Curam® 156,25 mg / 5 ml powder for oral suspension
Curam® forte 312,5 mg / 5 ml powder for oral suspension
Curam® 625 mg film-coated tablets

SANDOZ

Dear patient,
Please read the following instructions carefully. They contain important information about the use of this drug. If you have any further questions, please ask your doctor or pharmacist.

Composition
What does Curam® contain?

Curam® 156,25 mg / 5 ml powder for oral suspension
Medically active ingredients:
5 ml suspension ready for use contain:
143.5 mg of amoxycillin trihydrate, equivalent to 125 mg of amoxycillin
37.2 mg of clavulanic acid (potassium salt), equivalent to 31.25 mg of clavulanic acid
8.5 mg of aspartame as sweetener
Other ingredients:
lemon powder flavouring, peach apricot powder flavouring, anhydrous citric acid, anhydrous trisodium citrate, talc, orange powder flavouring, guar flour, precipitated silicon dioxide

Curam® 312,5 mg / 5 ml powder for oral suspension
Medically active ingredients:
5 ml suspension ready for use contain:
287.0 mg of amoxycillin trihydrate, equivalent to 250 mg of amoxycillin 74.5 mg of clavulanic acid (potassium salt), equivalent to 62.5 mg of clavulanic acid 8.5 mg of aspartame as sweetener
Other ingredients:
lemon powder flavouring, peach apricot powder flavouring, anhydrous citric acid, anhydrous trisodium citrate, talc, orange powder flavouring, guar flour, precipitated silicon dioxide

Curam® 625 mg film-coated tablets
Medically active ingredients:
1 film-coated tablet contains:
574.0 mg of amoxycillin trihydrate, equivalent to 500 mg of amoxycillin
148.9 mg of clavulanic acid (potassium salt), equivalent to 125 mg of clavulanic acid

Other ingredients:
magnesium stearate, talc, povidone, microcrystalline cellulose, croscarmellose sodium, triethyl citrate, ethyl cellulose, hypromellose, titanium dioxide E171

Pharmaceutical form: powder for preparation of suspension for oral administration film-coated tablets

Presentations:
Curam 156,25 mg/ 5ml
single pack 1 bottle with 5.4 g of powder (to make 60 ml of suspension)
single pack 1 bottle with 9.0 g of powder (to make 100 ml of suspension)
single pack 2 bottles, each with 5.4 g of powder (to make 2 x 60 ml of suspension)
Curam 312,5 mg/ 5ml
single pack 1 bottle with 7.5 g of powder (to make 60 ml of suspension)
single pack 1 bottle with 12.5 g of powder (to make 100 ml of suspension)
single pack 2 bottles, each with 7.5 g of powder (to make 2 x 60 ml of suspension)
Curam 625 mg
single pack 12, 16, 20, 30, 100 film-coated tablets

Pharmaceutical / therapeutic category and mode of action
How does Curam® work?
Curam® acts against certain bacteria (antibiotic).

Marketing authorization holder and manufacturer
Sandoz GmbH, Kundl, Austria

Indications
When is Curam® used?
To treat bacterial infections caused by gram-negative and gram-positive amoxycillin-resistant organisms whose resistance is due to β-lactamases but which are sensitive to a combination of amoxycillin and clavulanic acid. No additional amoxycillin is required with mixed infections caused by organisms sensitive to amoxycillin and resistant to amoxycillin but sensitive to amoxycillin/clavulanic acid.
If there are good reasons for suspecting that the above organisms are the cause of a particular infection, therapy with Curam® can be commenced before the results of sensitivity tests are available.

Curam® is suitable for treatment of the following indications:
Infections

have applied in the past - please ask your doctor.
Please notify your doctor:
- in the case of severe allergies or asthma, since allergic reactions are more likely in such instances;
- in the case of Pfeifer's glandular fever (infectious mononucleosis) or lymphatic leukaemia, since there is a higher likelihood of skin rash in such instances;
- in the case of severe hepatic dysfunction or if hepatic dysfunction has occurred in the past in connection with Curam®, since the drug should not be taken under these circumstances.

What precautions are required when driving, operating a machine or working without secure attachment?
According to findings to date Curam® does not affect concentration and reaction capability. In isolated cases side effects (see "Side effects") have been observed that would make such activities impossible (e.g. anaphylactic shock, convulsions).
Note:
Patients with phenylketonuria (an inborn metabolic disease) should note that Curam® 156,25 mg / 5ml and Curam® 312,5 mg/5ml powder for oral suspension contain the sweetener aspartame.

Keep out of reach of children!

Drug interactions

Please notify your doctor at all events if other drugs besides Curam® are being taken or have been taken recently.

What other substances or drugs influence the effect of Curam®?
Other specific antibiotics (e.g. tetracyclines, macrolides, sulphonamides or chloramphenicol) can reduce the efficacy of Curam®.
Probenecid increases the amoxycillin concentration in blood and bile.
Concurrent administration of allopurinol (for gout) during treatment with Curam® can increase the likelihood of allergic skin reactions.
Diuretics accelerate the excretion of amoxycillin, resulting in a lower active substance concentration in the blood.

What other substances or drugs are influenced by Curam®?
In rare instances amoxycillin can adversely affect the reliability of contraceptives (hormonal contraceptives, the Pill). It is therefore advisable to take other nonhormonal precautions in addition.
Curam® can increase the absorption by the body of digoxin (ingredient of various cardiac drugs).
Curam® should not be used together with disulfiram (for alcoholism).

What other interactions are possible?
The tendency to bleed can increase when Curam® is taken concurrently with specific anticoagulants (coumarins).
The efficacy of Curam® can be impaired if diarrhoe is present.
Non-enzymatic methods of urine sugar determination can produce false positive results. The identification of urobilinogen can also be affected.
Please note that this information can also apply to drugs taken in the recent past.

Dosage
The following information applies unless otherwise instructed by your doctor. Please observe the instructions, as otherwise Curam® will not work properly!
The tablets should not be split in half to obtain a half-dose. If a half-dose is prescribed (e.g. with renal impairment) Curam® powder for oral suspension should be used. Please consult your doctor accordingly.

How many Curam® 625 mg film-coated tablets should be taken and how often?
Adults, juveniles and children over 12 years of age weighing over 40 kg: 3 x 1 (625 mg) film-coated tablet per day.

Elderly patients:
As above, provided that there is no renal or hepatic impairment.

How much Curam® 156,25 mg / 5 ml or Curam® 312,5 mg / 5 ml powder for oral suspension should my child take and how often?

Children under two years of age:
37.5 mg to 50 mg of the active substances per kg weight and day (i.e. 30 to 40 mg amoxycillin + 7.5 to 10 mg clavulanic acid per kg per day).
Children aged 2 to 12 years:
37.5 mg to 75 mg of the active substances per kg weight and day (i.e. 30 to 60 mg amoxycillin + 7.5 to 15 mg clavulanic acid per kg per day).

Dosage examples:

Overdose and other misuses
What should you do if you have taken too much Curam® (intentional or accidental overdose)?
No specific measures are normally required in the case of overdose except for discontinuation of the drug. The symptoms of overdose are essentially the same as the side effects. With very high doses nausea, vomiting, abdominal pain and diarrhoea can occur.

What should you do if you have taken too little Curam® or have forgotten to take it at all?
If you have forgotten to take Curam® at the prescribed time, take it as soon as possible afterwards. The next administration should then take place at the planned time.

What should you do if you interrupt or prematurely discontinue the treatment?
Please do not discontinue treatment with Curam® without consulting your doctor. Your condition could deteriorate as a result.

Undesirable effects
What adverse reactions (side effects) can occur in connection with Curam®?
(Note that not all or any of the side effects described below will necessarily occur.)

Hypersensitivity reactions:
Skin reactions in the form of exanthemous rash and itching have been reported with some frequency. The typical measles-like rash occurs 5 to 11 days after the start of treatment. An immediate skin reaction in the form of a nettle rash usually indicates a real penicillin allergy, in which case treatment must be discontinued.
Severe allergic reactions, e.g. threatening (anaphylactic) shock, drug fever, increase in certain blood cells (eosinophilia), painful swelling of the skin and mucous membranes (Quincke's oedema), swelling of the inner larynx with constriction of the respiratory passages and difficulty in breathing (laryngeal oedema), serum sickness, haemolytic anaemia, and allergic vasculitis or nephritis, have been reported in rare instances as a result of sensitization to the 6-aminopenicillanic acid group. If any of these symptoms occur, you should seek medical assistance immediately.
In patients who have or have had a cutaneous fungal infection, hypersensitivity reactions (because of the antigens common to both cutaneous fungi and penicillin) cannot be ruled out even if they are receiving penicillin for the first time.
Hypersensitivity reactions of all degrees of severity up to and including allergy-induced (anaphylactic) shock have been observed even with orally administered penicillin, although they are much rarer than with injection (intravenous or intramuscular).
Inflammation of the mucous membranes, particulary in the mouth, can occur occasionally. Black tongue has been observed in very rare instances. Dryness of the mouth and changes in the sense of taste can occur. Severe skin reactions with life-threatening general reactions, such as Stevens-Johnson syndrome, Lyell's syndrome and exfoliative dermatitis (life-threatening disease with blistering of the skin) have been observed on rare occasions in coincidence with Curam® therapy.

Gastrointestinal tract:
Disorders in the form of pressure on the stomach, nausea (more frequent with higher dosage), vomiting, meteorism, soft stools or diarrhoea can occur occasionally in conjunction with amoxycillin/clavulanic acid. They are generally slight and frequently disappear during or at the latest on completion of the treatment. Tolerability is improved if amoxycillin/clavulanic acid is taken with meals.
Severe and persistent diarrhoea occuring during or in the first weeks following treatment is a possible indication of pseudomembranous colitis (in most cases caused by Clostridium difficile). This abdominal disorder resulting from antibiotic treatment can be life-threatening (see "What measures should be taken if side effects occur?").
Severe colonization of the abdomen with yeast fungi has been observed on rare occasions.

Liver:
A moderate increase in liver enzyme values can occur occasionally. In isolated cases as with some other penicilllins and some cephalosporins a temporary inflammation of the liver (hepatitis) and (cholestatic) jaundice caused by suppression of the bile flow have been observed. These hepatic dysfunctions can be severe (see "What measures should be taken if side effects occur?"). They are characterized by unusually severe itching, yellow coloration of the skin and eyeballs, and unusually dark urine and light stools. The hepatic dysfunction normally occurs during or shortly after treatment, but in some cases only several weeks after completion of the course, and is most frequent in

- of the upper and lower respiratory tract
  - otitis media (inflammation to the middle ear)
  - acute sinusitis
  - acute exacerbation of chronic bronchitis
  - pneumonia
- of the kidneys and lower urinary tract
- of the skin and soft tissues

Antibacterial spectrum of amoxycillin/clavulanic acid

gram-positive aerobes: Bacillus anthracis, Corynebacterium species, Enterococcus faecalis, Listeria monocytogenes, Nocardia asteroides, Staphylococcus aureus, coagulase-negative, staphylococci (including Staphylococcus epidermidis), Streptococcus pneumoniae*, Streptococcus pyogenes*, Streptococcus species*, Streptococcus viridans*

gram-positive anaerobes: Clostridium species, Peptococcus species*, Peptostreptococcus species*

* No β-lactamase producers have been reported to date for these species of bacteria.

gram-negative aerobes: Bordetella pertussis*, Brucella species*, Escherichia coli, Gardnerella vaginalis, Haemophilus influenzae, Helicobacter pylori*, Klebsiella species, Legionella species, Moraxella catarrhalis, Neisseria gonorrhoeae, Neisseria meningitidis*, Pasteurella multocida, Proteus mirabilis, Proteus vulgaris, Salmonella species, Shigella species, Vibrio cholerae, Yersinia enterocolitica

gram-negative anaerobes: Bacteroides species (including Bacteroides fragilis), Fusobacterium species

resistant organisms: methycillin-resistant staphylococci, Citrobacter, Enterobacter, Serratia, Proteus rettgeri, Morganella morganii, Providencia, Pseudomonas aeruginosa, Mycoplasma, Chlamydia, Rikettsia

* No β-lactamase producers have been reported to date for these species of bacteria.

Contraindications

When should Curam® not be used?

If the patient has had an allergic reaction to specific β-lactam antibiotics (e.g. penicillins, cephalosporins), there is a risk of allergy-induced (anaphylactic) shock.
Please inform your doctor accordingly.

Under what circumstances is caution advised?

Please inform your doctor if the patient has a liver function impairment (see "Dosage").
Please inform your doctor in the case of a kidney impairment. He will then decide how Curam® should be taken (see "Dosage").
Please inform your doctor in the case of a severe gastrointestinal disorder with vomiting and

1 measuring spoon of Curam® 156,25 mg / 5 ml = 5 ml = 125 mg amoxycillin + 31.25 mg clavulanic acid
1 measuring spoon of Curam® 312,5 mg / 5 ml = 5 ml = 250 mg amoxycillin + 62.5 mg clavulanic acid

Weight	Age	Standard dosage/day
6-12 kg	6-24 months	3 x 62.5-125 mg amoxycillin + 15.63-31.25 mg clavulanic acid (equivalent to 3 x ½-1 measuring spoon (5 ml) of Curam® 156,25 mg / 5 ml)
12-20 kg	2-6 years	3 x 125-250 mg amoxycillin + 31.25-62.5 mg clavulanic acid (equivalent to 3 x 1-2 measuring spoon (5 ml) of Curam® 156,25 mg / 5 ml) 3 x 125-250 mg amoxycillin + 31.25-62.5 mg clavulanic acid (equivalent to 3 x ½-1 measuring spoon (5 ml) of Curam® 312,5 mg / 5 ml)
20-40 kg	6-12 years	3 x 250-500 mg amoxycillin + 62.5-125 mg clavulanic acid (equivalent to 3 x 1-2 measuring spoon (5 ml) of Curam® 312,5 mg / 5 ml)

Patients with hepatic impairment:
If there are signs of damage to the liver, the liver function parameters should be monitored regularly by your doctor. If the values deteriorate during treatment with Curam®, termination of the therapy should be considered (see "Contraindications").

Patients with renal impairmend and dialysis patients:
Please notify your doctor if you have a kidney malfunction. He will then decide whether Curam® may be prescribed.
With renal impairment the dose should be reduced in accordance with the severity of the dysfunction and the patient's weight (see Table).

Adults and juveniles with renal impairment:
Dosage with renal impairment for a patient weighing 70 kg:

GFR (ml/min)	Plasma creatinine (mg/100 ml)	Single dose	Dosage interval
30-10	2.5-5.5	500 mg amoxycillin + 125 mg clavulanic acid	12 h
<10	>5.5	500 mg amoxycillin + 125 mg clavulanic acid	24 h

(modified according to Höffler)

Conversion formula based on actual body weight (according to Höffler)

$$Ywt = \frac{Y70 \times WT}{70}$$

Ywt = calculated dosage for patient with renal impairment
Y70 = dose for patient weighing 70 kg (see Table)
WT = weight of patient in kg

Children with renal impairment:
The following recommended dosages are based on theoretical considerations and pharmacokinetic data. No dose-finding studies have been carried out with these patients.
For children with renal impairment (GFR < 30 ml/min) the maximum single dose is 15 mg of amoxycillin + 3.75 mg of clavulanic acid per kg weight. The dosage interval is 12 hours for a GFR of 30-10 ml/min and 24 hours for a GFR of less than 10 ml/min.

men or elderly patients (60 years or over). The symptoms generally recede.

Haematological profile
In rare instances a temporary change in blood parameters, e.g. reduction in the number of white blood cells (leukopenia), reduction or increase in blood platelets (thrombocytopenia or thrombocytosis), can occur. Temporary changes in blood parameters such as reduction in the number of granulocytes (granulocytopenia), deficiency in all blood cell elements (pancytopenia), anaemia or increase in bleeding and coagulation times have been observed in isolated cases.

Central nervous system:
Isolated reports of hyperactivity, anxiety, insomnia, confusion, aggression and convulsions have been received.

Other side effects:
All antibiotics can cause proliferation of bacteria that are insensitive to the drug being used. Attention should be paid to signs of follow-up infections through these organisms. Such infections should be treated accordingly.

What measures should be taken if side effects occur?
The following extremely rare side effects (see above for more detailed explanation) can under certain circumstances be acutely life-threatening. You should therefore consult a doctor without delay if such an event occurs suddenly or becomes unexpectedly severe.

Pseudomembranous colitis:
Here the doctor will consider terminating treatment with Curam®, depending on the indication, and introduce suitable treatment immediately (e.g. vancomycin oral, 4 x 250 mg per day in adults). Drugs that inhibit abdominal motility (peristaltis) may not be taken.

Severe acute hypersensitivity reactions (e.g. anaphylaxis):
Treatment with Curam® must be terminated immediately and the normal emergency measures (e.g. antihistamines, corticosteroids, sympathomimetics and artificial respiration if required) taken.

(Epilepsy-like) convulsions:
The normal emergency measures (e.g. freeing of respiratory passages, anticonvulsants such as diazepam or barbiturates) are indicated.

Side effects affecting the liver:
Consult a doctor immediately if you observe the following symptoms: unusually severe itching, yellow coloration of the skin and eyeballs, unusually dark urine and light stools.
If side effects other than those described in this Patient Instruction Leaflet are observed, please notify your doctor or pharmacist.

Expiry date and storage

Please note the expiry date!
The expiry date is printed on the box lid and bottle. Do not use the drug after this date.
The prepared suspension can be used for seven days if stored in the refrigerator (2-8°C).

How should Curam® 625 mg film-coated tablets be stored?
Do not store at temperatures in excess of 25°C.

How should Curam® 156,25 mg / 5 ml and Curam® 312,5 mg / 5 ml powder for oral suspension be stored?

Curam® powder for oral suspension should not be stored as a powder mixture at temperatures in excess of 25°C.
Protect from moisture.
The prepared suspension should be kept in a refrigerator 2-8°C) and used within seven days.

Date of information:
September 1997

If you are unclear about any of the contents of this leaflet please ask your doctor or pharmacist.

diarrhoea, as adequate absorption of Curam® cannot be guaranteed in such cases.

What precautions need to be taken with children and elderly persons?
Elderly patients (aged 60 and over) should be treated with caution and their liver function monitored (see "Side effects").
There are no special precautionary measures for children provided that the kidney and liver function are not impaired.

What precautions need to be taken during pregnancy and breast-feeding?
No adverse effects on the foetus or neonate have been observed in connection with amoxycillin when taken during pregnancy. By way of a precaution, however, Curam® should only be used during pregnancy if, in the physician's judgement, the potential benefits outweigh the possible risks.
Both active substances reach the embryo/foetus by way of the placenta and are eliminate in breast milk. Breastfed babies may therefore have diarrhoea and colonization of the mucous membranes by yeasts, possibly resulting in a need to discontinue breastfeeding. The possibility of sensitization must also be taken into account.

Special warnings and precautions
What precautions need to be taken?
With prolonged therapy, kidney, liver and blood parameters should be regularly monitored. Patients with existing hepatic impairement should have their liver function closely monitored irrespective of the length of therapy. Should the parameters deteriorate during treatment, termination of the therapy should be considered.
Patients with a bladder catheter should inform their doctor, since a drug with substance combination (amoxycillin) can crystallize in high urine concentrations at room temperature.
Patients with severe gastrointestinal complaints with vomiting and/or diarrhoe should inform their doctor. The drug is contraindicated, since adequate absorption in the blood cannot be guaranteed.

Under what circumstances should you consult your doctor before taking Curam®?
In the following cases Curam® should be administered only under special circumstances and with special care. If such circumstances apply - or

Haemodialysis patients:
Adults and juveniles: 500 mg of amoxycillin + 125 mg of clavulanic acid every 24 hours, and the same dose during and at the end of haemodialysis.
The following recommended dosages for children are based on theoretical considerations and pharmacokinetic data. No dose-finding studies have been carried out with these patients. The dosage for children is 15 mg of amoxycillin + 3.75 mg of clavulanic acid per kg weight every 24 hours, and the same dose during and at the end of haemodialysis.

Nature and duration of administration
How and when should Curam® be taken?
The film-coated tablets are to be taken whole with fluid.

Preparation of Curam® powder for oral suspension

Fill the bottle with water until just under the ring and shake vigorously. Then top up with water exactly to the mark and shake vigorously again. Shake the bottle well every time you use the suspension.

Curam® is best taken at the start of a meal as it will act most effectively in this way and is also best tolerated. The active ingredients are also effective, however, if taken before or after meals.
The individual doses should be spread as evenly as possible throughout the day; if three doses per day are prescribed, they should be taken at eight-hour intervals.

How long should Curam® be taken?
The length ot treatment will be decided by the doctor.

Do not discontinue therapy of your own accord, even if you feel better. Normally treatment with Curam® should be continued for three to four days after recovery from the illness or disappearance of the symptoms.
Curam® should not be taken for more than 14 days without examination by your doctor.
If Curam® has been prescribed for the treatment of specific bacteria (β-haemolyzing streptococci), it must be taken for at least ten days to ensure adequate effect. Otherwise there is a risk of late complications (e.g. rheumatic fever, glomerulonephritis).

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