APPROVED PACKAGE INSERT

SCHEDULING STATUS

S4

PROPRIETARY NAMES AND DOSAGE FORM

Gentamycin Fresenius 20 mg/2 ml (vials)

Gentamycin Fresenius 80 mg/2 ml (vials)

Gentamycin Fresenius 20 mg/2 ml (ampoules)

Gentamycin Fresenius 40 mg/1 ml (ampoules)

Gentamycin Fresenius 80 mg/2 ml (ampoules)

Injection

COMPOSITION

Gentamicin sulphate equivalent to base 10 mg/ml (in 2 ml vials) - preserved with methylhydroxybenzoate 0,18 % *m/v* and propylhydroxybenzoate 0,02 % *m/v.*

Gentamicin sulphate equivalent to base 40 mg/ml (in 2 ml vials) - preserved with methylhydroxybenzoate 0,18 % *m/v* and propylhydroxybenzoate 0,02 % *m/v.*

Gentamicin sulphate equivalent to base 10 mg/ml (in 2 ml ampoules).

Gentamicin sulphate equivalent to base 40 mg/ml (in 1 ml ampoules).

Gentamicin sulphate equivalent to base 40 mg/ml (in 2 ml ampoules).

Inactive ingredients: methylhydroxybenzoate, propylhydroxybenzoate, water for injection.

PHARMACOLOGICAL CLASSIFICATION

A 20.1.1 Broad and medium spectrum antibiotics

PHARMACOLOGICAL ACTION

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

INDICATIONS

Gentamycin Fresenius injection is indicated for the following conditions, when caused by susceptible organisms:

1. Acute and chronic urinary tract infections;
2. Severe systemic infections, e.g. sepsis, peritonitis, meningitis;
3. Bone and soft tissue infections, e.g. acute osteomyelitis, wound and soft tissue infections;
4. Infected burns;
5. Respiratory tract infections;
6. Eye infections.

CONTRAINDICATIONS

Gentamycin Fresenius is contraindicated in patients with a known history of allergy to it, and those allergic to other aminoglycosides. Great care is required in patients with myasthenia gravis, parkinsonism, and other conditions characterised by muscular weakness. Impaired hepatic function or auditory function, bacteraemia, fever, and perhaps exposure to loud noises have also been reported to increase the risk of ototoxicity, while volume depletion or hypotension, liver disease, or female sex have been reported as additional risk factors for nephrotoxicity.

WARNINGS AND SPECIAL PRECAUTIONS

In patients with impaired renal function or those patients treated with **Gentamycin Fresenius** injection for longer periods or at higher dosage than recommended, ototoxicity (both vestibular and auditory) may occur, should gentamycin serum concentration levels exceed 12 µg/ml, for prolonged periods.

In such patients, the frequency of **Gentamycin Fresenius** administration should be reduced as indicated under “Dosage and directions for use”, by assessing blood urea, creatinine or creatinine clearance rates. It is also considered advisable to check auditory and vestibular function and to monitor peak (one hour) gentamycin serum levels, to ensure they do not exceed 12 µg/ml. Administer with caution to patients with myasthenia gravis.

INTERACTIONS

The concurrent use of **Gentamycin Fresenius** with diuretics such as ethacrynic acid and furosemide should be avoided, as these two diuretics may individually result in ototoxicity. Similarly **Gentamycin Fresenius** should not be administered concurrently with other potentially ototoxic medicines (e.g. kanamycin, neomycin, streptomycin, etc.). The nephrotoxicity due to cephalosporins may be potentiated by **Gentamycin Fresenius** and caution should generally be exercised in the simultaneous administration of potentially nephrotoxic substances together with **Gentamycin Fresenius.** Large doses of **Gentamycin Fresenius** should not be administered concurrently with neuromuscular blocking agents. As a result of this respiratory depression and muscular paralysis have been reported.

PREGNANCY AND LACTATION

Safety in pregnancy and lactation has not been established.

DOSAGE AND DIRECTIONS FOR USE

Intramuscular administration:

Gentamycin Fresenius injection is generally administered intramuscularly. Intravenous administration should only be utilised in special cases (Refer “Intravenous administration”). It is recommended that a needle not larger than 21 gauge is used to reduce fragmentation of the rubber stopper.

Adult patients with normal renal function:

1. *Urinary tract infections:*

   In infections of moderate severity: 2 mg/kg/day as a single daily dose or in 3 equal doses (8 hourly). In patients with severe infections 3 mg/kg/day as a single daily dose or in 3 equal doses (8 hourly). In the treatment of urinary tract infections with gentamycin, alkalis should be given concomitantly to raise the urinary pH above 7.

2. *Systemic infections:*

   In infections of moderate severity: 2 mg/kg/day as a single daily dose or in 3 equal doses (8 hourly). In patients with severe infections: 3 mg/kg/day as a single daily dose or in 3 equal doses (8 hourly).

3. *Life-threatening infections (e.g. sepsis):*

(a) *Adults:* for patients with life-threatening infections up to 5 mg/kg/day as a single daily dose or in 3 equal doses (8 hourly). This dosage should be reduced to 3 mg/kg/day as soon as clinically indicated.

(b) Children, infants and neonates:

Children: A dose of 3 to 6 mg/kg/day is administered in three equally divided doses every 8 hours.

Infants older than 1 week: Administer 3 to 6 mg/kg/day as for "Children" above or in two equal doses every 12 hours.

Neonates and infants less than 1 week: 6 mg/kg/day is administered in two equally divided doses every 12 hours.

Note: The dosing interval of **Gentamycin Fresenius** in paediatric patients may vary from every four hours to every twenty-four hours, depending on the medical condition of the patient (cystic fibrosis, burns, renal dysfunction); serum levels must be monitored.

Duration of treatment:

In all cases, the general duration of treatment is 7 to 10 days. When treatment exceeds this period, and in the administration of high dosage levels, it is advisable to monitor renal, auditory and vestibular functions (see "Warnings and special precautions").

Intravenous administration:

This form of administration is only recommended when circumstances do not permit the intramuscular route. The recommended dose and precautions for intravenous administration are identical to those stipulated for the intramuscular route. Intravenous administration is to be carried out slowly or may be infused over a period up to 2 hours.

Patients with impaired renal function:

Dosage must be adjusted in patients with impaired renal function. To minimize risk of toxicity in these patients, the first dose should be that normally recommended. Subsequent doses should be administered less frequently depending on the degree of renal impairment.

Since the serum half-life of gentamicin has a close correlation with creatinine clearance and serum creatinine, the serum half-life (in hours) of gentamicin may be estimated by multiplying the serum creatinine

(expressed in mg %), by four. The interval between doses, in hours, may be approximated by doubling the serum half-life.

Table 1 provides the guidance for adjustment of the interval between doses of **Gentamycin Fresenius** injection based on the aforementioned renal function tests. In those instances when only a blood serum urea concentration is available this value may be utilised initially; however, it should be supplemented with a serum creatinine level or creatinine clearance rate whenever possible.

This dosage schedule is not intended as a rigid recommendation. It is provided as a guide to dosage when the measurement of gentamicin serum levels is not feasible. It should be used in conjunction with close clinical and laboratory observation of the patient, and modified as deemed necessary by the treating medical practitioner.

TABLE 1

Approximate dosage guidelines for **Gentamycin Fresenius** Injection in adult patients based on renal function.

Mass of Adult Patient (kg)	**Dose (mg)**	**Renal Function Tests**			**Frequency of Administration**
		Creatinine Clearance Rate (ml/min)	**Serum Creatinine (mg %)**	**Blood Urea (mg %)**	
over 60	80 (2 ml)	over 70	less than 1,4	less than 38	every 8 hours
		35 – 70	1,4 – 1,9	36 – 63	every 12 hours
		24 – 34	2,0 – 2,8	64 – 84	every 18 hours
		16 –23	2,9 – 3,7	85 – 105	every 24 hours
		10 – 15	3,8 – 5,3	106 – 159	every 36 hours
		* 5 – 9	5,4 – 7,2	160 – 214	every 48 hours
60 or less (1,5 ml) (same as above)					

*When the clearance level is less than 5 ml/min, then haemodialysis is indicated. Gentamicin is dialysable and the dose should be individually adapted to the patient after each period of dialysis.

SIDE EFFECTS

In patients with normal renal function untoward side effects are not anticipated at the recommended dosage.

Ear and labyrinth disorders:

Frequent: Ototoxicity (both vestibular and auditory).

Renal and urinary disorders:

Frequent: Nephrotoxicity.

Immune system disorders:

Less frequent: Hypersensitivity reactions, especially after local use; cross-sensitivity between aminoglycosides may occur; anaphylactic reactions have occurred. Some hypersensitivity reactions have been attributed to the presence of sulphites in parenteral formulations.

Blood and lymphatic system disorders:

Less frequent: Blood dyscrasias, purpura.

Gastrointestinal disorders:

Less frequent: Nausea, vomiting, stomatitis.

Hepato-biliary disorders:

Less frequent Increased serum aminotransferase and increased serum bilirubin.

Nervous system disorders:

Less frequent Neuromuscular blockade (respiratory depression, muscular paralysis).

General disorders and administration site conditions:

Less frequent Endotoxic shock

Frequency unknown Electrolyte disturbances (notably hypomagnesaemia, but also hypocalcaemia and hypokalaemia) have occurred.

Eye disorders:

Frequency unknown Subconjunctival injection of gentamicin may lead to pain, hyperaemia, and conjunctival oedema, while severe retinal ischaemia has followed intra-ocular injection.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

In patients with renal impairment, gentamicin serum-blood levels in excess of 12 mcg/ml may result in ototoxicity. This is reversible if timeously observed and the dose is suitably adjusted. In the event of overdosage or toxic reactions, peritoneal dialysis or haemodialysis will aid in the removal of gentamicin from the blood.

IDENTIFICATION

A clear, colourless glass ampoule or vial containing a clear colourless to slightly yellow solution.

PRESENTATIONS

2 ml vials of 10 mg/ml (pack of 10 units)

2 ml vials of 40 mg/ml (pack of 10 units)

2 ml ampoules of 10 mg/ml (pack of 10 units)

1 ml ampoules of 40 mg/ml (pack of 10 units)

2 ml ampoules of 40 mg/ml (pack of 10 units)

STORAGE INSTRUCTIONS

Store at or below 30 ºC.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS

Gentamycin Fresenius 20 mg/2 ml (vials)	N/20.1.1/71
Gentamycin Fresenius 80 mg/2 ml (vials)	L/20.1.1/165
Gentamycin Fresenius 20 mg/2 ml (ampoules)	L/20.1.1/162
Gentamycin Fresenius 40 mg/1 ml (ampoules)	L/20.1.1/163
Gentamycin Fresenius 80 mg/2 ml (ampoules)	L/20.1.1/164

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATES OF REGISTRATION

Fresenius Kabi Manufacturing SA (Pty) Ltd

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