GARASENT INJECTION

DESCRIPTION:

GARASENT 80 mg INJ/2 ml amp: A clear, almost colourless liquid
GARASENT 280 mg INJ/2 ml amp: A clear, light straw coloured liquid

COMPOSITION:

GARASENT 80 mg INJ/2 ml amp: Each ampoule contains Gentamicin Sulphate equivalent to Gentamicin 80 mg per 2 ml
GARASENT 280 mg INJ/2 ml amp: Each ampoule contains Gentamicin Sulphate equivalent to Gentamicin 280 mg per 2 ml

PHARMACODYNAMICS:

Class. An aminoglycoside antibiotic which closely resembles kanamycin, tobramycin, amikacin and netilmicin in structure.
Gentamicin inhibits protein synthesis in susceptible bacteria. Cell death results. Gentamicin is active against a wide range of Gram-negative organisms including *Escherichia coli, Pseudomonas aeruginosa,* Proteus species (both indole positive and indole negative). Neiserria, Klebsiella, Enterobacter and Serratia species. It is also active against some Gram-positive organisms, eg. *Staphylococcus* (including methicillin and penicillin resistant strains.
Gentamicin shares the properties of ototoxicity and nephrotoxicity with other aminoglycosides. The aminoglycosides have been found to exacerbate impairment of neuromuscular transmission in clinical conditions such as myasthenia gravis.

PHARMACOKINETICS:

Gentamicin is rapidly absorbed after IM injection and peak serum levels are usually achieved within 30 to 90 minutes. Following parenteral administration gentamicin can be detected in tissue and body fluids. Penetration occurs into the bile, pleural and pericardial fluids, but little if any penetrates the blood/brain barrier.
Gentamicin is mainly distributed into the blood and urine. In the blood, it becomes bound to serum proteins (30%) and red blood cells (10%) and the rest is distributed mainly in extracellular fluids (15%).
Gentamicin is excreted almost entirely by renal glomerular filtration, hence the half-life of the drug is prolonged in the presence of renal failure. Adjustments in the frequency of administration of gentamicin are necessary to allow for the degree of renal failure.
The endogenous creatinine clearance rate and the serum creatinine level have a high correlation with the half-life of gentamicin in serum. Results of these tests may serve as guides for adjusting dosage in patients with renal impairment (see **Dosage and Administration**).
The serum half-life of gentamicin is approximately 2-3 hours in adults with normal renal function. It is prolonged in patients with impaired renal function and in premature or newborn infants.

INDICATION:

Gentamicin is effective in treating many gram-negative infections and should be considered for treatment of the following conditions, when caused by susceptible orgranisms: urinary tract infections, bacteraemia, respiratory tract infections, infected wounds, burns complicated by sepsis.

RECOMMENDED DOSAGE:

Gentamicin is normally given by I.M. injection. Intravenous administration is generally reserved for special indications and may be used when the I.M. route is not feasible, e.g. patients in shock, with haemorrhagic disorders, severe burns or reduced muscle mass. Whenever possible, and especially in patients with impaired renal function, peak and trough gentamicin serum concentrations should be determined and dosage adjusted where necessary, to maintain desired serum concentrations. In general, desired peak concentrations are between 4 and 10 mcg/mL, and trough concentrations are below 2 mcg/mL. Prolonged concentrations greater than these values may be associated with an increased risk of toxicity. Blood specimens for the determination of peak gentamicin concentrations should be obtained approximately one hour following I.M. administration and 30 minutes after completion of a 30 minute infusion, or at the completion of a 1 hour infusion. Blood specimens for trough gentamicin concentrations should be obtained immediately prior to the next I.M. or I.V. dose.

Intramuscular Administration: Dosage in patients with normal renal function:
1. Adults

Type of Infection	Dosage	Time Interval Between Doses	Duration of Therapy
Systemic and urinary tract infections*	3 mg/kg/day bodyweight > 60 kg: usual dose 80 mg; bodyweight ≤60 kg: usual dose 60 mg	8 hrs	7-10 days
Life threatening infections	5 mg/kg/day initially, then 3 mg/kg/day as soon as improvement is indicated	6-8 hrs	7-10 days Longer therapy may be required. If so, auditory renal and vestibular functions should be monitored

2. Paediatric

Infections	Age	Dosage	Frequency
Systemic	Up to 1 week	5 mg/kg/day	12 hourly
	1 week-1 year	6mg/kg/day	12 hourly
	1 year-12 years	4.5 mg/kg/day	8 hourly
Urinary tract infections		3 mg/kg/day	8-12 hourly
Life threatening infections	Up to 1 week	5 mg/kg/day	12 hourly
	1 week-1 year	7.5 mg/kg/day	8 hourly
	1 year-12 years	6 mg/kg/day	8 hourly

Dosage in patients with impaired renal function: In the presence of renal failure, it is particularly important to monitor renal, auditory and vestibular functions during gentamicin therapy. Dosage should be adjusted for patients with renal impairment to minimise the risk of toxicity. The first dose should be as normal; subsequent doses should be given less frequently, depending on the degree on renal impairment. The following table provides guidelines for adjustment of the interval between doses based on renal function tests:

Creatinine Clearance (mL/min)	Serum creatinine (mmol/Litre)	BUN (mmol/litre)	Interval between doses
Over 70	Less than 0.12	Less than 6.5	8 hours
35-70	0.12-0.17	6.5 – 10	12 hours
24-34	0.18-0.25	11-14	18 hours
16-23	0.26-0.33	15-18	24 hours
10-15	0.34-0.47	19-26	36 hours
5-9	0.48-0.64	27-36	48 hours

This table is provided as a guideline only, and is not intended as a rigid dose schedule. The measurement of gentamicin serum levels is highly desirable in patients with renal impairment to ensure optimal serum gentamicin concentrations.

Intravenous administration: The same dosage schedule as for I.M. administration may be used. For I.V. administration, the prescribed dose of gentamicin may be diluted in 100-200 mL of sterile normal saline or 5% glucose in water, the concentration of gentamicin in solution should not exceed 1 mg/mL. The solution should be infused over a period of 20-30 minutes.
Gentamicin has also been administered by injected directly into a vein or intravenous tubing. This may give rise, initially, to serum levels which are in excess of what is regarded as being safe from toxic side effects. The high serum level dose, however, fall rapidly. If this method of administration is used, the injection should be administered slowly over a period of 2-3 minutes.

[Revision Date: 28.05.2019]

ROUTE OF ADMINISTRATION:
For intramuscular or slow intravenous injection

CONTRAINDICATIONS:
Patients with a history of hypersensitivity to gentamicin; previous toxic reactions (ototoxicity, nephrotoxicity) resulting from aminoglycosides therapy.
Hypersensitivity to Disodium Edetate.

WARNINGS & PRECAUTIONS:
Gentamicin should be used with caution in patients with impaired renal function (including the elderly and premature infants). In such patients the frequency of administration should be reduced and renal function should be monitored along with evaluation of auditory and vestibular function. Serum concentrations of gentamicin should be monitored to avoid toxic levels.
In neonates, infants and children, the dosage and frequency of administration requirements are variable.
Myasthenia gravis. In myasthenia gravis and parkinsonism, gentamicin may aggravate muscle weakness because of its curare-effect on neuromuscular function.

WARNING FOR SODIUM METABISULPHITE: This preparation contains sodium metabisulphite, a sulphite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulphite sensitivity in the general population is unknown and probably low. Sulphite sensitivity is seen more frequently in asthmatic than non-asthmatic people.

INTERACTION WITH OTHER MEDICAMENTS:
Penicillins. Gentamicin is inactivated by solutions containing penicillins. This inactivation is brought about by the opening of the beta-lactam ring and combination of the penicillin with an amino group of gentamicin to form a biological inactive amide. For this reason, gentamicin and penicillins should not be administered simultaneously nor should they be combined in the intravenous fluid. The inactivation of gentamicin by penicillins may occur in vivo, especially in patients with renal failure. These patients maintain a higher level of the penicillin for a longer period of time compared to patients with normal renal function. Therefore, when gentamicin and penicillins are used together in patients with renal failure, the administration should be staggered so that several hours separate each infusion.

Although the inactivation of gentamicin and penicillin proceeds on an equimolar basis, in practice the gentamicin is present in such as excess that only the decline in activity of gentamicin is of concern. A combination of penicillin and gentamicin is often used in the treatment of enterococcal endocarditis.

Diuretics. Potent diuretics such as ethacrynic acid or frusemide may potentiate the ototoxic effects of gentamicin.

Neuromuscular blocking agents: Respiratory paralysis and prolongation of neuromuscular blockade may occur if a neuromuscular blocking agent such as succinylcholine or tubocurarine is administered to a patient receiving gentamicin.

Vitamin K: Gentamicin may inhibit the action of intravenous vitamin K upon the synthesis of clotting factors.

Cephalosporins: Increased nephrotoxicity of gentamicin has been observed during concurrent administration of cephalosporins.

Other drugs: Since ototoxic or nephrotoxic effects may be additive, the concurrent or sequential use of gentamicin and other drugs with similar toxic potentials should be avoided, if possible.

USE IN PREGNANCY & LACTATION:
Use in Pregnancy: Gentamicin and other aminoglycosides cross the placenta. There is evidence of selective uptake of gentamicin by the foetal kidney resulting in damage (probably reversible) to immature nephrons. Eighth cranial nerve damage has also been reported following in-utero exposure to some of the aminoglycosides. Because of their chemical similarity, aminoglycosides must be considered potentially nephrotoxic and ototoxic to the foetus. It should also be noted that therapeutic blood levels in the mother do not equate with safety for the foetus. It is advisable not to use gentamicin during pregnancy unless deemed essential by the physician.

Use in Lactation:
Since small amounts of Gentamicin have been detected in breast milk and because of the potential risk to newborns, it is recommended that breast feeding be discontinued during therapy unless the expected benefits outweigh any potential risk.

SIDE EFFECTS:
If serum levels of gentamicin are maintained within the therapeutic range, adverse reactions are not common. However, as with other aminoglycosides, ototoxicity and nephrotoxicity can occur, the incidence of either is approximately 2%.

Gentamicin nephrotoxicity is usually mild and reversible. However, severe renal impairment may occur and dialysis may be necessary. Nephrotoxicity may be increased by the concurrent administration of other drugs (see Interactions).
Infrequent adverse reactions reported include purpura, increased serum transaminases, increased serum bilirubin, hypersensitivity reactions (rash, urticaria), nausea, vomiting, headache, leucopenia, granulocytopenia, transient agranulocytosis, increased and decreased reticulocyte counts and thrombocytopenia.

SYMPTOMS AND TREATMENT OF OVERDOSE:
Overdosage: Patients on prolonged treatment with gentamicin or treated with larger dosage than recommended often demonstrated symptoms of nephrotoxicity and neurotoxicity like raised serum creatinine or oliguria and dizziness, vertigo, ataxia including tinnitus.

Treatment: Peritoneal dialysis or haemodialysis will aid in the removal of Gentamicin from the blood. This is particularly important in patients with renal malfunction.

INCOMPATIBILITIES:
When gentamicin is used in combination with any other drug, mixing the drugs before administration should be avoided at all costs.

STORAGE CONDITIONS:
Store below 30°C. KEEP OUT OF REACH OF CHILDREN. *JAUHKAN DARIPADA KANAK-KANAK.*

SHELF LIFE:
Please refer to outer package.

PACK SIZE:
Pack in 10's, 30's, 50's and 100's in 2 ml ampoules

PRODUCT REGISTRATION HOLDER & MANUFACTURER:
DUOPHARMA (M) SDN BHD
Lot 2599, Jalan Seruling 59 Kawasan 3,
Taman Klang Jaya, 41200 Klang, Selangor, MALAYSIA.

[Revision Date: 28.05.2019]