use Machines

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

## Adverse Reactions

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 to < 1/10

uncommon ≥ 1/1000 to < 1/100

rare ≥ 1/10,000 to < 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**

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|---|---|
| Uncommon | Dizziness, headache |
| Very rare | Reversible hyperactivity, aseptic meningitis, convulsions. Convulsions may occur in patients with impaired renal function or in those receiving high doses. |

**Gastrointestinal disorders**

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|---|---|
| Common | Diarrhoea, nausea, vomiting |

Nausea is more often associated with higher oral dosages. If gastrointestinal reactions are evident, they may be reduced by taking *AUGMENTIN* at the start of a meal.

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|---|---|
| Uncommon | Indigestion |

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|---|---|
| Very rare | Antibiotic-associated colitis (including pseudomembranous colitis and haemorrhagic colitis – see *Warnings and Precautions*). |
| | 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**

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|---|---|
| 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**

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|---|---|
| Uncommon | Skin rash, pruritus, urticaria |
| Rare | Erythema multiforme |
| Very rare | Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous exfoliative-dermatitis, acute generalised exanthemous pustulosis (AGEP), and drug reaction with eosinophilia and systemic symptoms (DRESS) |

If any hypersensitivity dermatitis reaction occurs, treatment should be discontinued.

**Renal and urinary disorders**

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|---|---|
| Very rare | Interstitial nephritis, crystalluria *(*see *Overdose)* |

## Overdose

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*).

*AUGMENTIN* may be removed from the circulation by haemodialysis.

# PHARMACOLOGICAL 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 *AUGMENTIN* infant drops anticipates this defence mechanism by blocking the beta-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 *AUGMENTIN* it produces an antibiotic agent of broad spectrum with wide application in hospital and general practice.

In the list below, organisms are categorised according to their *in vitro* susceptibility to *AUGMENTIN*.

| ***In vitro* susceptibility of micro-organisms to *AUGMENTIN*** |
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| Where clinical efficacy of *AUGMENTIN* has been demonstrated in clinical trials this is indicated with an asterisk (*).<br>Organisms that do not produce beta-lactamase are identified (with †). If an isolate is susceptible to amoxicillin, it can be considered susceptible to *AUGMENTIN*. |
| **Commonly susceptible species** |
| Gram-positive aerobes:<br>*Bacillius anthracis*<br>*Enterococcus faecalis*<br>*Listeria monocytogenes*<br>*Nocardia asteroides*<br>*Streptococcus pyogenes**†<br>*Streptococcus agalactiae**†<br>*Streptococcus* spp. (other beta-hemolytic)*†<br>*Staphylococcus aureus* (methicillin susceptible)* |

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| *Staphylococcus saprophyticus* (methicillin susceptible)<br>Coagulase negative staphylococcus (methicillin susceptible) |
| Gram-negative aerobes:<br>*Bordetella pertussis*<br>*Haemophilus influenzae**<br>*Haemophilus parainfluenzae*<br>*Helicobacter pylori*<br>*Moraxella catarrhalis**<br>*Neisseria gonorrhoeae*<br>*Pasteurella multocida*<br>*Vibrio cholerae* |
| Other:<br>*Borrelia burgdorferi*<br>*Leptospira ictterohaemorrhagiae*<br>*Treponema pallidum* |
| Gram positive anaerobes:<br>*Clostridium* spp.<br>*Peptococcus niger*<br>*Peptostreptococcus magnus*<br>*Peptostreptococcus micros*<br>*Peptostreptococcus* spp. |
| Gram-negative anaerobes:<br>*Bacteroides fragilis*<br>*Bacteroides* spp.<br>*Capnocytophaga* spp.<br>*Eikenella corrodens*<br>*Fusobacterium nucleatum*<br>*Fusobacterium* spp.<br>*Porphyromonas* spp.<br>*Prevotella* spp. |

| **Species for which acquired resistance may be a problem** |
|---|
| Gram-negative aerobes: |
| *Escherichia coli** |
| *Klebsiella oxytoca* |
| *Klebsiella pneumoniae** |
| *Klebsiella* spp. |
| *Proteus mirabilis* |
| *Proteus vulgaris* |
| *Proteus* spp. |
| *Salmonella* spp. |
| *Shigella* spp. |
| Gram-positive aerobes: |
| *Corynebacterium* spp. |
| *Enterococcus faecium* |
| *Streptococcus pneumoniae**[†] |
| Viridans group streptococcus |
| **Inherently resistant organisms** |
| Gram-negative aerobes: |
| *Acinetobacter* spp. |
| *Citrobacter freundii* |
| *Enterobacter* spp. |
| *Hafnia alvei* |
| *Legionella pneumophila* |
| *Morganella morganii* |
| *Providencia* spp. |
| *Pseudomonas* spp. |
| *Serratia* spp. |
| *Stenotrophomas maltophilia* |
| *Yersinia enterolitica* |
| Others: |
| *Chlamydia pneumoniae* |
| *Chlamydia psittaci* |
| *Chlamydia* spp. |

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| *Coxiella burnetti* |
| *Mycoplasma* spp. |

### Pharmacokinetics

The pharmacokinetics of the two components of *AUGMENTIN* are closely matched. Peak serum levels of both occur about 1 hour after oral administration. Absorption of *AUGMENTIN* is optimised at the start of a meal.

Doubling the dosage of *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.

## PHARMACEUTICAL PARTICULARS

### List of Excipients

*AUGMENTIN* dry powder for infant drops contains xanthan gum, hydroxypropyl methylcellulose, colloidal silica, succinic acid, silicon dioxide, aspartame, dry flavours (raspberry, orange and golden syrup).

### Incompatibilities

None known.

### Shelf Life

The expiry date is indicated on the packaging.

### Special Precautions for Storage

Do not take after the expiry date shown on the pack.

Store in a dry place in the original packaging to protect from moisture.

Do not store above 25°C.

Once reconstituted, the suspension must be stored in a refrigerator (2°C to 8°C) and used within 7 days. Do not freeze. (see also *Instructions for Use/Handling*).

## Nature and Contents of Container

*AUGMENTIN* infant drops for suspension is supplied in clear glass bottles with screw caps, containing powder for reconstitution.

Fill-lines are indicated on the bottle label. A syringe dosing device is also included.

## Instructions for Use/Handling

At time of use, the dry powder should be reconstituted to form an oral suspension, as detailed below:

- Check cap seal is intact before use.
- Invert and shake bottle to loosen powder.
- Fill the bottle with water to just below the mark on bottle label.
- Invert and shake well, then top up with water to the mark. Invert and shake again.
- Allow to stand for 5 minutes to ensure full dispersion.
- Shake well before taking each dose.

Once reconstituted, the adaptor that is supplied with the syringe dosing device should be inserted into the neck of the bottle before replacing the screw cap.

Discard any unused suspension after 7 days.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Not all presentations are available in every country.

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