Package leaflet: Information for the user

Amikacin Caragen 250 mg/ml solution for injection/infusion
amikacin

Read all of this leaflet carefully before you start using 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. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- 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 Caragen is and what it is used for

Amikacin Caragen contains amikacin which belongs to a group of antibiotics called 'aminoglycosides'. Amikacin Caragen is used in the treatment of serious infections caused by bacteria sensitive to amikacin.

2. What you need to know before you use Amikacin Caragen

Do not use this medicine
- if you are allergic (hypersensitivity) to amikacin or any of the other ingredients of this medicine (listed in section 6)
- If you have a history of allergy (hypersensitivity) or serious toxic reactions to other aminoglycoside antibiotics
- If you suffer from a disorder called myasthenia gravis (severe weakness of certain muscles of the body)

Warnings and precautions
Tell your doctor, pharmacist or nurse if
- you have kidney problems
- you have shown kidney or hearing problems after taking any other antibiotics
- you have hearing difficulties or tinnitus (ringing or buzzing in the ears)
- you are elderly
- you have any muscular disorders such a Parkinson's disease
- 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 Caragen 250 mg/ml solution for injection/infusion.

Talk to your doctor if any of the above applies to you before this medicine is used.

Other medicines and Amikacin Caragen
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

Some medicines may interact with others. Tell your doctor if you are taking:
- diuretics (e.g. furosemide or ethacrynic acid)
- other medicines that may affect your kidneys or hearing such as bacitracin (an antibiotic), cisplatin (an anti-cancer medicine), amphotericin B (an antifungal), ciclosporin (immune-suppressant), tacrolimus (immune-suppressant), cephaloridine (antibiotic), paromomycin (antimicrobial), viomycin (antibiotic), polymyxin B (antibiotic), colistin (antibiotic), vancomycin, or other aminoglycosides
- beta-lactam (penicillin type) medicinal products
- bisphosphonates (treatment of bone loss)
- vitamin B1
- platinum compound medicinal products (anti-cancer)
- muscle-relaxing drugs (drugs used for general anaesthesia)
- Indomethacin, an anti-inflammatory medicine, may increase that amount of amikacin absorbed in neonates.

Pregnancy and breast-feeding
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 taking this medicine. Your doctor will only use this medicine if the expected benefits outweigh any potential risk to your baby.
Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines
Do not drive or use machines if you experience any side effect (e.g. dizziness) which may lessen your ability to do so.

Amikacin Caragen contains sodium and sodium metabisulfite
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 of sodium for an adult.

May rarely cause severe hypersensitivity reactions and bronchospasm.

3. How to use Amikacin Caragen

This medicine is usually injected into a muscle. It may also be given into a vein, either as an injection or (following dilution) as an infusion (drip).

Dose
Your doctor will work out the correct dose of Amikacin for you and how often it must be given.

The dose will be different depending on your weight, your age, how well your kidneys are working, the infection you have, if you have poor hearing and any other medicines you may be taking.

The total daily dose by all routes of administration will generally not exceed 15mg/kg of your body weight per day.

It will usually be given once or twice a day, but may be given at a different interval depending on how well your kidneys function and the particular infection you have.

During the course of treatment, you are likely to undergo blood tests to monitor your kidney function and the level of amikacin in your blood, and you may be asked to provide urine samples. You will possibly also have hearing tests before and during treatment to look for signs of side effects. Your doctor may adjust your dose depending upon the results of these tests.

Paediatric use
Amikacin Caragen like all other aminoglycosides should be used with caution in premature and neonatal infants.

If you are given too much or too little Amikacin Injection

This medicine will be given to you in a hospital, under the supervision of a doctor. It is unlikely that you will be given too much or too little, however, tell your doctor or nurse if you have any concerns.

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

If any of the following happens, tell your doctor immediately as these are all serious. You may need urgent medical attention or hospitalisation.

- Severe allergic reaction (anaphylactic reaction, anaphylactic shock and anaphylactoid reaction), hypersensitivity-you may experience a sudden itchy rash (hives), swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing), and you may feel you are going to faint
- Paralysis
- Deafness
- Sudden loss of breathing, bronchopasm
- Severe kidney failure

(for each of the above side effects the expected frequency is unknown based on the available data).

Rare side-effects (may affect less than 1 person in 1 000):

- Ringing in the ear (tinnitus) or loss of hearing
- Decrease in the amount of urine you produce (oliguria)

If any of the following happens, tell your doctor as soon as possible:

Uncommon side effects (may affect less than 1 in 100 people):

- Superinfections or colonisation with bacteria or yeast which are resistant to amikacin
- Nausea, vomiting
- Skin rash

Rare side-effects (may affect less than 1 person in 1 000):

- Unusually low amounts of red blood cells in the blood (anaemia) or excessive amounts of the blood cells known as eosinophils (eosinophilia)
- low levels of magnesium in blood
- Tremor
- Abnormal tingling (paresthesia)
- Headache
- imbalance
- Blindness, retinal infarction
- Low blood pressure
- Itching or hives
- Joint pain, muscle spasms
- Fever
- Abnormal kidney blood tests and urine tests(e.g. blood cells in the urine)

Amikacin may lead to changes in your kidney function. Your doctor may take blood and urine samples to monitor for changes such as increased levels of creatinine or nitrogen in the blood and protein or red/white blood cells in urine. Your doctor may also ask you to undergo hearing tests.

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 Caragen

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 and vial label after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

Following dilution in 0.9 % (9 mg/ml) sodium chloride solution for injection or 5 % (50 mg/ml) glucose solution for injection, chemical and physical in-use stability has been demonstrated for 24 hours at 2-8 °C and at 25 °C, in non-PVC bags.

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 2-8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

Do not use this medicine if you notice particles in the vial, or if the solution does not appear colourless to pale yellow.

Do not throw away any medicines via wastewater. 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 Caragen contains

- The active substance is amikacin. Each ml of solution for injection/infusion contains 250 mg amikacin (as amikacin sulfate). Each vial of 2 ml of solution for injection/infusion contains 500 mg amikacin (as amikacin sulfate).
- The other ingredients are sodium citrate, sodium metabisulfite, sulfuric acid (for pH adjustment) and water for injections.

What Amikacin Caragen looks like and contents of the pack

Amikacin Caragen is a clear, colourless to pale yellow solution for injection/infusion which comes in a glass vial.
Pack size: 1 vial.

Marketing Authorisation Holder

Caragen Limited
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Manufacturer

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Schimatari Viotias, 32009,
Greece

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The following information is intended for healthcare professionals only:

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, therapy should be stopped and the antibiotic susceptibility pattern of the pathogen should be rechecked. Failure of the infection to respond may be due to resistance of the microorganism or to the presence of septic foci requiring surgical drainage.

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 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 %) glucose solution for injection.

For single use only.

Discard any unused contents.

Method of administration and posology
For most infections, the intramuscular route is preferred. However, in life-threatening infections or in patients for whom intramuscular administration is not possible, the medicine can be administered intravenously, either as is (2-3 minutes) or by slow infusion within 30 to 60 minutes. In infants, it should be administered as infusions lasting 1 to 2 hours.
Amikacin sulfate injection may be given intramuscularly or intravenously. When administered intravenously Amikacin sulfate should be given by either slow bolus (2 to 3 minutes) or infusion (0.25 % over 30 to 60 minutes).

Amikacin should not be physically premixed with other drugs, but should be administered separately according to the recommended dose and route.

Adults and children over 12 years old
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 q 12 h. 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 up to 12 years old

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 q 12 h. 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 q 12 h.

Premature infants
The recommended dose in prematures is 7.5 mg/kg in 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.

Urinary tract infections (other than pseudomonas infections)
Amikacin Caragen is indicated in non-pseudomonas urinary tract infections and may be administered in a single daily dose of 500mg or in two equally divided doses (250 mg twice per day).

Impaired renal function
For patients with impaired renal function daily doses 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 creatinine concentration is 2mg/100mL, 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.

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’