AMOKVART

Instructions for the medicinal product

Trade name: Amokvart.
International Nonproprietary Name: Amoxicillin.
Dosage form: Hard gelatin capsules.
Composition: Each hard gelatin capsule contains:
Amoxicillin Trihydrate BP eq. to Amoxicillin 500 mg.
Pharmacotherapeutic group: Antibiotic. Semisynthetic penicillin.
ATC Code: J01CA04.
Pharmacologic property:
Pharmacodynamics:
Amokvart is a broad spectrum antibiotic. It is rapidly bactericidal and possesses the safety profile of a penicillin. Like all penicillins it acts by interfering with the synthesis of the cell wall of the bacterium. It is active against aerobic Gram-positive bacteria: Staphylococcus spp. (Except for strains producing penicillinase), Streptococcus spp. and aerobic gram-negative bacteria: Neisseria gonorrhoeae, Neisseria meningitidis, Escherichia coli, Shigella spp., Salmonella spp., Klebsiella spp. Microorganisms producing penicillinase, resistant to the action of amoxicillin.
Pharmacokinetics:
The absolute bioavailability of amoxicillin depends on the dose and ranges between 75 and 90%. In the dose range between 250 mg and 1000 mg the bioavailability (parameters: AUC and Cmax) is linearly proportional to the dose. At higher doses the extent of absorption decreases. The absorption is not affected by concomitant food intake. Oral administration of a single dose of 500 mg amoxicillin results in plasma concentrations of 6 - 11 mg/l. After administration of a single dose of 3 g amoxicillin, the plasma concentrations reach 27 mg/l. Peak plasma concentrations are present about 1-2 hours after administration.
Protein binding for amoxicillin is approximately 17%. Therapeutic drug levels are rapidly achieved in serum, lung tissue, bronchial secretions, middle ear fluid, bile and urine. In healthy meninges amoxicillin diffuses badly in liquor cerebrospinalisis. Amoxicillin crosses the placenta and a small percentage is excreted into the breast milk.
The main route of excretion of amoxicillin is the kidney. About 60-80% of an oral dose of amoxicillin is excreted in unchanged active form in the urine within 6 hours of administration, and a small fraction is excreted in the bile. Approximately 7 - 25% of the administered dose is metabolised to inactive penicilloic acid. The serum half-life in patients with normal renal function is approximately 1 – 1,5 hour. In patients with end-stage renal failure the half-life ranges between 5 to 20 hours. The substance is haemodialysable.
Indications for use:
Amokvart capsules are indicated for the treatment of the following bacterial infections caused by amoxicillin-sensitive gram-positive and gram-negative pathogens:
- Infections of the upper respiratory tract, including infections of the ears, nose and throat: Acute otitis media, acute sinusitis and bacterial pharyngitis;
- Infections of the lower respiratory tract: Acute exacerbation of chronic bronchitis, community-acquired pneumonia;
- Infections of the lower urinary tract: Cystitis;
- Prophylaxis of endocarditis in patients at risk i.e. surgery in the oral cavity or upper airways

Consideration should be given to official guidance on the appropriate use of antibacterial agents.
Susceptibility of the causative organism to the treatment should be tested (if possible), although therapy may be initiated before the results are available.
Contraindications:
- Hypersensitivity (including to other penicillins, cephalosporins, carbapenems);
- Allergic diathesis;
- Bronchial asthma;
- Hay fever;
- Infectious mononucleosis;
- Lymphocytic leukemia;
- Liver failure;
- Gastrointestinal tract history (especially colitis associated with the use of antibiotics);
- Lactation.

Precautions: pregnancy, renal failure, bleeding in history.
Dosage and directions for use:
The preparations are administered orally.
Amokvart capsules should be taken, unchewed, with liquid (e.g. a glass of water).
The absorption of Amokvart is not reduced by food intake.
Adults and adolescents (> 40 kg body weight):
The usual dosage covers a range from 750 mg to 3g Amokvart daily in three divided doses. In some areas 1500 mg Amokvart daily in three divided doses are recommended as the upper usual dose.
Special dosage recommendation.
Acute exacerbation of chronic bronchitis in adults: 2 x 1 g per day.
Children (under 40 kg):
For infants and children Amokvart oral suspensions are recommended.
The daily dosage for children is 40 - 90 mg/kg/day in two to three divided doses (not exceeding 3 g/day) depending on the indication, severity of the disease and the susceptibility of the pathogen.
Children weighing more than 40 kg should be given the usual adult dosage.
Side-effects:
Infections and infestations: Uncommon- superinfections and colonization with resistant organisms or yeasts such as oral and vaginal candidiasis after prolonged and repeated use of amoxicillin.
Blood and the lymphatic system disorders: Rare - eosinophilia and haemolytic anaemia. Very rare- leucopenia, neutropenia, granulocytopenia, thrombocytopenia, pancytopenia, anaemia, myelosuppression, agranulocytosis, prolongation of bleeding time, and prolongation of prothrombin time. All were reversible on discontinuation of therapy.
Immune system disorders: Rare - laryngeal oedema, serum sickness, allergic vasculitis, anaphylaxis and anaphylactic.
Nervous system disorders: Rare- CNS effects including hyperkinesia, dizziness and convulsions. Convulsions may occur in patients with impaired renal function, epilepsy, meningitis or in those receiving high doses.
Gastrointestinal disorders: Common - Gastric complaints, nausea, loss of appetite, vomiting, flatulence, soft stools, diarrhoea, enanthemas (particularly in the region of the mouth), dry mouth, taste disturbances. These effects on the gastrointestinal system are mostly mild and frequently disappear either during the treatment or very soon after completion of therapy. The occurrence of these side effects can generally be reduced by taking amoxicillin during meals. Rare - Superficial discoloration of the teeth (especially with the suspension). Usually the discoloration can be removed by teeth brushing. Very rare - If severe and persistent diarrhoea occurs, the very rare possibility of pseudo membranous colitis should be considered. The administration of anti-peristaltic drug is contraindicated. Development of a black tongue.
Hepato-biliary disorders: Uncommon - Moderate and transient increase of liver enzymes. Rare - Hepatitis and cholestatic jaundice.
Skin and subcutaneous tissue disorders: Common - Cutaneous reactions such as exanthema, pruritus, urticaria; the typical morbilliform exanthema occurs 5 - 11 days after start of therapy. Immediate appearance of urticaria indicates an allergic reaction to amoxicillin and therapy should therefore be discontinued. Rare - Angioneurotic oedema (Quincke's oedema),erythema multiforme exsudativum, acute generalized pustulosis, Lyell's syndrome, Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous and exfoliative dermatitis.
Renal disorders: Rare - Acute interstitial nephritis, Crystalluria.
General disorders and administration site conditions: Rare - Drug fever.
Overdose:
Symptoms: gastrointestinal, renal and neuro-psychic disturbances and fluid and electrolyte imbalance. In patients with severely impaired renal function, large overdoses can result in signs of renal toxicity; crystalluria is possible.
Treatment: there is no specific antidote for an overdose of amoxicillin.
Treatment consists primarily of administration of activated charcoal (a gastric lavage is usually not necessary) or symptomatic measures. Particular attention should be paid to the water and electrolyte balance of the patients. Amoxicillin can be eliminated via haemodialysis.
Drug interaction:
Allopurinol.
Concomitant administration of allopurinol may promote the occurrence of allergic cutaneous reactions and is therefore not advised.
Digoxin.
An increase in the absorption of digoxin is possible on concurrent administration with amoxicillin. A dose adjustment of digoxin may be necessary.
Anticoagulants.
Concomitant administration of amoxicillin and anticoagulants from the coumarin class, may prolong the bleeding time. A dose adjustment of anticoagulants may be necessary. A large number of cases showing an increase of oral anticoagulant activity has been reported in patients receiving antibiotics. The infectious and inflammatory context, age and the general status of the patient appear as risk factors. In these circumstances, it is difficult to know the part of the responsibilities between infectious disease and its treatment in the occurrence of INR disorders. However, some classes of antibiotics are more involved, notably fluoroquinolones, marcolides, cyclines, cotrimoxazole and some cephalosporins.
Methotrexate.
Interaction between amoxicillin and methotrexate leading to methotrexate toxicity has been reported. Serum methotrexate levels should be closely monitored in patients who receive amoxicillin and methotrexate simultaneously. Amoxicillin decreases the renal clearance of methotrexate, probably by competition at the common tubular secretion system.
Cautions:
Before initiating therapy with Amokvart, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins and cephalosporins. The possibility of cross-hypersensitivity (10 % - 15 %) with cephalosporins should be taken into account.
In patients with renal function impairment the excretion of amoxicillin will be delayed and, depending on the degree of the impairment, it may be necessary to reduce the total daily dosage.
The prolonged use of amoxicillin may occasionally result in an overgrowth of non-susceptible organisms or yeasts. Patients should therefore carefully be watched for superinfections.
At high doses, adequate fluid intake and urinary output must be maintained to minimise the possibility of amoxicillin crystalluria.
Amokvart should not be used for the treatment of bacterial infections in patients with viral infections, acute lymphatic leukaemia, or infectious mononucleosis as erythematous (morbilliform) rashes have been associated with glandular fever in patients receiving amoxicillin.
Effects on ability to drive and use machines:
No studies on the effect on the ability to drive and use machines have been performed. However, undesirable effects may occur (e.g. allergic reactions, dizziness, convulsions), which may influence the ability to drive and use machines.
Presentation:
2x10, PVC blister in a monocarton.
Storage:
Keep in dry place, protected from light at a temperature below 30°C. Keep out of reach of children.
Shelf life:
Labeled. Do not use after expiry date.
Distribution Condition:
Prescribed medicine.