Augmentin Duo

Augmentin Trio Forte

Suspensions

Composition

Active ingredients
Amoxicillin, anhydrous, as amoxicillin trihydrate
lavulanic acid as potassium clavulanate

Excipients
- Suspension Trio Forte 312.5mg/5ml (250/62.5): Flavourings: vanillin et alia, aspartame; powder excipient
- Suspension Duo 457mg/5ml (400/57): Flavourings: vanillin et alia, aspartame; powder excipient

Pharmaceutical form (where applicable, after preparation) and active ingredient quantities per unit

Pharmaceutical form	Amoxicillin, anhydrous, as amoxicillin trihydrate	Clavulanic acid as potassium clavulanate	Ratio amoxicillin : clavulanic acid
5 ml suspension Trio Forte 312.5 mg (250/62.5)	250 mg	62.5 mg	4 : 1
5 ml suspension Duo 457 mg (400/57)	400 mg	57 mg	7 : 1

Indications/Uses

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

Augmentin is indicated in Gram-positive and Gram-negative bacterial infections with pathogens sensitive to Augmentin (especially organisms which are resistant to amoxicillin because they form beta-lactamase, see Properties/effects).

Augmentin Trio Forte

ENT infections:	Tonsillitis, pharyngitis, laryngitis, otitis media, sinusitis, mainly caused by *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis* and *Streptococcus pyogenes*.

Lower respiratory tract infections:	Acute bronchitis with bacterial superinfection and acute exacerbation of chronic bronchitis, bacterial pneumonia, mainly caused by *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis*.
Urinary tract infections:	Acute and chronic pyelonephritis, cystitis, urethritis, *inter alia* caused by *Escherichia coli*.
Venereal diseases:	Gonorrhoea (specific urethritis).
Skin and soft tissue infections:	Mainly caused by *Staphylococcus aureus* and *Streptococcus pyogenes*.
Gynaecological infections:	Salpingitis, adnexitis, endometritis, bacterial vaginitis.

Augmentin Duo
Tonsillitis
Lower respiratory tract infections
Otitis media

Susceptibility to amoxicillin-clavulanate will vary with geography and time. Local susceptibility data should be consulted where available, and microbiological sampling and susceptibility testing performed where necessary.

Dosage/Administration

The dose is dependent on the age, body weight and renal function of the patient, as well as on the severity of the infection.

Usual dosage

Adults and children over 40 kg

For the treatment of infections in adults and children over 40 kg see the Prescribing Information for Augmentin film-coated tablets.

Children up to 40 kg

General dosing guidelines

The general dosing guidelines per kg and per day (see below) should be observed.

The *Trio Forte* form of Augmentin must always be taken *three times daily*, the *Duo* suspension must only be taken *twice daily*.

Augmentin Trio Forte

The daily dose should be given in 3 divided doses.

Should it not be possible to give the stated dosages using the Augmentin Trio Forte (312mg/5ml) dosing aid, it is recommended that other medications containing amoxicillin and clavulanic acid be used (156.25mg/5ml).

Age	Daily dose
Under 2 years	25-50 mg/kg/day (20 mg AMX/5 mg CLV to 40 mg/10 mg)
Over 2 years	Mild to moderate infections: 25-37.5 mg/kg/day (20 mg AMX/5 mg CLV to 30 mg/7.5 mg)
	Severe infections: 50-75 mg/kg/day (40 mg AMX/10 mg CLV to 60 mg/15 mg)

Augmentin Duo

The daily dose should be given in 2 divided doses.
Augmentin Duo should only be used in the infections stated below. For other indications Augmentin Trio Forte should be considered.

Age	Daily dose
Under 2 years	***Acute otitis media:*** 29-51 mg/kg/day (25.4 mg AMX/3.6 mg CLV to 44.6 mg/6.4 mg)
Over 2 years	***Tonsillitis and mild to moderate lower respiratory tract infections:*** 29-51 mg/kg/day (25.4 mg AMX/3.6 mg CLV to 44.6 mg/6.4 mg)
	Otitis media: 51-80 mg/kg/day (44.6 mg AMX/6.4 mg CLV to 70 mg/10 mg)

Dosage recommendations

Augmentin Trio Forte

For the treatment of infections in neonates and infants up to 3 months of age, please refer to the Prescribing Information for Augmentin i.v.
Should it not be possible to give the stated dosages using the Augmentin Trio Forte (312mg/5ml) dosing aid, it is recommended that other medications containing amoxicillin and clavulanic acid be used (156.25mg/5ml).

Mild to moderate infections:

Weight	Age (approx.)	Pharmaceutical form	Dosage
5-9 kg	3-12 months	Other medication containing amoxicillin and clavulanic acid, 156.25mg/5ml (125/31.25), suspension	It is not possible to give Augmentin to this age group with the forms currently available.
10-19 kg	1-5 years	Trio Forte 312.5mg/5ml (250/62.5), suspension	2.5 ml three times daily
20-39 kg	5-12 years	Trio Forte 312.5mg/5ml (250/62.5), suspension	5 ml three times daily

> 40 kg	> 12 years	Film-coated tablets	See Prescribing Information for Augmentin film-coated tablets

Severe infections:

Weight	**Age (approx.)**	**Pharmaceutical form**	**Dosage**
5-9 kg	3-12 months	Other medication containing amoxicillin and clavulanic acid, 156.25mg/5ml (125/31.25), suspension	It is not possible to give Augmentin to this age group with the forms currently available.
10-12 kg	1-2 years	Trio Forte 312.5mg/5ml (250/62.5), suspension	2.5 ml three times daily
13-24 kg	2-7 years	Trio Forte 312.5mg/5ml (250/62.5), suspension	5 ml three times daily
25-39 kg	7-12 years	Trio Forte 312.5mg/5ml (250/62.5), suspension	10 ml three times daily
> 40 kg	> 12 years	Film-coated tablets	See Prescribing Information for Augmentin film-coated tablets

Augmentin Duo

Augmentin Duo 457 mg (400/57) suspension is used for certain infections in children aged 2 months and over (see "General dosing guidelines").

The 35 ml suspension pack contains a dosing pipette, in 0.2 ml steps to 5 ml.
The 70 ml and 140 ml packs contain a dosing cup, with 2.5, 5, 7.5 and 10 ml graduations.

Tonsillitis and mild to moderate lower respiratory tract infections:

Weight	**Age (approx.)**	**Dosage Augmentin Duo 457mg/5ml (400/57) suspension**
13-15 kg	2-3 years	2.5 ml twice daily
16-18 kg	3-5 years	3 ml twice daily
19-21 kg	5-6 years	3.5 ml twice daily
22-30 kg	6-10 years	5 ml twice daily
31-40 kg	10-12 years	7.5 ml twice daily

Acute otitis media:

Weight	**Age (approx.)**	**Dosage Augmentin Duo 457mg/5ml (400/57) suspension**
4-6 kg	2-6 months	1 ml twice daily
7-9 kg	6-12 months	1.6 ml twice daily
10-12 kg	1-2 years	2 ml twice daily
13-17 kg	2-4 years	5 ml twice daily
18-26 kg	4-8 years	7.5 ml twice daily
27-35 kg	8-10 years	10 ml twice daily
36-40 kg	10-12 years	12.5 ml twice daily

Special dosage instructions

Renal impairment

(Augmentin Trio Forte only, not Augmentin Duo 457 mg, should be used for the treatment of patients with creatinine clearance less than 30 ml/min.)

Children up to 40 kg:
Should it not be possible to give the stated dosages using the Augmentin Trio Forte (312mg/5ml) dosing aid, it is recommended that other medications containing amoxicillin and clavulanic acid be used (156.25 mg/5ml).

Creatinine clearance	Dosage
10-30 ml/min	15/3.75 mg/kg Augmentin Trio Forte every 12 hours (maximum 500/125 mg every 12 hours).
less than 10 ml/min	15/3.75 mg/kg Augmentin Trio Forte every 24 hours (maximum 500/125 mg every 24 hours).
haemodialysis	15/3.75 mg/kg Augmentin Trio Forte every 24 hours, plus one additional dose both during and at the end of dialysis.

Augmentin Duo should not be administered to patients with creatinine clearance less than 30 ml/min.
No dose adjustment is required where creatinine clearance is above 30 ml/min.

Method of administration
Augmentin is best taken at the start of a meal, thereby optimising absorption and gastrointestinal tolerance. The dose is dependent on the age, body weight and renal function of the patient, as well as on the severity of the infection. Parenteral therapies may be continued by the oral route.

Contra-indications
Augmentin is contra-indicated in patients with known hypersensitivity to penicillins and cephalosporins or to an ingredient of Augmentin, and also in patients who developed jaundice or hepatic dysfunction during previous treatment with Augmentin.
Infectious mononucleosis, lymphatic leukaemia: patients suffering from these diseases are particularly predisposed to exanthema when taking amoxicillin.

Warnings and precautions
– Augmentin Duo should not be administered in renal impairment (creatinine clearance less than 30 ml/min) (see "Special dosage instructions").
– Before treatment with Augmentin is started, it should be established whether hypersensitivity reactions to penicillins, clavulanic acid, cephalosporins or other allergens have occurred previously.
- Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions) have been reported in patient on penicillin therapy. If an allergic reaction occurs, Augmentin therapy should be discontinued and appropriate alternative therapy instituted
– Emergency measures in the event of anaphylactic or anaphylactoid reactions should be to hand. These reactions require immediate injection of adrenaline (beware cardiac arrhythmia). If necessary, the administration of adrenaline can be repeated. Then i.v. administration of glucocorticoids (e.g. 250-1000 mg prednisolone). The administration of glucocorticoids can be repeated if necessary. Oxygen, intravenous steroids and ventilation, including intubation, may also be necessary. In children the dosage of the preparations should be adjusted according to bodyweight or age. Further treatment measures such as intravenous administration of antihistamines and volume replacement should be considered. Careful monitoring of the patient is necessary, as the symptoms may recur.

– Proliferation of non-sensitive microorganisms can occur during long-term use. In such a case, suitable clarification and treatment must be initiated.
– The occurrence of diarrhoea, in particular severe, persistent and/or bloody diarrhoea, during or after treatment with Augmentin may be a symptom of a *Clostridium difficile* infection. The most severe form is pseudomembranous colitis. If a complication of this kind is suspected, discontinue treatment with Augmentin immediately and examine the patient thoroughly so that specific antibiotic therapy (e.g. metronidazole, vancomycin) can be initiated if required. The use of antiperistaltic agents is contraindicated in this clinical situation.

– During long-term treatment, the periodic monitoring of renal, hepatic and haemopoietic function is recommended.
– There have been rare reports of abnormal prolongation of prothrombin time (increased INR) in patients receiving amoxicillin-clavulanate and oral anticoagulants. If anticoagulants are prescribed concomitantly, appropriate monitoring should therefore be instituted. To maintain the desired degree of anticoagulation the dose of the oral anticoagulants may need to be adjusted.
– Augmentin should be administered with caution in hepatic impairment.
– The suspensions contain aspartame and should therefore be used with caution in patients with phenylketonuria.
– In the case of severe gastrointestinal disorders with vomiting and diarrhoea, sufficient absorption of Augmentin is no longer guaranteed. Parenteral administration should then be considered.
– In patients with reduce urinary excretion crystalluria has been observed very rarely, particularly during parenteral treatment. Acute renal failure may occur as a possible consequence of crystalluria. When high doses of amoxicillin are being administered, adequate fluid intake and corresponding urinary excretion should be ensured to reduce the possibility of amoxicillin crystalluria. Amoxicillin in high concentrations in the urine may be precipitated in a catheter at room temperature. Therefore normal urinary flow in the catheter should be regularly monitored.

Interactions
Probenecid inhibits renal tubular elimination of amoxicillin, but not of clavulanic acid. Co-administration with Augmentin may result in elevated and prolonged blood levels of amoxicillin. Co-administration is not recommended.

Oral contraceptives: during treatment with amoxicillin the enterohepatic circulation of oral contraceptives may be reduced or eliminated completely by impairment of the intestinal flora. This reduces the efficacy of the contraceptives.

As amoxicillin only works against bacteria in the growth phase, there is an interaction with bacteriostatic antibiotics.

There is the possibility of an interaction with glycosides (e.g. digoxin), because antibiotics can damage the intestinal flora, leading to increased absorption of glycosides in some patients.

The concomitant use of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions. No data are available on the combination of Augmentin and allopurinol.

Rare cases of increased International Normalised Ratio (INR) have been described in the literature in patients receiving acenocoumarol or warfarin who were prescribed amoxicillin therapy. If co-administration is necessary, the prothrombin time or International Normalised Ratio should be carefully monitored when adding or discontinuing 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/lactation

Pregnancy

Reproduction studies in animals (mice and rats at doses up to 10 times the human dose) with oral and parenteral Augmentin showed no teratogenic effects.
In a study in women with premature rupture of the foetal membrane, it was reported that prophylactic treatment with Augmentin may be associated with an increased risk of necrotising enterocolitis in neonates (incidence of proven necrotising enterocolitis in neonates 1.5% with Augmentin treatment versus 0.5% without Augmentin treatment).
Augmentin should not therefore be used during pregnancy unless absolutely necessary.

Lactation

As traces of Augmentin are excreted in breast milk, there is the possibility of a hypersensitivity reaction in sensitive neonates. Impairment of the intestinal flora of infants is conceivable in theory, but has not been observed to date at the recommended dosage. Mothers should not therefore breastfeed during treatment with Augmentin.

Effects on ability to drive and operate machines

Certain drug reactions varying from individual to individual (see Undesirable effects) may affect a patient's concentration and reactions to such an extent that the ability to drive or operate machines may be impaired.

Undesirable effects

The frequencies of very common to rare adverse effects have been taken from the data material of major clinical studies. The frequencies of the remaining undesirable reactions (i.e. with an incidence < 1/10,000) come predominantly from the data of post-marketing reports and therefore relate to the reporting frequency and not to the actual frequency of occurrence.

The following definitions were used for classifying the frequency of undesirable effects:
very common (≥1/10)
common (<1/10, ≥1/100)
uncommon (<1/100, ≥1/1,000)
rare (<1/1,000, ≥1/10,000)
very rare (<1/10,000)

Infections and infestations

Common Mucocutaneous candidiasis

Blood and lymphatic system disorders

Rare	Reversible leucopenia (including severe neutropenia) and thrombocytopenia
Very rare	Reversible agranulocytosis and haemolytic anaemia. Prolongation of bleeding time and prothrombin time (Quick value) (see "Warnings and precautions" and "Interactions").

Post-marketing data

Rare	Thrombocytosis

Immune system disorders

Very rare	Angioneurotic oedema, anaphylactic reaction, serum sickness-like syndrome, hypersensitivity vasculitis Anaphylactic shock requires immediate injection of adrenaline (see "Warnings and precautions").

Data from clinical studies

Common	Reversible eosinophilia (hypersensitivity reaction)

Post-marketing data

Very rare	Anaphylactic reactions (with symptoms such as urticaria, pruritic erythema, angioneurotic oedema; abdominal pain, vomiting, including abdominal symptoms; dyspnoea with bronchospasm or laryngeal oedema; circulatory symptoms such as fall in blood pressure or even anaphylactic shock). Herxheimer's reaction is possible in the treatment of typhoid fever, syphilis or leptospirosis. If a hypersensitivity reaction occurs the treatment must be discontinued immediately (see also "Skin and subcutaneous tissue diseases").

Nervous system disorders

Uncommon	Dizziness, headache
Very rare	Reversible hyperactivity and clonic seizures. Clonic seizures may occur in patients with renal impairment or in patients receiving high doses.

Post-marketing data

Very rare	Agitation, anxiety, insomnia, confusion, behavioural changes, stupor, dysaesthesia.

Gastrointestinal disorders

Very common	Diarrhoea
Common	Nausea, vomiting

Nausea occurs more frequently with higher oral doses. If gastrointestinal reactions do occur they can be minimised by taking Augmentin at the start of a meal.

Uncommon	Dyspepsia, loss of appetite, abdominal pressure, flatulence.
Rare	Glossitis, stomatitis.
Very rare	- Antibiotic-induced colitis (including pseudomembranous colitis and haemorrhagic colitis), see "Warnings and precautions"). - Reports of superficial discolouration of children's teeth, after using the suspension. Good oral hygiene could prevent the occurrence of tooth discolouration as it can generally be removed by cleaning the teeth. - Black hairy tongue (only after using the oral formulations). - A cohort study of 576 nine-year-old children showed that administration of amoxicillin at age 0-9 months significantly increases the risk of fluorosis of

the definitive maxillary incisors. Fluorosis can manifest as white stripes, cosmetically disturbing discolouration, enamel indentations and even deformation of the teeth.

Data from clinical studies

Very common	Soft stools
Common	Abdominal pain

Hepatobiliary disorders

Uncommon	- Moderate increase in AST and/or ALT level was observed in patients receiving Augmentin. - Transient increase in lactate dehydrogenase and alkaline phosphatase.
Rare	Hepatitis and cholestatic jaundice.

The risk appears to be slightly increased when the duration of therapy is prolonged, in patients aged ≥65 years and in males. Undesirable effects of this nature have been reported extremely rarely in children. The incidence of these effects during Augmentin therapy is approx. 5 times higher than with amoxicillin alone.

The signs and symptoms usually occur during or shortly after the treatment, but in isolated cases may not be observed until some weeks after the end of the treatment and are usually reversible. Events in the liver region may be severe and in extremely rare cases may even result in death. These cases occurred almost exclusively, however, in patients with a serious underlying disease or when Augmentin was taken concomitantly with medicines having a known side-effect potential in the liver region.

Skin and subcutaneous tissue disorders

Uncommon	Rash (in the form of maculopapular or morbilliform rash) and erythema, pruritus, urticaria
Rare	Erythema multiforme
Very rare	Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous exfoliative dermatitis, acute generalised exanthematous pustulosis (AGEP), and drug reactions with eosinophilia and systemic symptoms (DRESS).

The treatment should be discontinued if dermatitis occurs as a hypersensitivity reaction.

Renal and urinary disorders

Very rare	Interstitial nephritis, crystalluria. Renal impairment with elevation of serum BUN and creatinine concentration.

Overdose

In the event of overdose, gastrointestinal symptoms and fluid and electrolyte imbalance may occur. These can be treated symptomatically with activated charcoal and administration of fluids.
Augmentin can be removed from the circulation by haemodialysis.
In severe overdose with amoxicillin very high levels in the urine occur, particularly after parenteral administration.
There have been reports of amoxicillin crystalluria and accompanying acute renal failure (see "Warnings and precautions").

Properties/effects

– *ATC code:* J01CR02

– *Mechanism of action*

Augmentin is a bactericidal antibiotic. Amoxicillin is a semisynthetic aminopenicillin from the group of beta-lactam antibiotics and has a bactericidal activity against Gram-positive and Gram-negative pathogens. The bactericidal effect of amoxicillin is based on inhibition of bacterial cell wall synthesis by blocking the transpeptidases. Amoxicillin is acid-resistant but sensitive to penicillinases.

Clavulanic acid is a beta-lactam which has a low-level antibacterial effect against some pathogens. The main effect of clavulanic acid lies in its enzyme-inhibiting activity against many types of beta-lactamases.
In particular, it has good activity against the clinically important plasmid mediated beta-lactamases frequently responsible for transferred drug resistance. It is generally less effective against chromosomally-mediated type 1 beta-lactamases.
This inhibition protects amoxicillin against destruction by beta-lactamases and thus allows the amoxicillin to develop its antibiotic effect in full.

Due to the combination of amoxicillin and clavulanic acid, many pathogens which would be resistant to amoxicillin because of their production of beta-lactamase, become sensitive. This synergistic effect is seen at the concentrations of clavulanic acid achieved in the body after parenteral or oral administration.

Spectrum of action

In *vitro*-susceptibility of micro-organisms
In the following list the micro-organisms are classified following there susceptibility to Augmentin.

Where clinical efficacy of amoxicillin-clavulanate has been demonstrated in clinical trials this is indicated with an asterisk (*).

Organisms that do not produce beta-lactamase are identified (with †). If an isolate is susceptible to amoxicillin, it can be considered susceptible to amoxicillin-clavulanate.

Commonly susceptible species:

Gram-positive aerobes:

- Bacillus anthracis
- Enterococcus faecalis
- Listeria monocytogenes
- Nocardia asteroides
- Streptococcus pneumoniae*+
- Streptococcus pyogenes *+
- Streptococcus agalactiae*+
- Streptococcus viridans +

- Streptococcus spp. (andere β-hämolysierende Streptokokken)*+
- Staphylococcus aureus (Methicillin-empfindlich) *
- Staphylococcus saprophyticus (Methicillin-empfindlich)
- Coagulase-negative Staphylokokken (Methicillin-empfindlich)

Gram-negative aerobes:

- Bordetella pertussis
- Haemophilus influenzae*
- Haemophilus parainfluenzae
- Helicobacter pylori
- Moraxella catarrhalis*
- Neisseria gonorrhoeae
- Pasteurella multocida
- Vibrio cholerae

Other:

- Borrelia burgdorferi
- Leptospira ictterohaemorrhagiae
- Treponema pallidum

Gram-positive anaerobes:

- Clostridium spp.
- Peptococcus niger
- Peptostreptococcus magnus
- Peptostreptococcus micros
- Peptostreptococcus spp.

Gram-negative anaerobes:

- Bacteroides fragilis
- Bacteroides spp.
- Capnocytophaga spp.
- Eikenella corrodens
- Fusobacterium nucleatum
- Fusobacterium spp.
- Porphyromonas spp
- 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

Inherently resistant organisms

Gramnegative Aerobier:

- Acinetobacter spp.
- Citrobacter freundii
- Enterobacter spp.
- Hafnia alvei
- Legionella pneumophila
- Morganella morganii
- Providencia spp.
- Pseudomonas spp.
- Serratia spp.
- Stenotrophomas maltophilia
- Yersinia enterocolitica

Other:

- Chlamydia pneumoniae
- Chlamydia psittaci
- Chlamydia spp.
- Coxiella burnetti
- Mycoplasma spp.

Pharmacokinetics

Absorption

Amoxicillin and clavulanic acid are well absorbed in the intestine. For optimum absorption, administration at the start of a meal is recommended. The absorption curves of the two components are similar; the peak serum levels of amoxicillin and clavulanic acid are reached

about 1-1½ hours after oral administration. After consumption of a 375 mg tablet (250/125), they are around 5 mg/l (amoxicillin) and 3 mg/l (clavulanic acid).
The total quantities absorbed are usually 80% for amoxicillin and 70% for clavulanic acid.

Distribution
Amoxicillin and clavulanic acid are approx. 18% and approx. 25% bound to plasma proteins respectively. The volume of distribution is 22 litres for amoxicillin and 16 litres for clavulanic acid.
As high serum concentrations of amoxicillin and clavulanic acid are reached after oral administration of Augmentin, good penetration into body fluids can be expected.
Therapeutic concentrations of both active ingredients have been found in abdominal tissues, gall bladder, skin, adipose and muscle tissue and in following body fluids: synovial, peritoneal and pleural fluids, bile, sputum, pus.

Both active ingredients diffuse into the placenta; however, no adverse effects were observed in animal reproduction studies. There is limited clinical experience in humans.

The concentrations of amoxicillin in breast milk are low. Traces of clavulanic acid have also been found in breast milk. With the exception of the risk of a hypersensitivity reaction associated with this excretion, there are no known harmful effects for the breast-fed infant.

Metabolism
Amoxicillin is 10-25% metabolised into the corresponding inactive penicilloic acid, which is excreted renally. Clavulanic acid is 35-60% converted to inactive metabolites.

Elimination
Amoxicillin and clavulanic acid are excreted mainly by the kidneys. During the first 6 hours after oral administration, approx. 60-70% of the amoxicillin and 40-65% of the clavulanic acid administered are excreted in the urine in unchanged form.
The elimination half-life of both amoxicillin and clavulanic acid is approx. 1-1½ hours in patients with normal renal function.

Kinetics in special patient populations
In renal impairment the renal elimination of both active ingredients is delayed; the dose must be adjusted accordingly. The plasma concentration of both active ingredients is greatly reduced by haemodialysis.

Preclinical data
Administration of amoxicillin and clavulanate in combination (2:1) or of clavulanate alone did not reveal either in rats or mice any effect in the F0 generation in terms of mating behaviour, fertility, pregnancy (including embryonal and foetal development) or parturition. In addition, no adverse effects were observed on embryonal/foetal development and no negative effect observed on viability, growth, development, behaviour or reproductive function of F1 progeny.

Potassium clavulanate, administered alone and in combination with amoxicillin (1:2 or 1:4), was tested under *in vitro* and *in vivo* conditions in a battery of genotoxicity tests by which very different endpoints could be recorded. The results obtained led to the conclusion that the administration of amoxicillin or clavulanate does not entail any genotoxic risks.

Other information

– Incompatibilities
None known.

– Interference with diagnostic tests
Possibly falsified results of oestriol measurement in pregnant women.
Due to the high concentration of amoxicillin in the urine, the measurement of glucose using chemical methods (Benedict or Fehling solution or with Clinitest) may be affected (false positive results). It is therefore recommended that the measurement of glucose be conducted by enzymatic (glucose oxidase) methods (Dextrostix, Diastix or Clinistix).
The direct Coombs test can show positive without there being haemolysis.
In amino acid chromatography of the urine, amoxicillin or its breakdown products can give ninhydrin-positive spots.
Possible interference in urine and serum total protein measurements by means of a colour reaction (ninhydrin reaction after Ehrlich).
Possible false positive colour reaction in glycosuria determinations.
Falsely elevated serum uric acid concentrations may occur if the copper chelate method is used. The tungsten phosphate and uricase methods for uric acid determination are not affected by amoxicillin.

– Shelf-life
The medicine must not be used after the date shown on the container beside the letters "EXP".
Stability after reconstitution:
The Trio Forte 312.5mg/5ml (250/62.5) suspension and the Duo 457mg/5ml (400/57) suspension can be stored in a refrigerator (2-8°C) for 7 days after reconstitution.

– Special storage instructions
Store in a dry place, at room temperature (15-25°C) and out of the reach of children.

– Instructions for handing
Preparation of the suspensions:
The suspensions are normally prepared by the pharmacist.

Augmentin Trio Forte 312.5mg/5ml (250/62.5) suspension:
Shake the bottle containing the powder. Carefully fill with tap water (90 ml) up to the line on the label. Shake the bottle well and allow to stand for a short time. If necessary, add water again up to the mark. This produces 100 ml of ready-for-use suspension. Shake the bottle each time before use. One 2.5 ml spoonful = 156.25 mg of active ingredients (125 mg amoxicillin, 31.25 mg clavulanic acid). One 5 ml spoonful = 312.5 mg of active ingredients (250 mg amoxicillin, 62.5 mg clavulanic acid).

Augmentin Duo 457mg/5ml (400/57) suspension:
Shake the bottle containing the powder. Carefully fill with tap water (in 2 portions) up to the line on the label (31 ml for 35 ml, 62 ml for 70 ml or 124 ml for 140 ml of suspension). Shake the bottle well and allow to stand for a short time. If necessary, add water again up to the mark. This produces 35, 70 or 140 ml of ready-for-use suspension. Shake the bottle each time before use. 2.5 ml = 228.5 mg of active ingredients (200 mg amoxicillin, 28.5 mg clavulanic acid). 5 ml = 457 mg of active ingredients (400 mg amoxicillin, 57 mg clavulanic acid).

Authorisation numbers
Suspension Trio Forte 312.5mg/5ml (250/62.5): 45673 (Swissmedic)
Suspension Duo 457mg/5ml (400/57): 53974 (Swissmedic)

Packs

Augmentin Trio Forte 312.5mg/5ml (250/62.5): with 2.5 and 5 ml measuring spoon	Packs of 1 bottle with powder for the preparation of 100 ml suspension. **A**
Augmentin Duo 457mg/5ml (400/57): 35 ml with dosing pipette graduated in 0.6 ml steps to 5 ml. 70 ml and 140 ml with dosing cup, with graduations at 2.5, 5, 7.5 and 10 ml	Packs of 1 bottle with powder for the preparation of 35 ml, 70 ml or 140 ml suspension. **A**

Authorisation holder
GlaxoSmithKline AG, Münchenbuchsee

Date of information
January 2018