PACKAGE LEAFLET: Information for the patient

GENTAMYCINE

Solution for injection – 40 mg / 2 ml (40,000 UI)

Solution for injection – 80 mg / 2 ml (80,000 UI)

(Gentamicin sulfate)

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects becomes worse or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT GENTAMYCINE IS AND WHAT IT IS USED FOR

Gentamycine is a potent bactericidal antibiotic with a wide range activity against both Gram-positive and Gram-negative strains including Staphylococcus aureus, Escherichia coli, Klebsiella, Proteus, and Pseudomonas species.

Gentamycine solution for injection is indicated for the following cases:

- serious infections caused by *P.aeruginosa, Proteus species, E. coli, Klebsiella species, Enterobacter species, Serratia species, Citrobacter species, Staphylococcus species*;
- acute and chronic infections of the urinary tract;

- various systemic infections, such as: neonatal sepsis, peritonitis, meningitis;
- bone and soft tissue infections, such as: acute osteomyelitis, wound infections (including burns);
- bacterial septicemia;
- respiratory tract infections;
- empirical therapy for serious unknown infections.

2. BEFORE YOU TAKE GENTAMYCINE

Do not take Gentamycine if:

- you are sensitive (allergic) to gentamicin sulfate or other aminoglycosides or to any of the excipients of Gentamycine;
- you suffer from myasthenia gravis, Parkinson's disease and other causes of muscular weakness;
- you are pregnant.

Take special care with Gentamycine

Ask your doctor before taking Gentamycine:

- if you suffer from impaired renal function and especially if you are elderly nephrotoxicity may occur; in these cases, monitoring of the patient during use of Gentamycine and also reduction of dose frequency and of the dose itself is advisable;
- if you suffer from myasthenia gravis, Parkinson's disease or infant botulism because aminoglycosides, where gentamicin belongs, may cause block of neuromuscular activity with similar effect to curares; in these cases, monitoring of neuromuscular function of the patient is advisable;
- if you follow a limited diet or poor food because hypomagnesemia may occur;
- if you are breast-feeding;
- if you suffer from impaired hepatic and auditory function, bacteraemia and fever and especially if you are elderly because ototoxicity may occur (both vestibular and auditory); in these cases, monitoring of auditory function of the patient during use of Gentamycine is advisable;
- if you suffer from hypotension because the risk of nephrotoxicity increases.

Prolonged treatment should be avoided. The treatment usually lasts 7-10 days.
Monitoring is particularly important in patients receiving high doses or prolonged courses, in infants, children and the elderly, and in patients with cystic fibrosis or obesity.

Taking other medicines

Concomitant use with other drugs may affect or be affected by Gentamycine.
Tell your doctor or pharmacist if you are taking or have taken recently other drugs, including those without prescription. Remember to tell your doctor about the treatment with Gentamycine if you are given another drug during treatment.
It is especially important that your doctor is aware about the fact that you are being treated with:

- anticoagulants: gentamicin may increase the hypothrombinaemic effect of anticoagulants;
- similar drugs with gentamicin: gentamicin combined with kanamycin, neomycin, streptomycin, cyclosporine, acyclovir, polymyxin B, colistin, vancomycin, amphotericin B and some cephalosporins increases the risk of nephrotoxicity;
- diuretics: gentamicin combined with ethacrynic acid and less with furosemide increases the risk of ototoxicity; the intravenous injection of diuretics may cause increased serum concentration of gentamicin which may damage the eighth cranial nerve of the fetus;
- nondepolarizing myorelaxants and suxamethonium: gentamicin combined with succinylcholine or tubocurarine increases the risk for neuromuscular block, which may be associated with respiratory paralysis. Calcium and neostigmine salts may be used as antidote;
- botulinum toxin: gentamicin combined with botulinum toxin may increase the risk of toxicity due to enhanced neuromuscular block;
- antiemetics: they mask symptoms of vestibular impairment (nausea, dizziness) when patients use them concomitantly with gentamicin;
- carbenicillin and ticarcillin: gentamicin may inactivate them in vitro and in vivo;
- indomethacin: the plasmatic concentration of gentamicin may be increased when used concomitantly in premature babies;
- cytotoxics: like cisplatin and fludarabine, increased risk of nephrotoxicity and maybe ototoxicity when used with cisplatin;
- cholinergics: the effect of neostigmine and pyridostigmine is antagonised;
- biphosphonates: increased risk for hypocalcemia;

- tacrolimus: increased risk of nephrotoxicity;
- agalsidase alfa and beta: gentamicin possibly inhibits their action.

Taking Gentamycine with food and drinks

There are not enough data available.

Pregnancy

Ask for your pharmacist or doctor advice before taking this drug!

Gentamycine, like other aminoglycosides, should not be used during pregnancy because it may damage the eighth cranial nerve of the fetus.

Breastfeeding

It is very important to consult with your doctor before taking this drug.

Gentamicin passes into breast milk, but in low concentrations it does not cause harmful clinical effects in the newborn, whereas if high doses are used, the mother should not breastfeed the child.

Driving and using machines

There are no data available about the effects of this medicinal product on driving or using machines. You should be careful if you experience side effects that may affect the performance of these activities.

Important information about some of the excipients of Gentamycine

This drug contains sodium metabisulfite which may rarely cause severe hypersensitivity reactions and bronchospasm.

Gentamycine contains methyl hydroxybenzoate (nipagin) and propyl hydroxybenzoate (nipasol), which may cause allergic reactions (possibly delayed), and exceptionally, bronchospasm.

3. HOW TO TAKE GENTAMYCINE

Always take Gentamycine exactly as your doctor has told you. If you are not sure, talk to your doctor or pharmacist. If you feel that the effect of Gentamycine is too strong or too weak, talk to your doctor or pharmacist.

Gentamycine can be *injected into a muscle or vein* and in both cases it has the same dosage. It can be directly injected *into a vein* or through the catheter. The duration of injection is 2-3 minutes. When the daily dose of Gentamycine is injected as a single dose, the duration of injection should be continued up to 15 minutes. Below there is an overview of practical dosing of gentamicin in patients with normal renal function:

Age	**Daily dosage** **1 ampoule = 2 ml; 40 mg or 80 mg**
Adults and children over 12 years old	2 – 5 mg / kg weight, intramuscularly or intravenously in 1* to 3 separated doses**.
Children from 2 weeks to 12 years old	6 mg / kg weight, intramuscularly or intravenously in 1* to 3 separated doses**.
Neonates up to 2 weeks old	6 mg / kg weight, intramuscularly or intravenously in 2 separated doses.

** The total daily dose of gentamicin should not be injected as a single dose in patients with immune deficiency (neutropenia), in patients with severe impairment of renal function or infective endocarditis and in pregnant women.*

*** When gentamicin is injected into several separate doses, the initial dose for adults should be 1.5 to 2 mg/kg weight, regardless of renal function. This dose ensures a maximum suitable level in serum. In children, babies and neonates, the same doses adjusted based on body weight, will lead to lower serum concentrations compared to adults. Therefore, in this group of patients some higher therapeutic doses are needed. For safety reasons, it is recommended that in children the serum levels of gentamicin are determined on a daily basis. One hour after injection, serum levels of gentamicin should not exceed 2 mcg/mL. If the daily dose is injected as a single dose, then the level in serum, measured before the subsequent dose should not pass 1 mcg/mL.*

Dosage in patients with renal function impairment: Patients with impaired renal function should use the same initial dose as patients with normal renal function. During further treatment, doses should be adjusted either by increasing the interval between the two injections compared with the usual doses or by reducing the usual dose.

A practical overview for dosing gentamicin in this case is given below:

Urea, mg/100ml (mmol/L)	**Creatinine clearance mL/min (mL/s)**
<40 (< 6.8)	70 (1.16)
40-100 (6.8-17)	30-70 (0.5-1.16)
100-200 (17-34)	10-30 (0.16-0.5)
> 200 (>34)	5-10 (0.08 – 0.16)

Serum creatinine mg/100mL (mcmol/L)	**Doses and interval between doses**
<1.4 (<124)	80 mg*, every 8 hours
1.4-1.9 (124-168)	80 mg*, every 12 hours
1.9-2.8 (168-248)	80 mg*, every 18 hours
2.8-3.7 (248-327)	80 mg*, every 24 hours
3.7-5.3 (327-469)	80 mg*, every 36 hours
5.3-7.2 (469-636)	80 mg*, every 48 hours

** 60 mg if body weight is < 60 kg.*

The doses shown above are approximate.

Appropriate dosage adjustment is achieved upon the obtained level of gentamicin in serum. An appropriate level of gentamicin in serum, measured 30 to 60 minutes after injection into a muscle or vein is 50 mcg/mL. The dose at the end of each dialysis procedure is 1 to 1.5 mg / kg weight gentamicin. In peritoneal dialysis is needed to add 1 mg / kg weight gentamicin in 2 liters of dialysis solution. The duration of treatment is 7 to 10 days; in severe and complex infections a longer-term treatment may be needed.

Preparation of the solution for infusion: for short-term infusion in vein, gentamicin should be dissolved in 100 to 200 ml sterile 0.9% sodium chloride or 5% sterile glucose solution. The concentration of gentamicin in the solution should not exceed 1 mg / mL.

In all cases, treatment with Gentamycine lasts 7-10 days. When the treatment lasts beyond or it is administered at higher dosage levels, it is advisable to monitor renal, auditory and vestibular function.

If you take more Gentamycine than you should

If you take more Gentamycine than you should, or if the children have been taking this medicine by accident, please contact your doctor, the hospital, or call the emergency to get an opinion of the risk and advice on the action to be taken.

Symptoms of overdose are: vestibular syndrome and dizziness where toxicity is cumulative and irreversible, cochlear damage where the ciliar cells of the organ of Corti are damaged.

In patients with renal function impairment, the level of gentamicin in serum reaches 12 mcg / mL. This is reversible if at the same time the dose is adjusted and peritoneal dialysis or hemodialysis is applied to remove gentamicin from blood.

If you forget to take Gentamycine

If you forget a dose, take the next dose when it is the normal time to take it.

Do not take a double dose to make up for the forgotten dose.

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

4. POSSIBLE SIDE EFFECTS

Like all medicines, Gentamycine also can cause side effects, although not everybody may get them.

Most of the side effects are dose-related and disappear when the dose is reduced or the treatment is discontinued. Some side effects may appear at the beginning of treatment and disappear spontaneously during the treatment.

Tell your doctor straight away if you notice any of the following serious side effects – you may need urgent medical treatment:

- severe allergic reactions of the skin and mucous membranes accompanied by blistering and reddening of the skin which might in very severe cases affect inner organs and might be life threatening (Stevens-Johnson syndrome, toxic epidermal necrosis);
- allergic reactions including anaphylaxis, which may include:
  - an itchy, lumpy rash (hives) or nettle rash (urticaria);
  - swelling of the hands, feet, ankles, face, lips or throat which may cause difficulty in swallowing or breathing;

- fainting, dizziness, feeling lightheaded (low blood pressure).

- Nephrotoxicity is a serious side effect of gentamicin. Very rarely gentamicin may cause acute kidney failure. Nephrotoxicity may be manifested with increased creatinemia, hyposthenuria, leukocytes in urine, proteinuria, cylinders in urine and in severe cases with interstitial fibrosis, tubular necrosis and renal tubular acidosis. Nephrotoxicity is favored by high plasma concentrations, combination with other nephrotoxic drugs, total dose, duration of treatment and existing renal disease.
- Ototoxicity may be manifested with: irreversible hearing loss, deafness, (frequency unknown), hearing loss of high frequency, noise in the ears, dizziness, nausea. Cochleo-vestibular toxicity is favored by the duration of treatment and concomitant use with other ototoxic medicines.
- Neuromuscular blockade which is expressed with myasthenia.
- In the central and peripheral nervous system: headache, depression, confusion, hallucinations, convulsions, neurotoxicity, encephalopathy, lethargy, muscle twitch, peripheral neuropathies.
- In the gastrointestinal system: nausea, vomiting, anorexia, increased amount of saliva, stomatitis, stomach pain, diarrhoea.
- Pain during injection.
- Changes of liver enzymes.
- Decreased level of calcium, sodium, potassium, magnesium.
- Anemia, blood disorders.
- Infection with other gentamicin-resistant germs.
- Very rarely high urine levels of phosphate and aminoacids (so called Fanconi-like syndrome, associated with high doses given over long time) may occur.

If any of the side effects becomes worse or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE GENTAMYCINE

Keep out of the reach and sight of children!

Do not use Gentamycine after the expiry date which is stated on the package!

Do not store above 25°C!

Store in the original package to protect it from light!

6. FURTHER INFORMATION

What Gentamycine contains

The active substance is gentamicin sulfate.

Each 2 ml ampoule contains:

- gentamicin sulfate equivalent to 40 mg (40,000 UI) gentamicin base.
- gentamicin sulfate equivalent to 80 mg (80,000 UI) gentamicin base.

The excipients are: methyl hydroxybenzoate, propyl hydroxybenzoate, sodium metabisulfite, disodium edetate, sodium citrate, citric acid monohydrate, water for injection.

Contents of the pack

Box with 10 ampoules.

Marketing Authorisation Holder (MAH) and Manufacturer:

PROFARMA sh.a.,

St. “Skënder Vila”,

Tirana, Albania.

Tel.: +355 4 23 89 602

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