Curam® 600 mg i.v. – Powder for solution for injection/infusion

SANDOZ

Active substance: amoxicillin/clavulanic acid

Composition

What does Curam 600 mg i.v. – powder for solution for injection/infusion contain?

The medicinally active ingredients are amoxicillin and clavulanic acid. Each vial contains 500 mg amoxicillin (as sodium salt) and 100 mg clavulanic acid (as potassium salt).
The sodium content of each vial amounts to 1.7 mmol.
The potassium content of each vial amounts to 0.5 mmol.

Pharmaceutical form: powder for preparing a solution for injection
powder for preparing a solution for infusion
crystalline, white or off-white powder

Presentations: 10 vials

Pharmaceutical and therapeutic category and mode of action

How does Curam 600 mg i.v. – powder for solution for injection/infusion act?

Curam intravenous is an antibiotic with a broad range of activity from the group of the penicillins. Curam intravenous acts by quickly killing most bacteria through amoxicillin, with amoxicillin being protected from bacterial attack by clavulanic acid. The combination of the two active substances is therefore effective against many amoxicillin-resistant bacterial strains.

Registered owner and manufacturer

Sandoz GmbH, Kundl, Austria

Indications

When is Curam 600 mg i.v. – powder for solution for injection/infusion used?

Curam 600 mg i.v.– powder for solution for injection/infusion is indicated for parenteral treatment of infections caused by microbes which are resistant to amoxicillin and other beta-lactam antibiotics in cases where oral therapy is not indicated, such as in:

- infections of the airways
- infections of the abdominal cavity
- infections of the kidney and the urinary tract, excluding inflammation of the prostate
- genital infections
- infections of the skin and soft tissue
- generalized infections such as blood poisoning (sepsis) and inflammation of the lining of the abdominal cavity (peritonitis)

Treatment started with Curam 600 mg i.v.– powder for solution for injection/infusion can be continued orally once parenteral treatment is no longer necessary.

Contraindications

When must Curam 600 mg i.v. – powder for solution for injection/infusion not be used?

Curam 600 mg i.v.– powder for solution for injection/infusion must not be administered

- if you are hypersensitive (allergic) to beta-lactams (e.g. penicillins, cephalosporins) or clavulanic acid, because of the risk of an anaphylactic shock. It should therefore be carefully established whether you have a history of allergic reactions (e.g. after previous administration of penicillin or cephalosporin) before the start of therapy.
- to patients with severely impaired liver function and to patients developing an impairment of liver function during previous treatment with amoxicillin/clavulanic acid, for instance in conjunction with cholestatic jaundice caused by amoxicillin/clavulanic acid or another penicillin.
- to patients with infectious mononucleosis (glandular fever) and to patients with lymphoid leukaemia, since they are at an increased risk of developing exanthema.

Pregnancy and lactation

Ask your doctor or pharmacist for advice before taking any medicine.

Your doctor will decide on whether to use the product during pregnancy and lactation after weighing the benefits against the risks.

After use in pregnant women, Curam intravenous was not found to have any untoward effects on pregnancy or the health status of fetuses/newborn babies.

Curam intravenous must not be used in the first three months of pregnancy.

Both substances pass into breast milk. The breast-fed infant may therefore develop diarrhoea and an infection of mucous membranes with yeast-like fungi, which may require that breast-feeding is discontinued. The possibility of sensitization (development of an allergy) ought to be taken into consideration.

Precautions for use and special warnings

What must be borne in mind on use of Curam 600 mg i.v.–powder for solution for injection/infusion contain?

Curam intravenous may sometimes have undesirable effects, such as e.g. dizziness, which may impair the ability to drive a vehicle, to use machines or ensure safety at the workplace (see Undesirable effects section).

Patients with pre-existing liver function impairment should be treated with Curam intravenous only with caution. Use of Curam intravenous requires caution in patients with confirmed liver function disorders and care in patients with kidney function disorders. These patients should have their liver and kidney function determined and checked at regular intervals. This is particularly important in elderly patients and infants who may have diminished liver and kidney function.

Caution is advised in the treatment of elderly patients (60 years and older), with liver function tests being indicated for these patients (see "Undesirable effects").

Patients with signs of liver damage should have their liver function values checked at regular intervals, and discontinuation of therapy should be considered if these values deteriorate during treatment.

If severe persistent diarrhoea occurs, consideration should be given to the possibility of large bowel inflammation (pseudomembranous colitis) caused by Clostridium difficile, and therapy with Curam intravenous must not be continued. Antiperistaltics (e.g. the active substance loperamide) are contraindicated.

Care is required if this medicine is used in patients with pronounced allergies or asthma, as these patients are to be expected to develop allergic reactions more frequently.

Consideration should be given to the possibility of cross sensitivity (development of an allergy) with cephalosporins.

Amoxicillin may precipitate in the bladder catheter at room temperature if high concentrations are present in the urine; such a catheter must therefore be visually inspected for blockages at regular intervals.

As with other broad spectrum antibiotics, superinfections with resistant bacteria or yeast-like fungi may occur on prolonged use.

In newborn babies, prophylactic treatment with Curam intravenous may be associated with an increased risk of necrotizing enterocolitis (bowel inflammation).

For severe infections such as sepsis or peritonitis, combination treatment with another suitable antibiotic substance is recommended.

Treatment intervals of less than 4 hours should be avoided.

Regular checks of kidney and liver function and blood tests are indicated on long-term treatment.

The medicine contains 1.70 mmol of sodium per vial. This must be taken into account for patients on a controlled sodium diet.

The medicine contains less than 1 mmol (0.5 mmol) of potassium per vial, that is to say it is virtually potassium-free.

Incompatibilities (notes intended for your doctor)

Curam 600 mg i.v.– powder for solution for injection/infusion must not be mixed with amino acid solutions, lipid emulsions, blood and glucose solutions.

Curam 600 mg i.v.– powder for solution for injection/infusion is less stable in infusions comprising dextran or bicarbonate. The prepared solution should therefore not be added to such infusions, however, can be injected into the infusion tube within a period of three to four minutes.

Due to inactivation of aminoglycosides by amoxicillin, mixing *in vitro* should be avoided.

In a few instances, clouding may occur on mixing with a lidocaine solution. In this case it is advisable to discard the solution.

Please inform your doctor if you find out that you are pregnant.

Keep this medicine out of the reach and sight of children.

Interactions with other medicines

May Curam 600 mg i.v.–powder for solution for injection/infusion be used at the same time as other medicines?

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Interactions may occur in conjunction with:

Other antibiotics or chemotherapeutics
such as e.g. tetracyclines, macrolides, sulphonamides or chloramphenicol.

Probenecid

Allopurinol
The concurrent use may promote the onset of allergic skin reactions.

Methotrexate
Patients receiving amoxicillin at the same time should have their serum methotrexate concentrations checked frequently.

Digoxin

Disulfiram

Anticoagulants

Hormonal contraceptives
Amoxicillin may in rare cases impair the effectiveness of hormonal contraceptives ("the pill"). It is therefore recommended to use non-hormonal contraceptive measures in addition.

Diarrhoea may impair the uptake of other medicines and, as a result, their effectiveness.

Interference with laboratory tests
Determinations of glucose in urine may yield false-positive results. Likewise the urobilinogen test can be affected.

Dosage

How often should Curam 600 mg i.v. - powder for solution for injection/infusion be administered and in what quantity?

Curam intravenous may be administered only by a DOCTOR!

The dosage depends on the individual patient's age, weight and kidney function, on the severity and site of infection and the microbes suspected or confirmed to be involved.

The duration of treatment depends on the indication and on the severity of the infection.

Curam intravenous should not be used for more than 14 days without monitoring of liver function.

DOSAGE

This medicine for intravenous use is not suitable for intramuscular administration.

Curam 600 mg i.v.– powder for solution for injection/infusion is suitable exclusively for adults and children weighing more than 50 kg and suffering from impaired kidney function.

Dosage where kidney function is impaired
Elimination of clavulanic acid and amoxicillin via the kidneys is delayed in patients with impaired kidney function. The total daily dose of Curam intravenous should, depending on the severity of kidney function impairment, not exceed the values listed in the table below.

DOSAGE OF CURAM I.V.:

SEVERITY OF KIDNEY FUNCTION IMPAIRMENT	ADULTS and children weighing more than 50 kg
Glomerular filtration rate ml/min	
10-30 ml/min	Initial dose of 1000/200 mg, followed by 500/100 mg twice daily
< 10 ml/min	Initial dose of 1000/200 mg, followed by 500/100 mg per day
Haemodialysis	Initial dose of 1000/200 mg, followed by 500/100 mg per day and 500/100 mg after dialysis

Duration of therapy:
Therapy should be continued for another 3-4 days after symptoms have subsided. In conjunction with infections caused by Streptococcus pyogenes (group A β-haemolytic streptococci), treatment should last for at least 10 days to prevent complications such as rheumatic fever and glomerulonephritis (inflammation of the kidney).

Elderly patients
The same dosage as for "Adults" with normal kidney function.

Dosage where liver function is impaired
Amoxicillin/clavulanic acid must not be used in patients with severely impaired liver function and in patients developing an impairment of liver function during previous therapy with amoxicillin/clavulanic acid. Patients with signs of liver damage should have their liver function values checked at regular intervals. If these values deteriorate during administration, discontinuation of therapy should be considered. There are as yet not enough data available to provide special dosage recommendations for this patient group.

MODE OF ADMINISTRATION

The product is to be administered only by a doctor!

Preparation must take place under aseptic conditions. The solution must be visually inspected for particles before use. The solution may only be used when clear and free of particles. Any unused solution must be discarded.

For single use only.

Preparation of intravenous injections:
The vials containing 600 mg are diluted with 10 ml or up to 20 ml of water for injections.

Vial containing	Water for injections	Volume after preparation*	Concentration after preparation*
600 mg	10 ml	10.0 ml	50.0/10.0 mg/ml
600 mg	20 ml	20.2 ml	24.8/5.0 mg/ml

* Data are based on laboratory investigations

Preparation of intravenous infusions:
The vials containing 600 mg are diluted with 10 ml or up to 20 ml of water for injections.

Solutions for intravenous infusions should be administered completely within 60 minutes after preparation.
Transient pink discoloration may occur after dissolution in water for injections; however, the solution will become clear again shortly after.

Upon appropriate dissolution of Curam 600 mg i.v.– powder for solution for injection/infusion in water for injections, the solution can be mixed with the following fluids:
water for injections, physiological saline solution, sodium lactate 167 mmol/l, Ringer's solution, Hartmann's solution.

When too much amoxicillin/clavulanic acid (Curam) has been administered (overdose):

a) Symptoms of an overdose
Gastrointestinal symptoms such as e.g. nausea, vomiting and diarrhoea, and disturbances of fluid and electrolyte balance are possible in the event of an overdose. Convulsions may also occur. Reduced lucidity, muscular fasciculations, myoclonic jerks, coma, haemolytic reactions, kidney failure and acidosis are possible. Under exceptional circumstances, shock may occur within 20 to 40 minutes.

b) Treatment of an overdose:
There is no specific antidote for an overdose. Treatment is in the form of haemodialysis and symptomatic measures, with special attention to be paid to fluid and electrolyte balance.

Undesirable effects

What unwanted effects (undesirable effects) may Curam 600 mg i.v. – powder for solution for injection/infusion have, although they do not necessarily occur in all patients?

Like all medicines, Curam 600 mg i.v. – powder for solution for injection/infusion can cause undesirable effects.

Blood and lymphatic system disorders

Rare (>1/10 000, <1/1000)
- Blood count changes (thrombocytosis, haemolytic anaemia)

Very rare (<1/10 000)
- Blood count changes in the form of leucopenia, agranulocytosis, granulocytopenia, thrombocytopenia, pancytopenia, anaemia or myelosuppression and prolongation of bleeding and prothrombin time have been observed in a few cases. These symptoms are reversible upon cessation of therapy.

Immune system disorders

Rare (>1/10 000, <1/1000)
- Typical type-I allergic reactions (such as e.g. nettle rash, skin haemorrhages), swelling of the skin and mucous membranes and hypersensitivity symptoms may occur in rare cases.
- Severe skin disorders (e.g. erythema multiforme, Lyell's syndrome, Stevens-Johnson syndrome, toxic epidermal necrolysis, acute generalized erythematous pustulosis, bullous exfoliative dermatitis, serum disease and hypersensitivity vasculitis) may occur in rare cases.
- Drug-induced fever

Nervous system disorders

Rare (>1/10 000, <1/1000)
- Dizziness, headaches and convulsions occur rarely. Convulsions may occur with impaired kidney function and in patients receiving high doses.

Very rare (< 1/10 000)
- Hyperactivity, anxiety, sleeplessness, mental confusion and aggression.

Gastrointestinal disorders

Common (>1/100, <1/10)
- Gastrointestinal disorders such as e.g. nausea, vomiting, diarrhoea and itching have been observed. These undesirable effects are in most cases of mild intensity and subside again.

Rare (>1/10 000, <1/1000)
- As with amoxicillin, large bowel inflammation (pseudomembranous colitis) and inflammation of the mucosa of the large bowel with passing of blood (haemorrhagic colitis), as well as – albeit rarely – mucocutaneous candidiasis (fungal infection of the skin and mucous membranes) may occur.

Very rare (<1/10 000)
- Black discoloration of the tongue.

Hepatobiliary disorders

Rare (>1/10 000, <1/1000)
- A moderate increase in liver function values (AST and/or ALT values) has been reported in rare cases.

Very rare (<1/10 000)
- Inflammation of the liver (hepatitis) and cholestatic jaundice have been observed in rare cases. Hepatic events occur primarily in men and elderly patients, especially when aged over 60 years. The risk of developing these events increases with a duration of treatment of more than 14 days.
- These undesirable effects have also very rarely been observed in children.

Signs and symptoms usually occur during or shortly after treatment; however, in some cases they may not occur until several weeks after treatment has ended. The hepatic events are in general transient in nature. However, they may be very pronounced, and there have been very rare reports of a fatal outcome. Almost all of these occurred in patients with severe underlying disorders or in patients receiving potentially hepatotoxic drugs at the same time as Curam intravenous.

Skin and subcutaneous tissue disorders

Common (>1/100, <1/10)
- Allergic skin reactions occur significantly more often than with other penicillins.
- A "fifth-day rash" (skin rash) was observed in a few cases. This depends on the dose level and the condition of the patient.

Renal and urinary disorders

Very rare (<1/10 000)
- Interstitial nephritis (inflammation of the kidney) occurred on one single occasion. Crystalluria (urinary stones) has been observed.

General disorders and administration site conditions

Uncommon (>1/1000, <1/100)
- There have been occasional reports of clot formation and inflammation of superficial veins (thrombophlebitis) at the site of injection.

If you notice any other undesirable effect not listed in this leaflet, please tell your doctor or pharmacist.

Notes on expiry date and storage

How is Curam 600 mg i.v. – powder for solution for injection/infusion to be stored?

Keep out of the reach and sight of children.
Note the expiry date on the packaging.
The medicine must not be used after the expiry date stated on the packaging.

Do not store above 25 °C. Store in the original container.

Storage conditions after preparation: Do not store above 25 °C.

Prepared solution: From a microbiological point of view, the injection and infusions should be used immediately unless the method of preparation rules out the risk of microbial contamination. If they are not used immediately, the user holds responsibility for the duration and conditions of storage.

Date of information: December 2004

If you have further questions regarding Curam 600 mg i.v.– powder for solution for injection/infusion, please ask your doctor or pharmacist. E

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