Package leaflet: Information for the patient

Amikacin 250 mg/mL Solution for injection/infusion

(amikacin)

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Amikacin injection/infusion is and what it is used for

Amikacin 250 mg/ mL Solution for injection/infusion contains the active substance amikacin as amikacin sulfate. Each 2 mL ampoule contains 500 mg amikacin. Amikacin injection/infusion is an antibiotic and belongs to the group of medicines called aminoglycosides. Amikacin injection/infusion is used to treat serious infections caused by certain bacteria.

2. What you need to know before you take Amikacin injection/infusion

Do not take Amikacin injection/infusion:

- If you are allergic to amikacin or any of the other ingredients of this medicine (listed in section 6)
- If you suffer from a disorder called myasthenia gravis (a disease that causes muscle weakness)
- If you have had an allergic reaction to other antibiotics related to amikacin (aminoglycosides) in the past.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before taking Amikacin injection/infusion:

- If you have any kidney problems
- If you have had problems with your kidneys or hearing after taking other antibiotics
- If you have any hearing problems or other problems with your ears
- If you have any muscular disorders such as Parkinson’s Disease
- If you are elderly
- If you are dehydrated (ensure you are well hydrated during treatment).
- If you or your family members have a mitochondrial mutation disease (a genetic condition) or loss of hearing due to antibiotic medicines, you are advised to inform your doctor or pharmacist before you take an aminoglycoside; certain mitochondrial mutations may increase your risk of hearing loss with this product. Your doctor may recommend genetic testing before administration of Amikacin injection/infusion.

Children and adolescents
Amikacin injection/infusion should be used with caution in premature and neonatal infants.
Amikacin injection/infusion is not recommended to be given by injection into the abdominal cavity of young children.

Other medicines and Amikacin injection/infusion
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription. Some medicines can have an effect on the action of other medicines. It is especially important that you tell your doctor if you are taking:

- Diuretics (water tablet or injection) such as furosemide and ethacrynic acid
- Other antibiotics called beta-lactamases such as penicillins or cephalosporins
- Anaesthetics or muscle-relaxing medication
- Biphosphonates used to treat osteoporosis and similar diseases
- Platinum compounds used in the treatment of cancers
- Thiamine (Vitamin B1) as it may lose its effectiveness
- Other medicines that may affect your kidneys or hearing such as bacitracin (an antibiotic), cisplatin (anti-cancer medicine), amphotericin B (anti-fungal), ciclosporin (immune-suppressant), tacrolimus (immune-suppressant), cephaloridine (antibiotic), paromomycin (antimicrobial), biomycin (antibiotic), polymyxin B (antibiotic), colistin (antibiotic), vancomycin or other amino glycosides antibiotics.
- Indomethacin (an anti-inflammatory). This can increase the amount of amikacin which is absorbed in new born babies.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before you are given this medicine.

Driving and using machines
If you feel unwell or suffer from any of the side effects do not drive or operate machinery.

Amikacin injection/infusion contains sodium metabisulfite (E223) and sodium

- This medicine contains sodium metabisulfite (E223) which may rarely cause severe hypersensitivity reactions and bronchospasm.
- This medicine contains 15 mg sodium (main component of cooking/table salt) in each vial.

This is equivalent to 0.75 % of the recommended maximum daily dietary intake for an adult.

3. How to take Amikacin injection/infusion

Amikacin injection/infusion is usually injected into a muscle by a qualified healthcare professional (doctor or nurse). It may be given into a vein, either by injection or (following dilution) by infusion (drip). Your pre-treatment bodyweight should be obtained in order to calculate the correct dosage. The usual duration of the treatment is 7 to 10 days.
The total daily dose by all routes of administration should not exceed 15-20 mg/kg/day.

Adults and children over 12 years: The recommended dose is 15 mg/kg/day which is given once a day or divided into two doses which are given twice a day. The total daily dose should not exceed 1.5 g.

Elderly: Renal function should be assessed and dose adjusted as described under impaired renal function.

Children aged 4 weeks to 12 years: The recommended dose is 15 – 20 mg/kg/day which is given once a day or divided into two doses which are given twice a day.

Neonates: The recommended dose is initially 10 mg/kg followed by 7.5 mg/kg which is given twice a day.

Premature infants: The recommended dose is 7.5 mg/kg twice a day.

Life-threatening infection and/or those caused by Pseudomonas: The doses may be increased to 500 mg every eight hours, but should not exceed 1.5 g/day or be administered for a period longer than 10 days.

Urinary tract infections: The recommended dose is 7.5 mg/kg/day twice a day.

Impaired renal function: The daily dose should be reduced and/or the interval between doses increased to avoid build up of drug.

The doses may be increased in certain infections.

You may require hearing and kidney tests while receiving Amikacin injection/infusion as well as blood tests to check the amount of amikacin received.

You should start to see an improvement in 1-2 days. If there has been no improvement after 3-5 days, go back to see your doctor.

If you are given too much or too little Amikacin injection/infusion
Amikacin injection/infusion will be given by a qualified healthcare professional (doctor or nurse) who will ensure you are given the correct dose. It is unlikely that you will be given too much or too little Amikacin injection/infusion, however, tell your doctor or nurse if you have any concerns.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If you notice any of the following, stop taking Amikacin injection/infusion and contact your doctor immediately:

- Swelling of the face, lips or tongue
- Skin rash
- Difficulty breathing.

These may be signs of an allergic reaction or anaphylactic reaction.

Patients treated with Amikacin injection/infusion have reported the following side effects:
Uncommon: may affect up to 1 in 100 people

- Feeling sick (nausea) and being sick (vomiting)
- Infections with resistant bacteria or yeasts.
- Skin rash

Rare: may affect up to 1 in 1,000 people

- Abnormal white blood cells, which can be detected by blood tests
- Reduced magnesium levels in the blood
- Headache
- Tremor
- Muscle twitching
- Pins and needles
- Balance difficulty
- Blindness or other problems with your vision
- Low blood pressure
- Ringing in the ears
- Loss of hearing
- Joint pain
- Itching and hives
- Decrease in the amount of urine you produce (oliguria) and abnormal kidney blood tests and urine tests (e.g. blood cells in the urine)
- Fever
- Anaemia (reduction in red blood cells which make the skin pale cause weakness or breathlessness).

Not known: frequency cannot be estimated from the available data

- Inability of muscles to move
- Wheezing
- Temporarily stopping breathing
- Deafness.
- Kidney failure

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via:
HPRA Pharmacovigilance
Website: www.hpra.ie

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Amikacin injection/infusion

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

Do not use this medicine after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.

Do not store above 25°C.

Following dilution in 0.9% sodium chloride or 5% dextrose media, this medicine should be used immediately. However, if this is not possible prepared injections or infusions can be stored for up to 24 hours at 25 °C.

The ampoule is to be used once only. Any unused solution in the ampoule should be discarded. 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 protect the environment.

6. Contents of the pack and other information

What Amikacin injection/infusion contains

The active substance is amikacin. Each ampoule contains 2 ml of amikacin sulfate equivalent to 500 mg of amikacin (250 mg/mL).

The other ingredients are sodium metabisulfite (E223), sodium citrate, sulfuric acid and water for injection.

What Amikacin injection/infusion looks like and contents of the pack

Amikacin Solution for injection/infusion is a colourless to yellowish solution packed into glass ampoules containing 2 ml.

Amikacin Solution for Injection/Infusion is available in packs containing 5 ampoules.

Marketing Authorisation Holder

Athlone Pharmaceuticals Limited,

Connaught House,

1 Burlington Road,

Dublin 4,

Ireland

Manufacturer

HELP S.A.,
Pedini Ioanninon,
Ioannina,
45500
Greece

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Package leaflet: Information for Healthcare Professionals Amikacin 250 mg/mL Solution for injection/infusion

The following information is intended for healthcare professionals only:
Below is a summary of the dosage and administration of Amikacin injection/infusion. Reference should be made to the Summary of Product Characteristics (SmPC) for full prescribing information.

General dosing information
At the recommended dosage level, uncomplicated infections due to amikacin sensitive microorganisms should respond to therapy within 24 to 48 hours. If definite clinical response does not occur within 3 to 5 days, consideration should be given to alternative therapy.

Amikacin concentrations in serum should be measured to assure adequate, but not excessive levels. It is desirable to measure both peak and trough serum concentrations intermittently during therapy.

Instructions for use and other handling
The medicinal product should be inspected visually for particulate matter and discolouration prior to administration.

If required, suitable diluents for intravenous infusion use are 100 or 200 ml of 9 mg/ml (0.9%) sodium chloride solution for injection or 50 mg/ml (5%) dextrose solution for injection.

For single use only.

Incompatibilities:
Amikacin is incompatible with some penicillins and cephalosporins, amphotericin, chlorothiazide sodium, erythromycin gluceptate, heparin, nitrofurantoin sodium, phenytoin sodium, sodium thiopental, warfarin sodium, and depending on the composition and strength of the vehicle, tetracyclines, vitamins of the B group with vitamin C, and potassium chloride. This medicinal product must not be mixed with other medicinal products except those mentioned under 'Instructions for use and other handling'.

Method of administration and posology:
For most infections, the intramuscular route is preferred, however, in life-threatening infections, or in patients for whom intramuscular injection is not possible, the medicine can be administered intravenously, either as slow bolus (2 to 3 minutes) or by slow infusion over 30 to 60 minutes in adults. In paediatric patients, the solution should be administered as infusions lasting 1 to 2 hours.
Amikacin should not be mixed with other drugs, but should be administered separately according to the recommended dose and route.

<u>Adults and children over 12 years:</u>
The recommended intramuscular or intravenous dosage for adults and adolescents with normal renal function (creatinine clearance ≥50 mL/min) is 15 mg/kg/day which may be administered as a single daily dose or divided into 2 equal doses i.e. 7.5 mg/kg every 12

hours. The total daily dose should not exceed 1.5 g. In endocarditis and in febrile neutropenic patients dosing should be twice daily, as there is not enough data to support once daily dosing.

Children 4 weeks to 12 years:
The recommended intramuscular or intravenous (slow intravenous infusion) dose in children with normal renal function is 15-20 mg/kg/day which may be administered as 15-20 mg/kg, once a day; or as 7.5 mg/kg every 12 hours. In endocarditis and in febrile neutropenic patients dosing should be twice daily, as there is not enough data to support once daily dosing.

Neonates:
An initial loading dose of 10 mg/kg followed by 7.5 mg/kg every 12 hours.

Premature infants:
The recommended dose in premature infants is 7.5 mg/kg every 12 hours.
Aminoglycosides should be used with caution in premature and neonatal infants because of the renal immaturity of these patients and the resulting prolongation of serum half-life of these drugs.

Life-threatening infections and/or those caused by Pseudomonas:
The adult dose may be increased to 500 mg every eight hours but should never exceed 1.5 g/day nor be administered for a period longer than 10 days. A maximum total adult dose of 15 g (i.e. entire treatment course) should not be exceeded.

Urinary tract infections (other than pseudomonal infections):
7.5 mg/kg/day in equally divided doses (equivalent to 250 mg twice a day in adults). As the activity of amikacin is enhanced by increasing the pH, a urinary alkalising agent may be administered concurrently.

Impaired renal function:
For patients with impaired renal function, the daily dose should be reduced and/or prolonged intervals should be applied so as high trough drug concentrations are avoided. If the creatinine clearance rate is not available and the patient's condition is stable, a dosage interval in hours for the normal single dose (i.e., that which would be given to patients with normal renal function on a twice daily schedule, 7.5 mg/kg) can be calculated by multiplying the patient's serum creatinine by nine. For example if the serum concentration is 2 mg/100 mL, the recommended single dose (7.5 mg/kg) should be administered every 18 hours. Dose adjustment options are detailed in the SmPC. As renal function may alter appreciably during therapy, the serum creatinine should be checked frequently and the dosage regimen modified as necessary.

Other Routes of Administration:
Amikacin 250 mg/ mL Solution for injection/infusion in concentrations of 0.25% (2.5 mg/mL) may be used satisfactorily as an irrigating solution in abscess cavities, the pleural space, the peritoneum and the cerebral ventricles.

Intraperitoneal use
Following exploration for established peritonitis, or after peritoneal contamination due to faecal spill during surgery, amikacin may be used as an irrigant after recovery from

anaesthesia in concentrations of 0.25% (2.5 mg/mL). The intraperitoneal use of amikacin is not recommended in young children.

Storage Conditions:
Physicochemical compatibility - upon dilution with 0.9% sodium chloride or 5% dextrose the prepared injections or infusions can be stored for up to 24 hours at 25°C.

Microbiological compatibility - upon dilution with 0.9% sodium chloride or 5% dextrose from a microbiological point of view the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

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