CoAmox Acino™

CoAmox Acino™ 1000 Lactab™
CoAmox Acino™ 156.25/312.5/457 Suspension

Antibiotic (amoxicillin + clavulanic acid)

Composition
Active substances:
Amoxicillin (AMX)(in the form of trihydrate), clavulanic acid (CLV) (in the form of potassium salt).
CoAmox Acino 1000 Lactab
Excipients per film-coated tablet.
CoAmox Acino 156.25 Suspension
Preservative sodium benzoate (E211), saccharin sodium, aroma/flavour and other excipients.
CoAmox Acino 312.5 Suspension
Preservative sodium benzoate (E211), saccharin sodium, aroma/flavour and other excipients.
CoAmox Acino 457 Suspension
Saccharin sodium, aroma/flavour and other excipients.

Galenical form and amount of active substance per unit
CoAmox Acino 1000 Lactab
Each film-coated tablet contains: 875 mg amoxicillin (in the form of trihydrate), 125 mg clavulanic acid (in the form of potassium salt).
Amoxicillin/clavulanic acid ratio: 7:1
CoAmox Acino 156.25 Suspension
5 ml prepared suspension contain: 125 mg amoxicillin (in the form of trihydrate), 31.25 mg clavulanic acid (in the form of potassium salt).
Amoxicillin/clavulanic acid ratio: 4:1
CoAmox Acino 312.5 Suspension
5 ml prepared suspension contain: 250 mg amoxicillin (in the form of trihydrate), 62.5 mg clavulanic acid (in the form of potassium salt).
Amoxicillin/clavulanic acid ratio: 4:1
CoAmox Acino 457 Suspension
5 ml prepared suspension contain: 400 mg amoxicillin (in the form of trihydrate), 57 mg clavulanic acid (in the form of potassium salt).
Amoxicillin/clavulanic acid ratio: 7:1

Indications/Possibilities for use
CoAmox Acino is indicated for Gram-positive and Gram-negative bacterial infections with pathogens which are sensitive to CoAmox Acino (particularly organisms which, because of their beta-lactamase production, are resistant to amoxicillin).
CoAmox Acino 1000 Lactab
- Acute sinusitis
- Community acquired pneumonia
- Acute exacerbation of chronic bronchitis
- Pyelonephritis
- Complicated urinary tract infections

CoAmox Acino 156.25 and 312.5 Suspension
- *ORL infections*
  Tonsilitis, 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, amongst others, caused by *E. coli*.
- *GI infections*
  Typhoid fever, paratyphoid, shigellosis (bacillary dysentery).
- *Venereal diseases*
  Gonorrhoea (specific urethritis).
- *Infections of the skin and soft tissue*
  Mainly caused by *Staphylococcus aureus* and *Streptococcus pyogenes*.
- *Gynaecological infections*
  Salpingitis, adnexitis, endometritis, bacterial vaginitis.

CoAmox Acino 457 Suspension
- Tonsillitis.
- Lower respiratory tract infections.
- Otitis media.

Official recommendations for the appropriate use of antibiotics should be followed, especially recommendations for use to prevent increased resistance to antibiotics.

Posology/Method of administration
The dose is dependent on the patient's age, body weight and renal function, as well as the severity of the infection. Parenteral treatments can be continued orally.
Usual dosage
Adults and children over 40 kg
In acute sinusitis, community acquired pneumonia, acute exacerbation of chronic bronchitis, pyelonephritis and complicated urinary tract infections 2 x 1 g (875/125) per day.
If necessary the dose can be increased to a maximum of 3 x 1 g (875/125) per day.
Children up to 40 kg
CoAmox Acino film-coated tablets are not indicated for the treatment of infections in children.
a) General dosage guidelines
The general dosage guidelines per kg and day (see below) should be observed. The CoAmox Acino forms 156.25 and 312.5 must always be taken three times daily; CoAmox Acino 457 may only be taken twice daily.
CoAmox Acino 156.25 and 312.5 Suspension
The daily dose must be divided into three single doses.

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

CoAmox Acino 457 Suspension
The daily dose must be divided into two single doses.
CoAmox Acino 457 should only be used for the infections indicated here. For other indications CoAmox Acino 156.25 or 312.5 should be considered.

Age	Daily dose
Below 2 years	*Acute otitis media:* 29-51 mg/kg/day (25.4 mg AMX/3.6 mg CLV to 44.6 mg AMX/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 per day (44.6 mg AMX/6.4 mg CLV to 70 mg/10 mg)

b) Recommended dosage
CoAmox Acino 156.25 and 312.5 Suspension
Mild to moderately severe infections:

Weight	Age (approx.)	Galenical form	Dosage
5-9 kg	3-12 months	CoAmox Acino 156.25 mg/ 5 ml (125/31.25), Suspension	3 times daily 2.5 ml
10-19 kg	1-5 years	CoAmox Acino 156.25 mg/ 5 ml (125/31.25), Suspension or CoAmox Acino 312.5 mg /5 ml (250/62.5), Suspension	3 times daily 5 ml 3 times daily 2.5 ml
20-39 kg	5-12 years	CoAmox Acino 312.5 mg / 5 ml (250/62.5), Suspension	3 times daily 5 ml
>40 kg	> 12 years	film-coated tablets	see above

Severe infections:

Weight	Age (approx.)	Galenical form	Dosage
5-9 kg	3-12 months	CoAmox Acino 156.25 mg/5 ml (125/31.25), Suspension	3 times daily 2.5 ml
10-12 kg	1-2 years	CoAmox Acino 156.25 mg/5 ml (125/31.25), Suspension or CoAmox Acino 312.5 mg/5 ml (250/62.5), Suspension	3 times daily 5 ml 3 times daily 2.5 ml
13-24 kg	2-7 years	CoAmox Acino 312.5 mg/5 ml (250/62.5), Suspension	3 times daily 5 ml
25-39 kg	7-12 years	CoAmox Acino 312.5 mg/5 ml (250/62.5), Suspension	3 times daily 10 ml
> 40 kg	> 12 years	film-coated tablets	see above

CoAmox Acino 457 Suspension
CoAmox Acino 457 mg (400/57) Suspension is used for certain infections in children older than 2 months of age (see «General dosage guidelines»). Packs of 70 ml suspension contain a syringe dosing device with 0.5 ml graduations up to 5 ml.
Tonsillitis and mild to moderately severe lower respiratory tract infections

Weight	Age (approx.)	Dosage CoAmox Acino 457 mg/5 ml (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 CoAmox Acino 457 mg/5 ml (400/57) Suspension
4-6 kg	2-6 months	1 ml twice daily
7-9 kg	6-12 months	1.5 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 failure
Renal failure slows the excretion of amoxicillin and clavulanic acid. CoAmox Acino should therefore be given in the following dosage, dependent on the degree of renal failure, expressed as creatinine clearance:
a) Adults and children over 40 kg
CoAmox Acino 1000 (875/125) must not be given to patients with a creatinine clearance of less than 30 ml/min.
If the creatinine clearance is over 30 ml/min, no adaptation of the dose is necessary.
Haemodialysis
One additional normal dose during and at the end of dialysis (since haemodialysis reduces the plasma concentration of amoxicillin and clavulanic acid).
The 1 g film-coated tablets should only be given to patients with a creatinine clearance > 30 ml/min.
Elderly patients
No adaptation of the dose is necessary; dose as for adults. In the case of renal failure, the dose should be adapted according to the dosage for adults with renal failure.
b) Children up to 40 kg

Creatinine clearance	Dosage
10-30 ml/min	15/3.75 mg/kg CoAmox Acino 156.25 or 312.5 every 12 hours (max. 500/125 mg every 12 hours
Less than 10 ml/min	15/3.75 mg/kg CoAmox Acino 156.25 or 312.5 every 24 hours (max. 500/125 mg every 24 hours)
Haemodialysis	15/3.75 mg/kg CoAmox Acino 156.25 or 312.5 every 24 hours plus one additional dose during and one dose at the end of dialysis

CoAmox Acino 457 Suspension must not be used for the treatment of patients with a creatinine clearance of less than 30 ml/min.
If the creatinine clearance is over 30 ml/min no adaptation of the dose is necessary.
Correct method of use
CoAmox Acino should be taken preferentially at the beginning of meals to optimise absorption and gastrointestinal tolerance.
The film-coated tablets should be taken with at least half a glass of water.
Parenteral treatments can be continued orally.

Contraindications
CoAmox Acino is contraindicated in patients with known hypersensitivity to penicillins, cephalosporins or any of the ingredients of CoAmox Acino and in patients who have developed jaundice or hepatic dysfunction during earlier treatment with CoAmox Acino.
Infectious mononucleosis, lymphatic leukaemia
Patients suffering from these diseases are particularly predisposed to developing exanthema under amoxicillin therapy.

Special warnings and precautions for use
CoAmox Acino 457 and CoAmox Acino 1000 (875/125) should not be given to patients with limited renal function (creatinine clearance of less than 30 ml/min; see «Special dosage instructions»).
Before treatment with CoAmox Acino can be started, it should be checked whether the patient has already had allergic reactions to penicillins, clavulanic acid, cephalosporins or any other allergens.
Emergency measures should be prepared in case of anaphylactic or anaphylactoid reactions. Such reactions require the immediate injection of adrenaline (caution: cardiac arrhythmias). The adrenaline dose can be repeated if necessary. Intravenous glucocorticoids should then be given (e.g. 250-1000 mg prednisolone). The glucocorticoid dose can be repeated if necessary. Oxygen, intravenous steroids and ventilation, including intubation, may also be necessary. For children, the dose should be appropriately adapted according to body weight and age. Further treatment, such as the intravenous administration of antihistamines and volume replacement, should be considered. Careful monitoring of the patient is necessary as the symptoms can reoccur.
For patients with limited renal function the dosage intervals should be lengthened depending on the severity of the dysfunction (see «Special dosage instructions»).
With long-term use proliferation of non-sensitive pathogens can occur. In that case, suitable treatment must be started after carrying out appropriate investigations.
During long-term treatment periodic checks on the renal, hepatic and haematopoietic functions are recommended.
Abnormal prolongation of prothrombin times (INR increased) has rarely been reported in patients taking amoxicillin-clavulanic acid and oral anticoagulants. If anticoagulants are co-prescribed appropriate monitoring should therefore be undertaken. The dose of oral anticoagulants might need to be adapted in order to maintain the desired degree of anticoagulation.
In the case of hepatic dysfunction CoAmox Acino should only be used with caution.
In case of severe gastrointestinal disorders with vomiting and diarrhoea, sufficient absorption of CoAmox Acino can no longer be guaranteed. Parenteral administration should then be considered.
In patients with reduced urine excretion crystalluria has been observed on very rare occasions, particularly during parenteral treatment. As a possible consequence of crystal formation acute renal failure can occur. If high doses of amoxicillin are given, sufficient fluid intake and appropriate urine excretion must be ensured in order to reduce the possibility of amoxicillin crystalluria. In the case of high concentrations in the urine, amoxicillin can precipitate in the bladder catheter at room temperature. The catheter should therefore be checked regularly to ensure that the urine excretion is normal.
Pseudomembranous colitis has been reported on rare occasions. If this infection should occur, the medicine must be discontinued immediately and suitable treatment started.
Medicines that inhibit peristalsis are contraindicated.
Since orally administered antibiotics can reduce the efficacy of oral contraceptives, patients should be warned to take additional anti-conceptive measures during treatment with CoAmox Acino.
CoAmox Acino 156.25 and 312.5 Suspension contain sodium benzoate which is a mild irritant to skin, eye and mucous membrane. The risk of jaundice in newborns may be increased.

Interaction with other medicinal products and other forms of interaction
Probenecid
Probenecid inhibits the renal tubular elimination of amoxicillin, but not of clavulanic acid. Concurrent administration with CoAmox Acino can result in increased and prolonged blood levels of amoxicillin. Concurrent administration is therefore not advised.
Oral contraceptives
During treatment with amoxicillin the damage to the intestinal flora can impair or even completely eliminate the enterohepatic circulation of oral contraceptives. The efficacy of contraceptives is thereby reduced.
Bacteriostatic antibiotics
Because amoxicillin only affects bacteria in the growth phase, there is an interaction with bacteriostatic antibiotics.
Glycosides
There is the possibility of interaction with glycosides (e.g. digoxin), because antibiotics can cause damage to the intestinal flora which leads to increased absorption of the glycosides in some patients.
Allopurinol
Concurrent administration of allopurinol during treatment with amoxicillin may increase the incidence of allergic skin reactions.
There is no information available on the combination of CoAmox Acino with allopurinol.
Oral anticoagulants
In the literature rare cases are described of increased international normalised ratio (INR) in patients maintained on acenocoumarol or warfarin who have been prescribed a course of amoxicillin. If co-administration is necessary, the prothrombin time or international normalised ratio should be carefully monitored if amoxicillin is added or withdrawn.

Fertility/Pregnancy/Lactation
Pregnancy
Reproduction studies on animals (mice and rats with up to ten times higher doses than used for humans) with CoAmox Acino administered orally and parenterally did not show any teratogenic effects.
In a study in women with premature rupture of the foetal membranes it was reported that prophylactic treatment with CoAmox Acino can be associated with an increased risk of necrotising enterocolitis in new-born babies (incidence of proven necrotising enterocolitis in neonates of 1.5% with CoAmox Acino treatment compared with 0.5% without CoAmox Acino treatment).
CoAmox Acino should therefore not be used during pregnancy unless it is absolutely necessary.
Lactation
Since traces of CoAmox Acino are passed into breast milk, there is the possibility of an allergic reaction in sensitive neonates. Damage to the intestinal flora of infants is theoretically possible, but has so far not been found when the recommended dosage is given.
Lactation should therefore be avoided during treatment with CoAmox Acino.

Effects on ability to drive and use machines
Certain responses to the medicine, which vary from individual to individual (see «Undesirable effects») can affect the patient's concentration and reactions to such a degree that their ability to drive or to operate machines can be impaired.

Undesirable effects
The incidences of very common to rare undesirable effects were taken from data gathered in large-scale clinical studies. The incidences of the remaining adverse reactions (i.e. with an incidence of less than 1/10,000) are taken mainly from post-marketing reports and therefore relate to the frequency of notification rather than the actual frequency of occurrence.
The following definitions are used to classify the frequency of undesirable effects:
Very common (≥ 1/10); *common* (≥ 1/100 to < 1/10); *uncommon* (≥ 1/1,000 to < 1/100); *rare* (≥ 1/10,000 to < 1/1,000); *very rare* (<1/10,000); *not known* (cannot be estimated from the available data).
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's value; see «Special warnings and precautions for use»).
Post-marketing data
Rare: thrombocytosis.
Immune system disorders
Very rare: angioneurotic oedema, anaphylactic reaction. Serum sickness-like syndrome, hypersensitivity vasculitis. Anaphylactic shock requires the immediate injection of adrenaline (see «Special warnings and precautions for use»).
Data from clinical studies
Common: reversible eosinophilia (allergic reaction).
Post-marketing data
Very rare: anaphylactic reactions (with symptoms such as urticaria, itching erythema, angioneurotic oedema, abdominal pain, vomiting and other abdominal signs; dyspnoea with bronchospasm or laryngeal oedema; circulatory symptoms ranging from a drop in blood pressure to anaphylactic shock). A Herxheimer reaction is possible in the treatment of typhus, syphilis or leptospirosis. If a hypersensitivity reaction occurs, the treatment must be stopped immediately (see also «Skin and subcutaneous tissue disorders»).
Nervous system disorders
Uncommon: vertigo, headache.
Very rare: reversible hyperactivity and clonic convulsions. Clonic convulsions can occur in patients with impaired renal function or in patients on high doses.
Post-marketing data
Very rare: excitement, anxiety, sleeplessness, confusion, behavioural changes, drowsiness, dysaesthesia.
Gastrointestinal disorders
Very common: diarrhoea.
Common: nausea, vomiting.
Nausea occurs more often with higher oral doses. If gastrointestinal reactions occur, these can be reduced by taking CoAmox Acino at the beginning of a meal.
Uncommon: dyspepsia, loss of appetite, gastric discomfort, flatulence.
Rare: glossitis, stomatitis.
Very rare: colitis caused by antibiotics (including pseudomembranous colitis and haemorrhagic colitis).
There are reports of superficial discoloration of teeth in children after using the suspension. Good oral hygiene could prevent the discoloration of teeth as this discolouration can normally be removed by cleaning the teeth.
Black hairy tongue (only after use of oral forms).
A cohort study with 576 children of 9 years of age showed that the risk of fluorosis of the permanent maxillary incisors was significantly increased by administration of amoxicillin at the age of 0-9 months.
Fluorosis may manifest as white striations, cosmetically unpleasant discolourations, enamel pitting and even deformities of the teeth.
Data from clinical studies
Very common: loose stools.
Common: abdominal pain.
Hepatobiliary disorders
Uncommon: a moderate increase in AST and/or ALT levels has been observed in patients taking CoAmox Acino. Temporary increase in lactate dehydrogenases and alkaline phosphatases.
Rare: hepatitis and cholestatic jaundice.
The risk appears to be slightly increased with longer period of treatment, age ≥ 65 years and in men. Such side-effects have very rarely been reported in children. The incidence of these side-effects is approximately five times higher with CoAmox Acino than with amoxicillin alone.
The signs and symptoms normally occur during or shortly after treatment, although in individual cases they may only become apparent a few weeks after the end of treatment, and they are normally reversible. Effects on the liver can be serious and in extremely rare circumstances can even lead to death. However, these cases have occurred almost exclusively in patients with a serious underlying disease or concomitant treatment with medicines with a known potential for side-effects on the liver.
Skin and subcutaneous tissue disorders
Uncommon: skin rash (in the form of maculopapular or morbilliform exanthema) and reddening of the skin, pruritus, urticaria.
Rare: erythema multiforme.
Very rare: Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous exfoliative-dermatitis, acute generalised exanthematous pustulosis (AGEP).
If dermatitis occurs as a hypersensitivity reaction, the treatment should be discontinued.
Renal and urinary disorders
Very rare: interstitial nephritis, crystalluria. Renal dysfunction with increased BUN and creatinine concentration in the serum.

Overdose
In the event of an overdose gastrointestinal symptoms and a disorder of the fluid and electrolyte balance can occur. This can be treated symptomatically with activated charcoal and fluids.
CoAmox Acino can be removed from the organism by means of haemodialysis.
In the event of a severe overdose of amoxicillin, very high urine levels occur, particularly following parenteral administration.
Amoxicillin crystalluria and associated acute renal failure have been reported (see «Special warnings and precautions for use»).

Properties/Effects
ATC code: J01C R02
Mechanism of action
CoAmox Acino is a bactericidal antibiotic. Amoxicillin is a semisynthetic aminopenicillin of the beta-lactam group of antibiotics and has a bactericidal activity against Gram-positive and Gram-negative bacteria. The bactericidal effect of amoxicillin is based on the inhibition of bacterial cell wall synthesis by blocking the transpeptidases. Amoxicillin is acid-stable, but is sensitive to penicillinases.
Clavulanic acid is a beta-lactam which has a mild antibacterial effect against some bacterial strains. The main effect of clavulanic acid is its enzyme-inhibiting activity on many types of beta-lactamases.
Amongst the beta-lactamases which are inhibited by clavulanic acid are those of staphylococci and many chromosomally and plasmid induced beta lactamases of Gram-negative organisms such as *Haemophilus influenzae, Escherichia coli, Klebsiella pneumoniae* and anaerobic organisms such as *Bacteroides fragilis*. This inhibition protects amoxicillin against destruction by beta lactamases, thus enabling the amoxicillin to have its full antibiotic effect.
The combination of amoxicillin and clavulanic acid means that many organisms which would be resistant to amoxicillin because of their beta lactamase production become sensitive. This synergistic effect is shown with the clavulanic acid concentrations which are achieved in the body after parenteral or oral administration.
Pharmacodynamics
Spectrum of activity

	MIC (mg/l) for CoAmox Acino*		
	< 0.5	0.51-4.0	4.1-16
Gram-positive aerobes			
*Staphylococcus aureus*** (beta)	x	0	
*Staphylococcus epidermidis***	x	0	
Streptococcus pyogenes	0		
Streptococcus viridans	0		
Streptococcus pneumoniae	0		
Streptococcus faecalis (Enterococcus)	0		
Listeria monocytogenes	0		
Gram-positive anaerobes			
Clostridium spp.	0		
Peptococcus spp.	0		
Peptostreptococcus	0		
Gram-negative aerobes			
Neisseria meningitidis	0		
Neisseria gonorrhoeae (beta)		0	
Moraxella catarrhalis (beta)	0		
Haemophilus influenzae (beta)		0	
Escherichia coli (beta)		x	0
Salmonella spp.		x	0
Shigella spp.		x	0
Klebsiella spp. (beta)		x	0
Proteus mirabilis (beta)	x	0	
Proteus vulgaris (beta)		x	0
Helicobacter pylori	0		
Campylobacter jejuni			0
Yersinia enterocolitica			x
Gram-negative anaerobes			
Bacteroides fragilis (beta)	x	0	
Fusobacterium spp.	x	0	

* value for amoxicillin, ratio 2:1
** not including methicillin-resistant staphylococci
(beta) = including beta-lactamase producing strains
x = ≈ 50% of the strains sensitive
0 = ≈ 90 % of the strains sensitive
Resistant organisms
Methicillin-resistant staphylococci, *Pseudomonas aeruginosa, Serratia, Providencia, Morganella morganii, Citrobacter, Enterobacter, Proteus rettgeri,* mycobacteria, *Acinetobacter*.

Pharmacokinetics
Absorption
Amoxicillin and clavulanic acid are well absorbed in the gut. For optimum absorption it is recommended that the medicine should be taken at the beginning of a meal. The absorption curves of the two components are similar; maximum serum levels of amoxicillin and clavulanic acid are reached approximately 1-1½ hours after oral administration. After administration of a 375 mg (250/125) tablet the levels are approximately 5 mg/l (amoxicillin) and 3 mg/l (clavulanic acid).
The total amounts absorbed are generally 80% for amoxicillin and 70% for clavulanic acid.
Distribution
Amoxicillin is approximately 18% and clavulanic acid approximately 25% bound to plasma proteins. The distribution volumes are 22 litres for amoxicillin and 16 litres for clavulanic acid.
Since high serum concentrations of amoxicillin and clavulanic acid are achieved after oral administration of CoAmox Acino, good penetration into the body fluids can be expected.
Therapeutic concentrations of both active substances have been found in the abdominal tissues, gall bladder, skin, adipose tissue and muscle tissue and in the following body fluids: synovial, peritoneal and pleural fluid, bile, sputum and pus.
Both active substances diffuse through the placental barrier; reproduction studies on animals did not show any adverse effect; there is limited clinical experience in humans.
The concentrations of amoxicillin in breast milk are small. Traces of clavulanic acid were also found in breast milk. With the exception of the risk of a hypersensitivity reaction which is associated with this excretion, no harmful effects for the infant are known.
Metabolism
Amoxicillin is 10-25% metabolised into the corresponding inactive penicilloic acid, which is excreted renally. Clavulanic acid is 35-60% transformed into inactive metabolites.
Elimination
Amoxicillin and clavulanic acid are mainly excreted renally. Six hours after oral administration approximately 60-70% of amoxicillin and 40-65% of clavulanic acid taken is excreted unchanged in the urine, still in its active form.
The elimination half-lives of amoxicillin and clavulanic acid are approximately 1-1½ hours, assuming normal renal function.
Kinetics in particular groups of patients
In the case of renal failure the renal elimination of both active substances is delayed; the dose must be adapted accordingly. The plasma concentrations of both active substances are severely reduced by haemodialysis.

Preclinical safety data
Concomitant administration of amoxicillin and clavulanate (2:1) or clavulanate alone did not produce any effect in the F0 generation of either rats or mice with regard to mating behaviour, fertility, gestation (including embryonic and foetal development) or parturition. In addition, no adverse effects on the embryonic-foetal development or any negative effect on viability, growth, development, behaviour or reproductive function were detected in the F1 offspring.
Potassium clavulanate was tested when given alone and in combination with amoxicillin (1:2 or 1:4) in an extensive series of genotoxicity tests under *in-vitro* and *in-vivo* conditions, in which very varied endpoints were recorded. The results obtained led to the conclusion that administration of amoxicillin or clavulanate does not involve any genotoxic risks.

Further remarks
Incompatibilities
Not applicable.
Interference with diagnostic methods
Possibly false results when determining oestriol during pregnancy.
Owing to the high concentration of amoxicillin in the urine, the measurement of glucose with chemical methods (Benedict or Fehling solution or with Clinitest) can be affected (falsely positive results). Glucose measurement with enzymatic (glucose-oxidase) methods (Dextrostix, Diastix or Clinistix) is therefore recommended.
The direct Coombs' test can give a positive result, but without haemolysis occurring.
In amino acid chromatography of urine, amoxicillin or its degradation products can result in ninhydrin-positive spots.
Possible interference in determining the total protein in the urine and serum by means of colour reaction (ninhydrin reaction according to Ehrlich).
Possible falsely positive colour reaction when determining glycosuria.
Falsely high concentrations of uric acid in the serum can be shown if the copper-chelate method is used. The tungsten phosphate and uricase methods of determining uric acid are not affected by amoxicillin.
Shelf life
Do not use this medicine after the expiry date which is stated on the carton after «EXP». The expiry date refers to the last day of that month.
Storage following reconstitution
The suspensions can be kept in a refrigerator at 2-8°C for up to seven days after reconstitution.
Special precautions for storage
Keep this medicine out of the sight and reach of children.
Store dry below 25°C.
Instructions for handling
Preparation of the suspensions
The suspensions are normally prepared by the pharmacist.
CoAmox Acino 156.25 Suspension (125/31.25 mg)
Shake the bottle to loosen the powder. Carefully fill with tap water (86 ml) up to the ring marking on the bottle. Shake the bottle well and allow it to stand for a short time. If necessary add more water up to the ring marking. This gives 100 ml of ready-to-use suspension. Shake the bottle each time before use.
One 2.5 ml dosing syringe = 78.1 mg of the active substances (62.5 mg amoxicillin, 15.6 mg clavulanic acid). One 5 ml dosing syringe = 156.25 mg of the active substances (125 mg amoxicillin, 31.25 mg clavulanic acid).
CoAmox Acino 312.5 Suspension (250/62.5 mg)
Shake the bottle to loosen the powder. Carefully fill with tap water (85 ml) up to the ring marking on the bottle. Shake the bottle well and allow it to stand for a short time. If necessary add more water up to the ring marking. This gives 100 ml of ready-to-use suspension. Shake the bottle each time before use.
One 2.5 ml dosing syringe = 156.25 mg of the active substances (125 mg amoxicillin, 31.25 mg clavulanic acid). One 5 ml dosing syringe = 312.5 mg of the active substances (250 mg amoxicillin, 62.5 mg clavulanic acid).
CoAmox Acino 457 Suspension (400/57 mg)
Shake the bottle to loosen the powder. Carefully fill with tap water (62 ml) up to the mark on the label. Shake the bottle well and allow it to stand for a short time. If necessary add more water up to the mark on the label. The bottle now contains 70 ml ready-to-use suspension. Shake the bottle each time before use.
One 2.5 ml dosing syringe = 228.5 mg of the active substances (200 mg amoxicillin, 28.5 mg clavulanic acid). One 5 ml dosing syringe = 457 mg of the active substances (400 mg amoxicillin, 57 mg clavulanic acid).
Disposal of unused or expired medicines
Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

Presentation
CoAmox Acino 1000 Lactab
White to off-white, oblong film-coated tablets with bevelled edges, scored and debossed with 875/125 on one side and debossed with AMC on the other side.
The film-coated tablets are packed in Aluminium-Aluminium blisters.
Packs of 12 film-coated tablets.
CoAmox Acino 156.25 Suspension
White to yellowish white, crystalline powder.
The powder is packed into an amber glass bottle closed with aluminium screw cap.
Packs with one bottle of dry powder for the preparation of 100 ml suspension with syringe dosing device with 1 ml graduations up to 5 ml or ¼, ½, ¾, 1 syringe.
CoAmox Acino 312.5 Suspension
White to yellowish white, crystalline powder.
The powder is packed into an amber glass bottle closed with aluminium screw cap.
Packs with one bottle of dry powder for the preparation of 100 ml suspension with syringe dosing device with 0.5 ml graduations up to 5 ml.
CoAmox Acino 457 Suspension
White to yellowish white, crystalline powder.
The powder is packed into an amber glass bottle with plastic tamper-evident screw cap.
Packs with one bottle of dry powder for the preparation of 70 ml suspension with syringe dosing device with 0.5 ml graduations up to 5 ml.
Not all pack sizes may be marketed.

Date of information
October 2009.

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 reach of children.

Council of Arab Health Ministers, Union of Arab Pharmacists.

Manufactured by Lek, Prevalje, Slovenia
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