PRODUCT MONOGRAPH

PrGENTAMICIN(E)

GENTAMICIN (AS SULFATE) IN 0.9% SODIUM CHLORIDE INJECTION
(1.0 mg/mL and 1.6 mg/mL)

ANTIBIOTIC

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GENTAMICIN(E)
Gentamicin (as sulfate) in 0.9% sodium chloride injection

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Intravenous	Solution for Intravenous Injection/ • 1.0 mg/mL Gentamicin (as sulfate) in 0.9% sodium chloride injection • 1.6 mg/mL Gentamicin (as sulfate) in 0.9% sodium chloride injection	None are clinically relevant *For a complete listing see Dosage Forms, Composition and Packaging section.*

INDICATIONS AND CLINICAL USE

Gentamicin(e) (Gentamicin (as sulfate) in 0.9% sodium chloride injection) is indicated in the treatment of patients with the following serious infections:

> bacteremia/septicemia, respiratory tract infections, urinary tract infections, bone, skin and soft tissue infections (including burns), and intra-abdominal infections, including peritonitis.

Gentamicin(e) is clinically effective in serious infections caused by susceptible strains of the following bacteria: *Pseudomonas aeruginosa*, *Proteus* species (indole negative and indole positive), *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter aerogenes*, *Serratia marcescens* and *Staphylococcus* species (methicillin-susceptible strains only)*.

*Gentamicin(e) may be considered for the treatment of *Staphylococcus* infections when other less potentially toxic drugs are contraindicated and bacterial susceptibility tests and clinical judgment indicates its use.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of gentamicin and other antibacterial drugs, Gentamicin(e) should be used only to treat infections that are proven or suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Geriatrics (≥ 65 years of age):

Due to age related decline in glomerular filtration rate, dosage adjustment may be required for elderly patients. Gentamicin(e) should be used with caution in persons with preexisting vestibular or cochlear dysfunction (**See WARNINGS AND PRECAUTIONS; DOSAGE AND ADMINISTRATION, Geriatrics [≥ 65 years of age])**.

Pediatrics (≤ 12 years):

Dosage adjustment is required in children (including infants, neonates and pre-term/full-term newborns). Gentamicin(e) may not be appropriate for use in children therefore other higher concentration gentamicin products (such as Gentamicin for injection 10 mg/mL or 40 mg/mL injection vial may be used for gentamicin dosing in this population. Gentamicin for injection should be administered with caution and only when no other treatment option is available (**See WARNINGS AND PRECAUTIONS, Special Populations, Pediatrics; DOSAGE AND ADMINISTRATION, Pediatrics [≤12 years of age]; PART II: SCIENTIFIC INFORMATION, DETAILED PHARMACOLOGY**).

CONTRAINDICATIONS

- Gentamicin(e) (Gentamicin (as sulfate) in 0.9% sodium chloride injection) is contraindicated in patients with a history of hypersensitivity or serious toxic reactions to other aminoglycosides because of known cross-sensitivity of patients to drugs in this class.

- Gentamicin(e) is contraindicated in patients with known hypersensitivity to gentamicin, or to any of the ingredients in the formulation or components of the container (See **DOSAGE, FORMS, COMPOSITION AND PACKAGING)**.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

- Aminoglycosides including Gentamicin(e) (Gentamicin (as sulfate) in 0.9% sodium chloride injection) are potentially nephrotoxic therefore renal function should be assessed prior to and regularly during treatment. Adequate therapeutic peak and trough serum concentrations of gentamicin should be maintained and higher potentially toxic levels should be avoided during therapy. Dosage adjustment is required in children and in patients with renal dysfunction (See **WARNINGS AND PRECAUTIONS, Renal, Special Populations, Geriatric (≥ 65 years of age)** and **Pediatric (≤ 12 years of age), Monitoring and Laboratory Tests, Renal; ADVERSE REACTIONS; DOSAGE AND ADMINISTRATION; ACTION AND CLINICAL PHARMACOLOGY**).
- Aminoglycosides including Gentamicin(e) are potentially ototoxic therefore, patients receiving Gentamicin(e) should be closely monitored for eighth cranial nerve toxicity. The ototoxicity is usually associated with high serum levels and renal insufficiency. (See **WARNINGS AND PRECAUTIONS, Ear/Nose/ Throat, Ototoxicity, Monitoring and Laboratory Tests, Audiometric Testing; ADVERSE REACTIONS**).
- The prior/concurrent and/or sequential system or topical use of other potentially nephrotoxic/neurotoxic drugs should be avoided with Gentamicin(e) treatment (See **WARNINGS AND PRECAUTIONS, Ear/Nose/Throat, Ototoxicity, Renal; DRUG INTERACTIONS, Drug-Drug Interactions**).

General

Gentamicin(e) (Gentamicin (as sulfate) in 0.9% sodium chloride injection) is a ready to use isotonic solution and should be used for intravenous infusion only. It must not be administered by any other route.

Not all strains of these bacteria are susceptible to gentamicin. In serious or life-threatening infections known or suspected to be caused by these organisms, initial empiric combination therapy should be considered until results of susceptibility tests become available.

To reduce the risk of Gentamicin(e) toxicity, careful attention must be given to appropriate dosage. Caution should be exercised when Gentamicin(e) is prescribed to patients with known or suspected renal, auditory, vestibular, or neuromuscular dysfunction.

Periodic electrolyte determinations should be performed in patients with low potassium reserves, and the possibility of hypokalemia should be kept in mind with patients who have potentially low potassium reserves and who are receiving cytotoxic therapy or diuretics.

This product contains gentamicin sulfate in a 0.9% sodium chloride solution (9 mg/mL). Solutions containing sodium ions should be used with great care, if at all, in patients with

congestive heart failure, severe renal insufficiency, and in clinical states in which there exists edema with sodium retention.

Patients should be well hydrated during treatment.

Treatment with Gentamicin(e) may result in overgrowth of non susceptible or resistant organisms. If treatment failure occurs, prescribe appropriate therapy.

Cardiovascular

QT Interval Prolongation

The effect of Gentamicin for injection on prolonged cardiac repolarisation, QT interval and increased risk of developing cardiac arrhythmia and torsades de pointes is not known.

Ear/Nose/Throat

Ototoxicity

In patients receiving Gentamicin(e) therapy, the function of the eighth cranial nerve (auditory and vestibular branches) should be carefully monitored as these changes may not be manifested until after completion of therapy, and are usually irreversible. Ototoxicity manifested by loss of high frequency auditory perception usually precedes clinically detectable hearing loss, and may be detected by audiological assessment. Ototoxicity (tinnitus, roaring in the ears), including serious irreversible complete hearing loss, usually bilateral; and vestibular toxicity (nausea, vomiting, dizziness, eighth nerve disorder, nystagmus, vertigo, ataxia) have been reported, primarily in patients with renal dysfunction, or in patients receiving high doses and/or prolonged therapy. To reduce the risk of ototoxicity, if a patient reports tinnitus or hearing loss during therapy, the physician should refer them for audiological assessment. If ototoxicity occurs in a patient receiving Gentamicin(e), stop the drug and substitute treatment with an alternative non-ototoxic agent. If discontinuation is not possible, then the dosage should be adjusted so that trough serum concentration falls below 2 mcg/mL. Additionally, the patient must be well-hydrated to reduce the risk of ototoxicity. (See **Monitoring and Laboratory Tests; Audiological Assessment**). In high risk patients, it may be necessary to consider audiological assessment before initiating the therapy.

Gentamicin(e) should be used with caution with the understanding that toxic effects may be cumulative in patients with sensorineural hearing deficit, elderly, visual impairment patients, liver disease, bacteremia, high temperature, and dehydration. In addition, some individuals have a genetic predisposition to aminoglycoside-induced ototoxicity.

The prior use of other aminoglycosides and concomitant administration of diuretics, have been associated with 8th cranial nerve dysfunction and therefore use of Gentamicin(e) in patients receiving sequential/concomitant treatment with these agents should be avoided. (See **ADVERSE REACTIONS; DRUG INTERACTION, Drug-Drug Interactions; DOSAGE AND ADMINISTRATION**).

Gastrointestinal

Clostridium difficile-associated disease (CDAD) has been reported with use of many antibacterial agents, including Gentamicin for injection. CDAD may range in severity from mild diarrhea to fatal colitis. It is important to consider this diagnosis in patients who present with diarrhea or symptoms of colitis, pseudomembranous colitis, toxic megacolon, or perforation of the colon subsequent to the administration of any antibacterial agent. CDAD has been reported to occur over 2 months after the administration of antibacterial agents.

Treatment with antibacterial agents may alter the normal flora of the colon and may permit overgrowth of *Clostridium difficile*. *C. difficile* produces toxins A and B, which contribute to the development of CDAD. CDAD may cause significant morbidity and mortality. CDAD can be refractory to antimicrobial therapy.

If the diagnosis of CDAD is suspected or confirmed, appropriate therapeutic measures should be initiated. Mild cases of CDAD usually respond to discontinuation of antibacterial agents not directed against *Clostridium difficile*. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial agent clinically effective against *Clostridium difficile*. Surgical evaluation should be instituted as clinically indicated since surgical intervention may be required in certain severe cases (see **ADVERSE REACTIONS**).

Immune

Hypersensitivity

Anaphylaxis (including fatality), hypotensive shock, angioedema, laryngeal edema and bronchial spasm have been reported following administration of Gentamicin for injection to patients. Gentamicin(e) is contraindicated in patients with a known history of hypersensitivity (allergic) reaction to any aminoglycoside. Gentamicin(e) should be discontinued if a hypersensitivity reaction to Gentamicin(e) occurs. Serious acute hypersensitivity (anaphylaxis or air way constriction) requires emergency treatment as clinically indicated (See **ADVERSE REACTIONS**).

Neurologic

Neurological adverse reactions (vertigo, gait ataxia, dizziness, numbness, skin tingling, muscle twitching, convulsions, seizure) including serious adverse drug reactions, (e.g., peripheral motor and/or sensory polyneuropathy, encephalopathy) have been reported following administration of Gentamicin for injection to patients. If a neurotoxic reaction occurs, discontinue use of Gentamicin(e) immediately.

During or following Gentamicin for injection therapy, paresthesia, tetany, positive Chvostek and Trousseau signs and mental confusion have been reported in patients with hypomagnesemia, hypocalcemia and hypokalemia. When this has occurred in infants, tetany and muscle weakness

has been reported. Electrolytes should be monitored in patients receiving Gentamicin(e). If paresthesia and positive Chvostek and Trousseau signs do occur, corrective electrolyte therapy should be initiated both in adults and infant patients (See **Monitoring and Laboratory Tests, Electrolytes; ADVERSE REACTIONS)**.

Neuromuscular Blocking Action

Caution should be exercised when Gentamicin(e) is prescribed to patients with known or suspected neuromuscular disorders such as myasthenia gravis or Parkinson's disease. If signs of respiratory paralysis do occur, discontinue administration of Gentamicin(e) immediately. Provide supportive care as clinically indicated.

Aminoglycosides, including Gentamicin for injection, may aggravate muscle weakness because of their potential curare-like effects on the neuromuscular junction. Neuromuscular effects occur more commonly after application to serosal surfaces (e.g., after intrapleural injection or peritoneal instillation). Neuromuscular blockade (flaccid paralysis, dilated pupils and weakness of the respiratory musculature), is generally dose dependent and self-limiting. Neuromuscular blockade and myasthenia gravis-like syndrome have been reported with Gentamicin for injection therapy. Recovery from gentamicin-induced neuromuscular blockade may be slow, and prolonged blockade has been described with chronic administration. Neuromuscular blockage and respiratory paralysis have been reported in cats receiving high doses (40 mg/kg) of gentamicin sulfate (See **ADVERSE REACTIONS, Post-Market Adverse Drug Reactions**).

Rapid injection of aminoglycoside antibiotics including gentamicin can cause neuromuscular blockade therefore, infuse Gentamicin(e) over at least 30 minutes.

Avoid concurrent use of neuromuscular blocking curariform muscle relaxants and other potential neurotoxic agents which may precipitate respiratory depression. The possibility of neuromuscular blockade and respiratory paralysis should be considered if Gentamicin(e) is administered to patients receiving muscle relaxants or paralytic agents, which are commonly used in patients undergoing anesthesia. Patients receiving massive transfusions of citrate anticoagulated blood may also experience weakness caused by a decreased free calcium concentration. In both adults and infants, if neuromuscular blockade occurs, calcium salts or neostigmine should be administered to counteract gentamicin associated neuromuscular blockade. (See **ADVERSE REACTIONS, Post-Market Adverse Drug Reactions; DRUG INTERACTIONS**, **Drug-Drug Interactions).**

Ophthalmologic

Serious adverse reactions (reduced visual acuity, oscillopsia and partial loss of eyesight) have been reported with Gentamicin for injection. If signs of visual disorders appear, discontinue Gentamicin(e) treatment or adjust dosage (See **ADVERSE REACTIONS**).

Renal

Acute renal failure, tubular necrosis, toxic nephropathy and interstitial nephritis with hospitalization and dialysis have been reported with Gentamicin for injection. Acute renal failure including fatality has been reported in a patient receiving inadvertent gentamicin for injection outside the recommended dose. Development of toxic nephropathy also has been described even with a single aminoglycoside dose. Acute renal injury is usually reversible following discontinuation of the aminoglycoside, but can also lead to severe uremia and possibly death. On rare occasions, changes in renal function may not manifest until soon after completion of therapy. Assess baseline renal function and monitor laboratory tests of urine and renal function regularly because patients receiving high dose or treatment for longer duration have demonstrated increased risk of nephrotoxicity (See **ADVERSE REACTIONS, Post Market Adverse Drug Reactions**). If nephrotoxicity occurs in a patient receiving Gentamicin(e), stop the drug and substitute treatment with an alternative non-nephrotoxic agent. If discontinuation is not possible, then adjust dosage so that trough serum concentration falls below 2 mcg/mL.

Caution should be exercised while prescribing Gentamicin(e) to patients with known or suspected renal dysfunction, or if patient develop signs of nephrotoxicity, in patients with higher serum concentrations, dehydration/hypovolemia/shock and liver disease and also children (including neonates, pre-term/full-term newborns), elderly and females. Adjust Gentamicin(e) dosage to ensure therapeutically adequate, but not potentially toxic excessive drug levels in blood. Avoid peak serum concentrations above 12 ug/mL and trough concentrations above 2 mcg/mL during therapy.

Avoid prior use of other potentially nephrotoxic agents and concomitant use of Gentamicin(e) with diuretics, antimicrobials and antineoplastic agents. A proximal renal tubular dysfunction, causing a Fanconi-like syndrome (glycosuria, aminoaciduria, metabolic acidosis and electrolyte wasting) and renal failure has been reported in some adults and infants being given aminoglycosides, including Gentamicin for injection. Electrolyte disturbance and Fanconi-like syndrome may develop even in the absence of an aminoglycoside-induced reduction in creatinine clearance. When this occurs, administer corrective electrolyte therapy as clinically indicated (See **DRUG INTERACTIONS, Drug-Drug Interactions**; **ADVERSE REACTIONS, Post-Market Adverse Drug Reactions; DOSAGE AND ADMINISTRATION, Dosing Considerations**).

Susceptibility/Resistance

Development of Drug Resistant Bacteria

Prescribing Gentamicin(e) in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and risks the development of drug-resistant bacteria.

Special Populations

Pregnant Women

Gentamicin(e) should not be used in pregnant women unless the potential benefits outweigh the potential risk to the fetus. The use of Gentamicin for injection in pregnant women has not been

evaluated. Aminoglycosides, including gentamicin, crosses the placenta and may be found in fetal serum and amniotic fluid and there have been several reports of total irreversible bilateral congenital deafness in children whose mothers received streptomycin during pregnancy. Severe muscle weakness in the newborn has been reported with Gentamicin for injection.

Nursing Women

Due to the potential for serious adverse drug reactions from Gentamicin(e) in infants being nursed by mothers, a decision should be made to either discontinue nursing or discontinue the administration of Gentamicin(e), taking into account the importance of Gentamicin(e) treatment to the mother. The safety and efficacy of Gentamicin for injection in nursing women have not been established. Gentamicin is excreted in human breast milk, and nursing infants may have detectable gentamicin levels.

Geriatrics (≥ 65 years of age):

Due to the age-related decline in glomerular filtration rate, elderly are likely to have renal dysfunction and elimination of gentamicin may be prolonged in elderly which may not be evident in the results of routine screening tests such as BUN or serum creatinine. A creatinine clearance determination may be more useful in these patients. Renal function should be assessed prior to and regularly during Gentamicin(e) therapy. Caution should be exercised when prescribing Gentamicin(e) to patients with known or suspected renal, auditory, vestibular or neuromuscular dysfunction. Gentamicin(e) should be used with caution in persons with preexisting vestibular or cochlear dysfunction. (See **DOSAGE AND ADMINISTRATION, Geriatrics [≥ 65 years of age]; ACTION AND CLINICAL PHARMACOLOGY**).

Pediatrics (≤ 12 years)

Higher serum levels and prolonged half-life has been reported in children (including infants, neonates, and pre-term/full-term newborns). Dosage adjustments are required in children. Gentamicin(e) may not be appropriate for use in children (including newborns, neonates, and infants). Use other higher concentration gentamicin injection products (e.g., Gentamicin for injection 10 mg/mL or 40 mg/mL) with caution and assess serum concentration and renal function regularly during treatment.

During and following Gentamicin for injection therapy, paresthesia, tetany, positive Chvostek and Trousseau signs and mental confusion have been described in patients with hypomagnesemia, hypocalcemia and hypokalemia. When this occurred in infants, tetany and muscle weakness have been described. A Fanconi-like syndrome, with aminoaciduria and metabolic acidosis has been reported in some adults and infants being given Gentamicin for injection. Appropriate corrective electrolyte therapy in both adults and infants is required (See **DOSAGE AND ADMINISTRATION, Pediatrics [≤ 12 years of age]**; **ACTION AND CLINICAL PHARMACOLOGY, Pharmacokinetics**).

Monitoring and Laboratory Tests

Gentamicin for injection has demonstrated the following laboratory test abnormalities. While clinical laboratory test abnormalities may be isolated findings, they may be associated with clinically related signs and symptoms (See **ADVERSE REACTIONS**). For example, tetany and muscle weakness may be associated with hypomagnesemia, hypocalcemia, and hypokalemia. The following tests should be conducted at the discretion of the treating physician.

Renal

Assess laboratory tests of urine and renal function prior to and regularly during treatment.

Serum Drug Levels

Monitor peak and trough gentamicin serum concentrations during Gentamicin(e) therapy to assure adequate serum levels and to avoid potentially toxic levels. Avoid peak serum concentrations above 12 ug/mL and trough concentrations above 2 ug/mL. Discontinue Gentamicin(e) if concentrations exceed these levels. If discontinuation is not possible adjust dosage so that trough serum concentration falls below 2 mcg/mL.

Electrolytes

Monitor electrolytes in patients receiving Gentamicin(e).

Audiological Assessment

For patients with known or suspected auditory or vestibular dysfunction and those who are at increased risk for auditory dysfunction, it may be necessary to consider audiological assessment before initiating Gentamicin(e) therapy. If a patient reports tinnitus or hearing loss during Gentamicin(e) therapy, the physician should refer them for audiological assessment.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

The most frequently reported serious adverse drug reactions associated with Gentamicin(e) include nephrotoxicity (including acute renal failure, renal tubular necrosis, toxic nephropathy) and ototoxicity (including irreversible hearing loss).

Clinical Trial Adverse Drug Reactions

Data from clinical trials are not available. Drug-related adverse reactions are derived from adverse drug reporting from retrospective studies and therefore frequency of common and uncommon drug-related adverse reactions that could occur with gentamicin cannot be determined.

Blood and lymphatic system disorders

Anemia, leukopenia, granulocytopenia, transient agranulocytosis, eosinophilia, increased and decreased reticulocyte counts and thrombocytopenia.

Ear and labyrinth disorders

Irreversible hearing loss, tinnitus, roaring in the ears, loss of high frequency hearing perception, eighth nerve disorder, dizziness, vertigo, ataxia, nystagmus.

Eye disorders

Visual disturbances.

Gastrointestinal disorders

Anorexia, nausea, increased salivation, vomiting, decreased appetite, weight loss, stomatitis, gastrointestinal hemorrhage.

General disorders and administration site conditions

Local irritations, generalized burning, phlebitis, alopecia, pain at the injection site, subcutaneous atrophy or fat necrosis suggesting local irritation, febrile response, infection at the site of injection, venous thrombosis or phlebitis extending from the site of injection, extravasation.

Hepatobiliary disorders

Splenomegaly, transient hepatomegaly.

Immune system disorders

Stevens-Johnson syndrome, laryngeal edema, bronchial spasm, anaphylactoid reactions, toxic epidermal necrolysis, erythema multiforme, purpura, splenomegaly, transient hepatomegaly, numbness, skin tingling, pyrexia, rash, urticaria, pruritus, itching.

Investigations

Increased levels of serum transaminase (SGOT, SGPT), serum LDH, bilirubin, decreased haemoglobin, and hematocrit.

Metabolism and nutrition disorders

Hypervolemia.

Musculoskeletal and connective tissue disorders

Joint pain.

Nervous system disorders

Fifth nerve paresthesia, dizziness, vertigo, ataxia, nystagmus, numbness, tingling, muscle twitching, tremor, peripheral neuropathy, encephalopathy, convulsions, a myasthenia gravis-like syndrome, seizures, pseudotumor cerebri, headache, lethargy, confusion, depression.

Psychiatric disorders

Acute organic brain syndrome.

Renal and urinary disorders

Renal failure, rising BUN, increased blood creatinine, oliguria, proteinuria, nonoliguric azotemia, casts, cells, aminoaciduria, metabolic acidosis, electrolyte wasting, hyponatremia, hypokalemia, hypocalcemia, hypomagnesemia.

Respiratory, thoracic and mediastinal disorders

Respiratory depression, respiratory distress, pulmonary fibrosis.

Vascular disorders

Tachycardia, hypotension, hypertension.

Abnormal Hematologic and Clinical Chemistry Findings

Test	Effect	Clinical Comment
Serum creatinine	Increased	An increase in BUN and serum creatinine over baseline is an indication of nephrotoxicity. Acute kidney injury (AKI) for patients with normal renal function is defined as an absolute increase in the serum level of creatinine of ≥0.3 mg/dL (26.4 mM) from baseline; or a percentage increase in the serum level of creatinine of ≥50%. For patients with chronic kidney disease, AKI is defined as an increase in serum creatinine of ≥50%. In patients with initially normal renal function, an increase in BUN of 10 mg/dL, and in those patients with chronic kidney disease, an increase in BUN of ≥50% is considered a marker of AKI. If nephrotoxicity occurs during treatment with Gentamicin(e) (Gentamicin (as sulfate) in 0.9% sodium chloride injection), discontinue Gentamicin(e) treatment and substitute treatment with an alternative non-nephrotoxic agent. If discontinuation is not possible, then adjust dosage so that trough serum does not rise above 2 mcg/mL and monitor renal function.
BUN	Increased	

Post-Market Adverse Drug Reactions

Ear and labyrinth disorders

Deafness, ototoxicity, hearing impaired, vestibular disorders (ataxia, balance disorder).

Eye disorders

Oscillopsia, visual impairment, visual acuity reduced, vision blurred.

General disorders and administration conditions

Infusion reactions: tremor, chills.

Immune system disorders

Hypersensitivity reactions, including angioedema, dyspnea, anaphylaxis (including fatality*), serum sickness*, hypotensive shock.

Musculoskeletal, connective tissue and bone disorders

Muscle weakness, muscle spasm.

Nervous system disorders

Neuromuscular blockade.

Renal and urinary disorders

Toxic nephropathy, acute tubular necrosis, interstitial nephritis; Fanconi-like syndrome; glycosuria; electrolyte losses leading to hypokalemia, hypocalcemia, hypomagnesemia, hypophosphatemia; metabolic alkalosis.

*Causal attribution of the reaction to Gentamicin(e) is uncertain.

DRUG INTERACTIONS

Serious Drug Interactions

Avoid concurrent and/or sequential systemic or topical use of Gentamicin(e) (Gentamicin (as sulfate) in 0.9% sodium chloride injection) with drugs with neurotoxic, nephrotoxic or ototoxic potential (See **Drug-Drug Interactions**).

Avoid concurrent use of Gentamicin(e) with other drugs with potential of neuromuscular blockade (See **Drug-Drug Interactions**).

Overview

Gentamicin(e) (Gentamicin (as sulfate) in 0.9% sodium chloride injection) should not be administered concurrently/subsequently with the following drugs with nephrotoxic, ototoxic or neurotoxic potential. Neuromuscular blockade and respiratory paralysis have been reported in

cats receiving high doses (40 mg/kg) of gentamicin. The possibility of this phenomenon in man should be considered if aminoglycosides including Gentamicin(e) are administered by any route to patients receiving anesthetics, or to patients receiving neuromuscular blocking agents, or in patients receiving massive transfusions of citrate-anticoagulated blood.

Drug-Drug Interactions

Name	Ref	Effect	Clinical Comment
Antimicrobials Aminoglycosides (e.g., Amikacin, Kanamycin, Parmomycin, Streptomycin, Tobramycin) Amphotericin B Cephalosporins (e.g., cephaloridine, cephalothin) Clindamycin Polymyxin B, Polymyxin E (colistin) Vancomycin	L	Increased risk of nephrotoxicity and/or neuro-/ototoxicity.	Avoid concomitant and/or sequential use. Monitor laboratory tests of urine and renal function. If nephrotoxicity occurs, stop the drug and substitute treatment with an alternative non-nephrotoxic agent. If discontinuation is not possible, then adjust dosage so that trough serum concentration falls below 2 mcg/mL. Conduct/refer for audiological assessment.
Carbenicillin, Piperacillin	L	A reduction in gentamicin serum half-life has been reported in patients with severe renal impairment receiving carbenicillin and piperacillin concomitantly with Gentamicin for injection.	Avoid concomitant and/or sequential use.
Cholinergic agents (e.g., neostigmine, pyridostigmine)	L	Gentamicin antagonizes the effect of neostigmine and pyridostigmine.	Avoid concomitant use.
Loop Diuretics (e.g., Bumetanide, Ethacrynic acid, Furosemide, Piretanide)	L	Increases the risk for ototoxic and nephrotoxic effects of aminoglycosides, including gentamicin.	Concomitant use of Gentamicin(e) with potent loop diuretics should be avoided. Monitor laboratory tests of urine and renal function. If renal dysfunction occurs, adjust dosage of Gentamicin(e). Monitor for signs of ototoxicity.
Neuromuscular blocking agents and opioid-analgesics (e.g., Atracurium, Alfentanyl, Decamethonium, Fentanyl, Succinylcholine, Sulfentanil, Trimethaphan, Tubocurarine, Vecuronium)	L	Increased risk of neuromuscular blockade.	Avoid concomitant use. Monitor respiratory function. Provide supportive care if an interaction occurs.

Name	Ref	Effect	Clinical Comment
Anti-neoplastic Agents (e.g., Carboplatin, Cisplatin)	L	Increased risk of nephrotoxicity and/or neurotoxicity	Avoid concomitant and/or sequential use. Monitor laboratory tests of urine and renal function. If nephrotoxicity occurs, stop the drug and substitute treatment with an alternative non-nephrotoxic agent. If discontinuation is not possible, then adjust dosage so that trough serum concentration falls below 2 mcg/mL.
Immunosuppresive Agents (e.g., Cyclosporine, Tacrolimus)	L	Increased risk of nephrotoxicity and/or neurotoxicity	Avoid concomitant and/or sequential use. Monitor laboratory tests of urine and renal function. If nephrotoxicity occurs, stop the drug and substitute treatment with an alternative non-nephrotoxic agent. If discontinuation is not possible, then adjust dosage so that trough serum concentration falls below 2 mcg/mL.
Zalcitabine	L	Increased risk of nephrotoxicity and/or neurotoxicity	Avoid concomitant and/or sequential use. Monitor laboratory tests of urine and renal function. If nephrotoxicity occurs, stop the drug and substitute treatment with an alternative non-nephrotoxic agent. If discontinuation is not possible, then adjust dosage so that trough serum concentration falls below 2 mcg/mL.
Mannitol	L	Increased risk of nephrotoxicity and/or neurotoxicity	Avoid concomitant and/or sequential use. Monitor laboratory tests of urine and renal function. If nephrotoxicity occurs, stop the drug and substitute treatment with an alternative non-nephrotoxic agent. If discontinuation is not possible, then adjust dosage so that trough serum concentration falls below 2 mcg/mL.
Agalsidase α and β	L	Inhibition of intracellular α-galactosidase	Avoid concomitant use.
Indomethacin	L	Increased gentamicin serum concentrations in infants	Avoid concomitant use. Monitor laboratory tests of urine and renal function. If nephrotoxicity occurs, stop the drug and substitute treatment with an alternative non-nephrotoxic agent. If discontinuation is not possible, then adjust dosage so that trough serum concentration falls below 2 mcg/mL.
Magnesium	L	Increased neuromuscular blockade	Avoid concomitant use. Concomitant use may potentiate muscle relaxant effect.

L = Literature

Drug-Vaccine Interactions

Gentamicin(e) may interfere with the immunological response of live typhoid vaccine and reduce effectiveness of BCG (Bacillus of Calmette and Guerin) vaccine and should not be concomitantly administered.

Gentamicin(e) may have an additive risk of neuromuscular blockade if administered concomitantly with Botulism toxin. Avoid concurrent use. If given together, monitor respiratory function.

DOSAGE AND ADMINISTRATION

Dosing Considerations

Gentamicin(e) (Gentamicin (as sulfate) in 0.9% sodium chloride injection) is a ready to use isotonic gentamicin sulphate solution for intravenous infusion only. Do not use Gentamicin(e) for intramuscular administration.

Gentamicin(e) container system may be inappropriate for use in children (including infants, neonates; and pre-term/full-term newborns). Gentamicin for injection (10 mg/mL or 40 mg/mL injection vial) may be more appropriate for gentamicin dosing in this population. The pharmacokinetics of gentamicin differs in neonates, and pre-term or full-term newborns compared with older children in that renal clearance of the drug is prolonged in neonates, and pre-term or full-term newborns. Specialized references and other gentamicin products with higher concentration (i.e., Gentamicin for injection 10 mg/mL or 40 mg/mL) may be considered for use in children (See **ACTION AND CLINICAL PHARMACOLOGY, Pharmacokinetics**).

Gentamicin(e) should be infused over a period of half hour to 2 hours to minimize the possibility of neuromuscular blockade.

Individualized dose of Gentamicin(e) should be administered based upon severity of infection, patient's weight, age and renal function. Patient's pretreatment body weight should be obtained for calculation of correct dosage. In obese patients the initial dose based on patient's adjusted body weight should be calculated.

Give special consideration in elderly, renal dysfunction, and in conditions which may pre-dispose the patient to gentamicin toxicity, (i.e., diabetes, auditory vestibular dysfunctions, otitis media, a history of otitis media, previous use of ototoxic drugs) and in patients with genetically determined high sensitivity to aminoglycoside induced ototoxicity.

Gentamicin is eliminated primarily by the kidneys and therefore assess renal function prior to and regularly during treatment in all patients. Serum creatinine concentration has a high correlation with the serum half-life of gentamicin therefore consider using this laboratory guidance for adjustment of the interval between doses.

Adjust dosage in patients with renal dysfunction to assure therapeutically adequate, but not excessive potentially toxic gentamicin is used. Assess gentamicin therapeutic levels at steady state and weekly thereafter.

For measurement of adequate therapeutic levels which are critical, while at the same time avoiding potentially toxic concentrations, assess a post-dose (peak) and pre-dose (trough) serum concentration of gentamicin. When monitoring peak concentration (30 to 60 minutes following the cessation of infusion), adjust dosage so that levels above 12 mcg/mL are avoided. When monitoring trough concentrations (less than 30 minutes prior to the infusion of next dose), adjust dosage so that levels above 2 mcg/mL are avoided. Limit Gentamicin(e) treatment to the shortest duration consistent with the treatment goal and acceptable risks for the individual patient.

Recommended Dose and Dosage Adjustment

Urinary Tract Infections

Gentamicin is highly concentrated in urine and renal tissue. The recommended dosage of Gentamicin(e) in patients with chronic or recurrent lower urinary tract infection and normal renal function is either 160 mg once daily or 80 mg twice daily for 7 to 10 days. For adults weighing less than 60 kg, the single daily dose of 3.0 mg/kg of body weight is recommended.

Patients with upper urinary tract infections, such as pyelonephritis, and more particularly if there are signs of systemic involvement, should be treated according to one of the dosage schedules for systemic infections.

Since gentamicin activity is increased at pH 7.5, it is advantageous to alkalinize the urine of patients treated for urinary tract infections.

Systemic Infections

The recommended dosage of Gentamicin(e) in patients with serious infections and normal renal function is 3 mg/kg/day administered in three (3) equally divided doses every eight hours (Table 1).

For patients with life-threatening infections, dosages up to 5 mg/kg/day may be administered in three (q8h) or four (q6h) equally divided doses. The dosage should be reduced to 3 mg/kg/day as soon as clinically indicated (Table 1).

In patients with extensive burns, altered pharmacokinetics may result in reduced serum concentrations of gentamicin therefore in such patients adjust Gentamicin(e) dosage based upon serum concentration.

Table 1. Dosage schedule guide for adults with normal renal function (dose at eight-hour intervals)			
Patient's weight*		**Dosage for serious infections**	**Dosage for life-threatening infections**
kg	**(lb)**	**Total average daily dosage (3 mg/kg/day) Usual dose for serious infections q8h dose: 1 mg/kg**	**Total average daily dosage (5 mg/kg/day) (reduce as soon as clinically indicated) q8h dose: 1.7 mg/kg†**
		mg/dose q8h	**mg/dose q8h**
40	(88)	40	66
45	(99)	45	75
50	(110)	50	83
55	(121)	55	91
60	(132)	60	100
65	(143)	65	108
70	(154)	70	116
75	(165)	75	125
80	(176)	80	133
85	(187)	85	141
90	(198)	90	150
95	(209)	95	158
100	(220)	100	166

* The dosage of Gentamicin(e) in obese patients should be based on a patient's adjusted body weight
† For every q6h schedules, dosage should be recalculated.

The usual duration of treatment is 7 to 10 days. In cases where longer than 10 days of therapy is required, assess renal, auditory and vestibular functions on day 7 and weekly thereafter since toxicity is more apt to occur with extended treatment. Reduce dosage if clinically indicated.

Dosing in Special Populations

Pediatrics (≤ 12 years of age)

Gentamicin(e) container system may be inappropriate for use in children (including infants, neonates; and pre-term/full-term newborns) and other higher concentration gentamicin products (such as Gentamicin for injection 10 mg/mL and 40 mg/mL injection vials) may be used to reduce infusion volume in children. These dosage recommendations are included for completeness.

The recommended dosage of Gentamicin for injection in children with serious infections and normal renal function is 6 to 7.5 mg/kg/day (2 to 2.5 mg/kg administered every eight (8) hours). The treatment precautions in children are the same as those for adults.

For children with renal dysfunction the dosing interval can be adjusted as follows:

- mild-moderate renal impairment: 2.5 mg/kg every 12 hours
- severe renal impairment: 2.5 mg/kg every 24-48h.

Infants and Neonates (>1 week of age)

In infants and neonates older than 1 week, Gentamicin for injection dosage of 7.5 mg/kg/day (2.5 mg/kg administered every 8 hours) is recommended. Using these recommended doses, considerable variation in the serum levels between individual children has been observed therefore monitor serum levels regularly.

Pre-term or Full-Term Newborns (≤1 week of age)

In pre-term and full-term newborns, one week of age or less, a dosage of 5 mg/kg/day (2.5 mg/kg) administered every 12 hours is recommended. Use Gentamicin for injection with caution in pre-term newborns (post conceptional age of ≤38 weeks) because of their renal immaturity.

The above dosage schedules are not intended as rigid recommendations but are provided as guides to dosage. A variety of methods (e.g., microbiologic, enzymatic and radioimmunoassay techniques) are available to measure gentamicin concentrations in body fluids.

Geriatrics (≥ 65 years of age)

Dosage adjustment is not required in elderly patients with normal renal function. However, since elderly are more likely to have decreased renal function, assess renal function prior to and regularly during therapy.

Patients with Renal Impairment

Dosage adjustment is required in patients with renal impairment. One method of dosage adjustment is to increase the interval between administrations of the usual doses. Since the serum creatinine concentration has a high correlation with the serum half-life of gentamicin this laboratory test may provide guidance for adjustment of the interval between doses. The interval between doses (in hours) may be approximated by multiplying the serum creatinine level (mg/100 mL) by 8. For example, a patient weighing 60 kg with a serum creatinine level of 2 mg/100 mL could be given 60 mg (1 mg/kg) every 16 hours (2 x 8).

In patients with serious systemic infections and renal impairment, it may be desirable to administer the antibiotic more frequently but in reduced dosage. After the usual initial dose, a rough guide for determining reduced dosage at eight-hour intervals is to divide the normally recommended dose by the serum creatinine level (Table 2). For example, after an initial dose of 60 mg (1 mg/kg), a patient weighing 60 kg with a serum creatinine level of 2 mg/100 mL could be given 30 mg every eight hours (60 ÷ 2).

The status of renal function may be changing over the course of the infectious process. Deteriorating renal function requires a greater reduction of dosage than that specified in the guidelines below for patients with stable renal impairment.

Table 2. Dosage Adjustment Guide For Patients With Renal Impairment (Dosage At Eight-Hour Intervals After The Usual Initial Dose)

Serum Creatinine (mg%)	Approximate Creatinine Clearance (ml/min/1.73m²)	Percent Of Usual Doses Shown In Table 1
≤1	>100	100
1.1 - 1.3	70 - 100	80
1.4 - 1.6	55 - 70	65
1.7 - 1.9	45 - 55	55
2 - 2.2	40 - 45	50
2.3 - 2.5	35 - 40	40
2.6 - 3	30 - 35	35
3.1 - 3.5	25 - 30	30
3.6 - 4	20 - 25	25
4.1 - 5.1	15 - 20	20
5.2 - 6.6	10 - 15	15
6.7 - 8	<10	10

In adults with renal failure undergoing hemodialysis, the amount of gentamicin removed from the blood may vary. An eight hour hemodialysis may reduce serum concentrations of gentamicin by approximately 50%. The recommended Gentamicin(e) dosage at the end of each dialysis period is 1 to 1.7 mg/kg depending upon the severity of infection.

In adult patients receiving continuous ambulatory peritoneal dialysis 3 to 4 mg of gentamicin will be lost per litre of dialysate each day. Thus in a patient receiving 8 L of dialysate per day a total of 24 to 32 mg will be lost daily. Gentamicin(e) can be administered by the intravenous route to replace drug lost through peritoneal dialysis. Calculate the correct volume considering the gentamicin concentration used and the amount of drug needed.

Gentamicin(e) should be used for intravenous administration only. Gentamicin(e) should not be added directly to peritoneal dialysis fluid for the treatment of peritonitis. Treatment duration should be determined by the clinical response. Please note systemic toxicity can occur when gentamicin is given by the intraperitoneal route.

Patients with Hepatic Impairment

Gentamicin is not metabolized by the liver therefore no dosage adjustments are required in

patients with hepatic dysfunction. However, patients with severe hepatic dysfunction are at increased risk of nephrotoxicity, therefore monitor renal function carefully in these patients.

Administration

Gentamicin(e) containing gentamicin as sulfate and 0.9% sodium chloride is available in VIAFLEX plastic containers as pre-mixed ready-to-use isotonic gentamicin sulfate solution for IV infusion and should not be diluted or buffered prior to administration. No other drug should be added to this solution (See **DOSAGE FORMS, COMPOSITION AND PACKAGING**).

Gentamicin(e) should be administered using sterile equipment and intravenous apparatus be replaced at least once every 24 hours. If administration is controlled by a pumping device, care must be taken to discontinue pumping action before the containers runs dry or air emboli may result.

Visually inspect the container. If the administration port protector is damaged, detached, or not present, discard container as solution path sterility may be impaired.

INCOMPATIBILITIES

Gentamicin(e) (gentamicin (as sulfate) in 0.9% sodium chloride injection) should not be mixed with other drugs before injection and where co-administration of beta-lactam antibiotics (penicillins, cephalosporins, etc.), erythromycin, lipiphysan, sulfadiazine, furosemide and heparin is necessary, the drugs should be administered separately (See **PART II, MICROBIOLOGY**, **Chemical Interaction with Other Antimicrobials**).

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre.

As in the case of other aminoglycosides, gentamicin toxicity (e.g., nephrotoxic, ototoxic effects and neuromuscular blockade) can occur when serum drug levels reach above a critical value.

In the event of overdosage or toxic reactions, hemodialysis may aid in the removal of gentamicin from the blood, and is especially important if renal function is, or becomes compromised. The rate of removal of gentamicin is considerably lower by peritoneal dialysis than it is by hemodialysis.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Gentamicin is a member of the aminoglycoside class of antibiotics. Aminoglycosides including gentamicin act by inhibiting normal protein synthesis in susceptible microorganisms. Aminoglycosides are characterized by concentration-dependent killing and demonstrate

significant post-antibiotic effect (PAE). Gentamicin is water soluble, a property that limits its ability to cross lipid-rich cellular membranes. Gentamicin is less active in an acidic environment. Gentamicin is active against a wide variety of pathogenic Gram-negative bacteria including *Escherichia coli*, *Proteus* species (indole-positive and indole-negative), *Pseudomonas aeruginosa*, species of the *Klebsiella-Enterobacter-Serratia* group, and *Citrobacter* species. Amongst Gram-positive cocci, methicillin-sensitive *Staphylococcus aureus* (MSSA) are sensitive but methicillin-resistant *S. aureus* (MRSA) are resistant to gentamicin. Due to the facultative anaerobic metabolism of streptococci and enterococci, which reduces the transmembrane potential and thereby limits drug intake of the oxygen-dependent aminoglycoside, gentamicin is minimally active against all streptococci, including *Streptococcus pneumonia* and enterococci. However, due to synergy between an aminoglycoside and a cell-wall active antibiotic, certain streptococci and enterococci can be inhibited with a combination of aminoglycoside and β-lactam/glycopeptides antibiotics. Because aminoglycosides require aerobic metabolism to exert an antibacterial effect, all anaerobic organisms, including *Bacteriodes* species or *Clostridium* species are resistant to aminoglycosides, including gentamicin.

Mechanism of Resistance

There are four mechanisms of resistance to aminoglycosides including gentamicin: reduced uptake or decreased cell permeability, alterations at the ribosomal binding sites, production of aminoglycoside modifying enzymes or presence of plasmid-mediated resistance factor.

Cross-Resistance

Cross-resistance of gentamicin with other aminoglycosides may occur on the basis of common sensitivity to modifying enzymes. Since multiple enzymes exist, resistance may be specific to one aminoglycoside or to multiple aminoglycosides. Gentamicin may be active against bacteria resistant to other aminoglycosides and other aminoglycosides may be active against gentamicin-resistant bacterial strains. Cross-resistance may also occur with drugs of other classes. For example, plasmids conferring resistance to aminoglycosides may also contain resistance factors for beta-lactams, fluoroquinolones, chloramphenicols, sulphonamides, or tetracyclines.

Pharmacodynamics

Aminoglycosides are rapidly bactericidal, and their rate of bacterial killing increases as the antibiotic concentration is increased, regardless of the inoculum. Bactericidal concentration of gentamicin is usually one to four times the minimum inhibitory concentration. In the neutropenic thigh model, the therapeutic efficacy of aminoglycosides correlates with the peak serum concentration and the area under the concentration versus time curve over time.

Pharmacokinetics

Table 3: Pharmacokinetic Parameters of Gentamicin

Population	Dose (mg/kg)/Route		Cmax (ug/mL)	Tmax (h)	T ½ (h)	Distribution Volume (L/kg)
	IM	IV				
Adult						
Normal Renal	1		4-7.6	0.5-1.5	2-3	0.2-0.3
Severe Renal Impairment	1				24-60	
Children						
2-24 months	2-2.5		2.8-8.6			
6 months – 5 years		1	1.58			
5-10 years		1	2.03			
> 10 years		1	2.81			
Infant				0.5-1		
Over 1 week full-term (> 2 kg)	1.5-2.5	0.75-1	3.6-4.1 2.3		3-3.5 2.7	
Under 1 week full-term or > 2 kg premature	1.5-2.5	0.75-1	2.6-3.9 2.6		5.25-5.5 4.6	0.5-0.7 0.5-0.7
Under 1 week low birth weight infants						
Under 1.5 kg	1.5		1.9	2	11.5	
1.5 – 2 kg	1.5		2.6	0.5	8	
Over 2 kg	1.5		2.6-2.8	0.5-1	4.5-5	

Aminoglycosides are minimally absorbed from the gastrointestinal tract and thus must be administered intravenously or intramuscularly in order to treat systemic infections.
After intramuscular (IM) administration of gentamicin, bioavailability is approximately 100%. Peak serum concentrations usually occur between 30 to 60 minutes and serum levels are measurable for 6 to 8 hours. When gentamicin is administered by intravenous (IV) infusion over 20 minutes to two-hour period, the serum concentrations are similar to those obtained by intramuscular administration. The dosing for gentamicin for intravenous and intramuscular administration is identical.

Gentamicin administered at 1 mg/kg every eight hours for the usual 7- to 10- day treatment period to patients with normal renal function does not accumulate in the serum. However, adults given dosages of 4 mg/kg/day or higher for 7 to 10 days have resulted in a slight, progressive raise in both peak and trough concentrations. Concentrations in renal cortex sometimes may be eight times higher than the usual serum levels.

Gentamicin binding to protein is low and varies from 0 and 30%. Gentamicin is highly water soluble and is distributed in the vascular space and interstices of most tissues. Drug concentrations in interstitial fluids at steady state approximate those of plasma. However, the volume of distribution increases in certain clinical situations including extensive burns, ascites, pregnancy and the postpartum state. In severely burned patients, the half-life may be significantly decreased and resulting serum concentrations may be lower than anticipated from the mg/kg dose. The volume of distribution of gentamicin per kg bodyweight is increased in premature newborns as compared with adolescents, therefore for adequate peak levels; a higher dose per kg bodyweight is required. Aminoglycosides have poor penetration into bronchial secretions and abscesses.

Following parenteral administration, gentamicin can be detected in serum, lymph, subcutaneous tissue, lung, sputum, and bronchial, pleural, pericardial, synovial, and peritoneal fluids. A lower concentration in bile suggests minimal biliary excretion. Since aminoglycosides diffuse poorly into the subarachnoid space after parenteral administration, concentrations of gentamicin in cerebrospinal fluid are often low and dependent upon dose, rate of penetration, and degree of meningeal inflammation. There is minimal penetration of gentamicin into ocular tissues following intramuscular or intravenous administration.

Gentamicin crosses the placenta and is distributed into fetal circulation and amniotic fluid. Gentamicin is excreted in breast milk and achieves detectable levels in the circulation of breast-fed infants.

Gentamicin is excreted unchanged primarily by glomerular filtration. This results in high urinary concentration of the antibiotic. In adults with normal renal function, 50-90% of a single IM dose of gentamicin is excreted within 24 hrs. Peak urine concentrations of gentamicin may range from 113-423 mcg/mL 1 hour after a single IM dose in patients with normal renal function. Complete recovery of the dose in urine requires 10-20 days in patients with normal renal function, and terminal elimination half-lives of greater than 100 hour, have been reported in adults with normal renal function following repeated IM or IV administration of the drug. In newborn babies gentamicin elimination rate is reduced because renal function is immature, however as they have a larger volume of distribution a higher dose/kg of gentamicin in newborns, but longer dosing interval for gentamicin than in other age groups is required.

Renal clearance of gentamicin is similar to that of endogenous creatinine. As with other aminoglycosides, a small amount of gentamicin may be retained in the tissues, especially in the kidneys. Minute quantities of aminoglycosides have been detected in the urine weeks after the drug administration was discontinued.

Special Populations and Conditions

Geriatrics (≥ 65 years of age)

Elderly may have significant renal impairment due to the age-related decline in glomerular filtration rate. The terminal elimination half-life of gentamicin may be prolonged in elderly

patients. Renal function should be determined prior to and during gentamicin therapy and the dosage must be individualized according to renal function.

Renal Insufficiency

The terminal elimination half-life of gentamicin is prolonged in patients with renal dysfunction in proportion to the extent of the impairment in glomerular filtration rate. Gentamicin(e) must be used with caution and the dosage must be individualized in patients with renal impairment. Monitoring of renal function (i.e., BUN and serum creatinine) is recommended during treatment.

Gentamicin is cleared from the body more slowly than in patients with normal renal function. The more severe the impairment, the slower the clearance.

In patients with marked impairment of renal function, there is a decrease in the concentration of aminoglycosides in urine and in their penetration into defective renal parenchyma. Therefore, the possibility of decreased drug excretion, together with the potential nephrotoxicity of aminoglycosides, should be considered when treating such patients who have urinary tract infections.

In adult patients, treatment with gentamicin dosages of 4 mg/kg/day or higher for seven to ten days may result in a slight, progressive rise in both peak and trough concentrations. Gentamicin, like all aminoglycosides, may accumulate in the serum and tissue of patients with impaired renal function. Dosage must be adjusted.

The endogenous creatinine clearance rate and 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.

Probenecid does not affect renal tubular transport of gentamicin.

Hepatic Insufficiency

The pharmacokinetics of gentamicin in patients with hepatic impairment have not been studied.

STORAGE AND STABILITY

Gentamicin(e) (Gentamicin (as sulfate) in 0.9% sodium chloride injection) should be stored between 15°- 25°C.
Gentamicin(e) should not be administered unless the solution is clear and the seal is intact.
Gentamicin(e) should not be physically premixed with, or infused simultaneously through the same tubing with other drugs before injection, but should be administered separately in accordance with the recommended route of administration and dosage schedule. Addition of Gentamicin(e) to solutions containing bicarbonate should be avoided because it may lead to the release of carbon dioxide.

SPECIAL HANDLING INSTRUCTIONS

Directions for Use of VIAFLEX Plus Plastic Container

WARNING: Do not use plastic container in series connections. Such use could result in air embolism due to residual air being drawn from primary container before administration of the fluid from the secondary container is completed.
TO OPEN: Tear overwrap down side at slit and remove solution container. Check for leaks.
Preparation for administration:
1. Suspend container from eyelet support.
2. Remove plastic protector from outlet port at bottom of container.
3. Attach administration set.
DO NOT ADD OTHER DRUGS TO GENTAMICIN(E) (GENTAMICIN (AS SULFATE) IN 0.9% SODIUM CHLORIDE INJECTION).
DO NOT USE UNLESS SOLUTION IS CLEAR.
DISCONTINUE INFUSION IF ADVERSE REACTION OCCURS.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Gentamicin(e) (Gentamicin (as sulfate) in 0.9% sodium chloride injection is available in 50 mL and 100 mL VIAFLEX plastic containers having the following compositions:
1.6 mg/mL in 50 mL VIAFLEX
1.0 mg/mL in 100 mL VIAFLEX

NOTE:
Do not remove unit from overwrap until ready for use. The overwrap is a moisture barrier. The inner bag maintains the sterility of the product. After removing the overwrap, check for minute leaks by squeezing inner bag firmly. If leaks are found discard solution as sterility may be impaired.

Composition:
Gentamicin(e) contains gentamicin sulfate and 0.9% sodium chloride in VIAFLEX Plus plastic container made of polyvinyl chloride. It is sterile, isotonic solution having a pH which ranges from 3.0 -5.5.

Gentamicin(e) (Gentamicin (as sulfate) in 0.9% sodium chloride injection) is available in 50 mL and 100 mLVIAFLEX plastic containers having the following compositions:
80 mg/50 mL - Each mL contains 1.6 mg Gentamicin (as sulfate)
100 mg/100 mL - Each mL contains 1.0 mg Gentamicin (as sulfate)

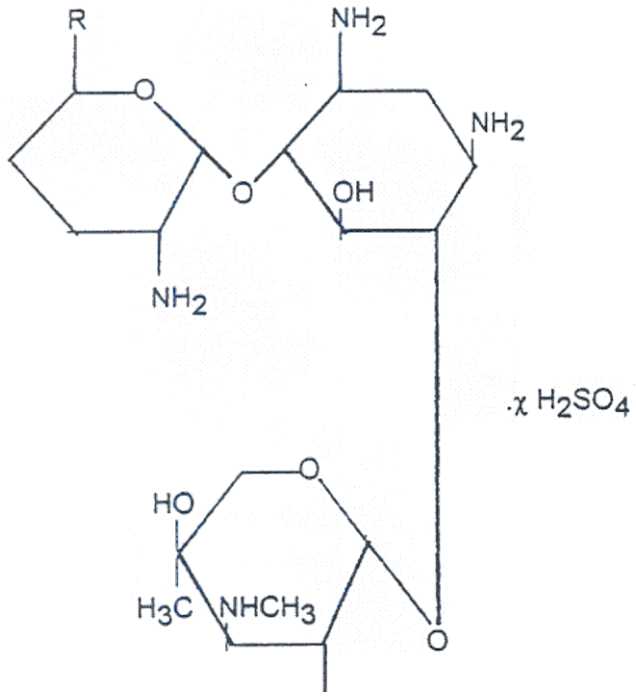
For all solution concentrations each mL contains 9.0 mg sodium chloride, sodium hydroxide or sulfuric acid to adjust the pH, and water for injection q.s.

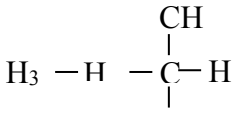
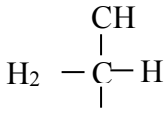
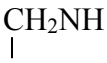
PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substances

Proper Name: Gentamicin Sulfate.
Chemical Name (for Gentamicin C_{1a} base): O-3-deoxy-4-C-methyl-3-(methylamino)-β-L-arabinopyranosyl-(1->6)-O-[2,6-diamino-2,3,4,6-tetradeoxy-α-D-erythro-hexopyranosyl-(1->4)]-2-deoxy-D-streptamine.
Structural formula:



Gentamicin	R
C_1	
C_2	
C_{1A}	

The relative ratio of C_1:C_{1A}:C_2 is variable in a range of 25-50: 10-35: 25-55%, respectively.

Description

Gentamicin Sulfate is a complex substance with three components, sulfates of gentamicin C_1, C_2 and C_{1a}. It is white to cream-coloured powder, readily soluble in water, moderately soluble in methanol, ethanol and acetone but practically insoluble in benzene and halogenated hydrocarbons.

CLINICAL TRIALS

Data from original clinical studies are no longer available.

DETAILED PHARMACOLOGY

Pharmacodynamics

In the neutropenic thigh model, the therapeutic efficacy of aminoglycosides including gentamicin correlated with the peak serum concentration and the area under the concentration versus time curve (AUC) over time. Because the half-life of aminoglycosides in small animals is short (<1 hour), results of the peak serum concentration can be separated from the AUC. The short drug half-life also predicts a long interval of sub-MIC serum levels, implying an *in vivo* post antibiotic effect (PAE). In a study of the neutropenic mouse thigh infected with 15 clinical isolates of *Enterobacteriaceae*, the *in vivo* PAE after gentamicin therapy varied from 1.4 to 6.9 hours.

Urine is known to inhibit the activity of aminoglycosides against urinary tract pathogens. Inhibition is believed to result from the low pH and high osmolality caused by the high salt and glucose concentrations.

Pharmacokinetics

Absorption

Aminoglycosides, including gentamicin, are poorly absorbed from the gastrointestinal tract. Aminoglycosides may also be absorbed through the peritoneal cavity. Absorption may be delayed in patients with hypotension or poor tissue perfusion.

Distribution

Aminoglycosides distribute to intravascular and interstitial tissues in the body. The volume of distribution is typically on the order of 0.2 to 0.3 L/kg. There is minimal penetration of gentamicin into ocular tissues following intramuscular or intravenous administration. Following parenteral administration, gentamicin can be detected in serum, lymph, tissues, sputum, and in pleural, synovial, and peritoneal fluids. Concentrations in bile, in general, have been low and suggest minimal biliary excretion. Concentrations of gentamicin in CSF of infants with purulent meningitis range from 0.2 ug/mL to 3.5 ug/mL after a dose of 1.5 to 2.5 mg/kg. Peak values are found 4 to 6 hours after the dose, and are dependent on degree of meningeal inflammation and dosage. In one study intrathecal administration of 4 mg of gentamicin resulted in CSF concentrations of the drug of 19-46 mcg/mL for 8 hours and less than 3 mcg/mL at 20 hours.

Metabolism

Gentamicin is not metabolized.

Excretion

The drug is excreted unchanged primarily by glomerular filtration. Aminoglycosides, including gentamicin, accumulate in the cells of the proximal convoluted tubule to concentrations that exceed those in plasma. Nephrotoxicity is probably due to time-dependent accumulation of drug within cells of the proximal convoluted tubule. Thus, minimizing exposure to the drug, as with extended interval administration, may minimize the risk of nephrotoxicity. The elimination half-life may be shortened in patients with febrile conditions. The elimination is prolonged in elderly patients and in those with renal dysfunction and remains in proportion to the extent of the impairment in glomerular filtration rate.

MICROBIOLOGY

Mode of Action

Aminoglycosides, including gentamicin, require aerobic energy to enter the cell and bind to rRNA, on the 30S subunit of prokaryotic ribosomes. This results in a conformational change in the structure of the ribosomal subunit and prevents protein synthesis by impairing messenger RNA translation and translocation. The drug also binds electrostatically to the lipopolysaccharide layer of Gram-negative bacteria, an effect that ultimately disrupts the permeability of the bacterial cell wall.

Aminoglycosides are bactericidal antibiotics and have a significant post-antibiotic effect. Antibacterial activity is enhanced in media with an alkaline pH and reduced in media with an acidic pH.

Mechanisms of Resistance

There are four general mechanisms of resistance to aminoglycosides including gentamicin:

(1) modification and inactivation of aminoglycosides including gentamicin by one or more of the following families of bacterial enzymes: aminoglycoside acetyltransferases (AACs), aminoglycoside nucleotidyltransferases (ANTs), and aminoglycoside phosphotransferases(APHs);

(2) exclusion of aminoglycosides including gentamicin from the site of activity by increased permeability of the bacterial membrane and/or removal of the drug via an efflux pump;

(3) modification of the target ribosome either by methylation or (rarely) mutation of the nucleotide sequence of the target rRNA, or

(4) the presence of a plasmid-mediated resistance factor which is acquired by conjugation.

Any of these mechanisms of resistance may be transferred from one organism to another by way of conjugation, transposons, plasmid exchange, or may arise by spontaneous mutation.

Cross-Resistance

Cross-resistance of gentamicin with other aminoglycosides may occur on the basis of common sensitivity to modifying enzymes. Since multiple enzymes exist, resistance may be specific to one aminoglycoside or to multiple aminoglycosides. Gentamicin may be active against bacteria resistant to other aminoglycosides and other aminoglycosides may be active against gentamicin-resistant bacterial strains. Cross-resistance may also occur with drugs of other classes. For example, plasmids conferring resistance to aminoglycosides may also contain resistance factors for beta-lactams, fluoroquinolones, chloramphenicol, sulphonamides, or tetracycline.

Spectrum of Activity

Gentamicin is active against the majority of the following aerobic Gram-positive and Gram-negative bacteria both *in vitro* and in clinical infections:

Aerobic Gram-Positive Bacteria

Staphylococcus aureus (methicillin-susceptible only)
Staphylococcus epidermidis

Aerobic Gram-Negative Bacteria

Escherichia coli
Klebsiella pneumonia
Pseudomonas aeruginosa
Enterobacter cloacae
Serratia marcescens
Proteus mirabilis
Klebsiella oxytoca
Acinetobacter baumanii

Not all strains of these bacteria are susceptible to gentamicin. In serious or life-threatening infections known or suspected to be caused by these organisms, initial empiric combination therapy should be considered until results of susceptibility tests become available.

The aminoglycosides, including gentamicin, show no inhibitory activity against *Stenotrophomonas maltophilia*. All streptococci, including *Streptococcus pnuemoniae*, and enterococi are resistant to gentamicin. All anaerobic organisms are resistant to this class of drugs.

Susceptibility Test Methods

Dilution Techniques

Quantitative methods are used to determine antimicrobial minimum inhibitory concentrations (MICs). MICs provide estimates of the susceptibility of bacteria to antimicrobial compounds. MIC values should be determined using a standardized procedure. Standardized procedures are based on a dilution method (broth or agar) or equivalent with standardized inoculum

concentrations and standardized concentrations of gentamicin powder. The MIC values should be interpreted according to the criteria provided in Table 4.

Diffusion Techniques

Quantitative methods that require measurement of zone diameters also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. One such standardized procedure requires the use of standardized inoculum concentrations. This procedure uses paper disks impregnated with 10 mcg of gentamicin to test susceptibility. Results should be interpreted according to the criteria in Table 4.

Anaerobic Techniques

Not applicable for gentamicin.

Table 4: Susceptibility Interpretive Criteria for Gentamicin

	Minimum Inhibitory Concentrations (mcg/ml)			Disk Diffusion (Zone diameters in mm)		
Pathogen	**S**	**I**	**R**	**S**	**I**	**R**
Enterobacteriaceae[a]	≤4	8	≥16	≥15	13-14	≤12
Pseudomonas aeruginosa	≤4	8	≥16	≥15	13-14	≤12
Staphylococcus spp.	≤4	8	≥16	≥15	13-14	≤12

These standards apply to testing done with Mueller-Hinton medium (cation-adjusted for broth) without blood or other nutritional supplements. n/a = not applicable
a-For *Salmonella* spp. and *Shigella* spp., gentamicin may appear active *in vitro* but is not clinically effective

A report of *Susceptible* indicates that the antimicrobial is likely to inhibit growth of the pathogen if the antimicrobial compound in the blood reaches the concentrations usually achievable. A report of *Intermediate* indicates that the result should be considered equivocal, and, if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where a high dosage of drug can be used or where a prolonged infusion of drug can be used. This category also provides a buffer zone that prevents small, uncontrolled technical factors from causing major discrepancies in interpretation. A report of *Resistant* indicates that the antimicrobial is not likely to inhibit growth of the pathogen if the antimicrobial compound in the blood reaches the concentrations usually achievable; other therapy should be selected.

Quality Control

Standardized susceptibility test procedures require the use of quality control microorganisms to control the technical aspects of the test procedures. Standard gentamicin powder should provide the MIC values noted in Table 5. For diffusion techniques using a 10 mcg gentamicin disk, the criteria noted in the table should be achieved.

Table 5: Acceptable Quality Control Ranges for Susceptibility Testing

QC Organism	Minimum Inhibitory Concentrations (mcg/ml)	Disk Diffusion (zone diameters in mm)
Escherichia coli ATCC 25922	0.25-1	19-26
Pseudomonas aeruginosa ATCC 27853	0.5-2	16-21
Staphylococcus aureus ATCC 29213	0.12-1	n/a
Staphylococcus aureus ATCC 25923	n/a	19-27

These standards apply to testing done with Mueller-Hinton medium (cation-adjusted for broth) without blood or other nutritional supplements.
n/a = not applicable

Synergy/Antagonism with Other Antimicrobials

Aminoglycosides, including gentamicin often exhibit synergistic antimicrobial activity when combined with cell-wall active drugs such as beta-lactams or glycopeptides. This phenomenon forms the basis for the clinical use of aminoglycosides and penicillins as a synergistic combination against certain pathogens. Concomitant exposure of enterococci and certain species of streptococci to a cell wall-active drug such as ampicillin or vancomycin facilitates access of aminoglycosides to their ribosomal target site and this synergy results in an antibacterial effect.

Chemical Interaction with Other Antimicrobials

Cationic aminoglycosides interact chemically with beta-lactam antibiotics with a reaction that results in a nucleophilic opening of the β-lactam ring, with acylation of an amino group of the aminoglycoside and mutual loss of β-lactam antibacterial activity. Therefore penicillin and aminoglycosides should not be mixed in the same solution before infusion.

TOXICOLOGY

Gentamicin has been shown to affect vestibular and renal functions in animals. Chronic administration of 5 mg/kg for 50 days in dogs, 10 mg/kg for 40 days in cats and 20 mg/kg for 24 days in rats resulted in mild toxicity in some animals studied. Higher toxic doses resulted in damage to renal and vestibular function which appeared to be dose related. Proteinuria, a rise in blood urea nitrogen or serum creatinine has also occurred.

REFERENCES

1. AHFS Drug Information 2011. Aminoglycosides 8:12.02. Gentamicin Sulfate. 2011, pp.61-67.

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3. Warner, W.A. and Sanders, E.: Neuromuscular Blockade Associated with Gentamicin Therapy. JAMA. 215:1153-1154, Feb. 15, 1971.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE
PATIENT MEDICATION INFORMATION

[Pr]Gentamicin(e)
Gentamicin (as sulfate) in 0.9% sodium chloride injection
(1.0 mg/mL and 1.6 mg/mL)

Read this carefully before you start taking **Gentamicin(e)** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Gentamicin(e)**.

Serious Warnings and Precautions

- Aminoglycosides, including Gentamicin(e), may cause:
  - Serious kidney problems
  - Serious hearing problems and hearing loss. Hearing loss may be permanent in some cases.
- While you are using Gentamicin(e), your healthcare professional may do bloodwork to check how your kidneys are working. Sometimes you may also take a hearing test to check if Gentamicin(e) is not affecting your hearing
- Tell your healthcare professional about all the medications you are taking. The risk that you will develop serious kidney, hearing, or other problems is greater if you are taking certain medications.
- See the following sections of the Patient Medication Information for further information and signs of kidney or hearing problems:
  - "To help avoid side effects and ensure proper use…"
  - "Interactions with this medication"
  - "Serious side effects and what to do about them"

What is Gentamicin(e) used for?
Gentamicin(e) is used to treat serious bacterial infections such as:

- Blood infection (septicemia)
- Chest infections
- Infections of system that carries urine out of the body (urinary tract infections)
- Bone, and tissue infections
- Infected wounds or burns
- Intra-abdominal (belly) infections

Antibacterial drugs like Gentamicin(e) treat only bacterial infections. They do not treat viral infections. Although you may feel better early in treatment, Gentamicin(e) should be used exactly as directed. Misuse or overuse of Gentamicin(e) could lead to the growth of bacteria that will not be killed by Gentamicin(e) (resistance). This means that Gentamicin(e) may not work for you in the future.

How does Gentamicin(e) work?
Gentamicin(e) is an antibiotic that belongs to a group of medicines called aminoglycosides. It works by preventing bacteria from growing and killing them.

What are the ingredients in Gentamicin(e)?
Medicinal ingredients: Gentamicin (as sulfate)
Non-medicinal ingredients: Sodium Chloride, Sodium Hydroxide or Sulfuric Acid (For pH adjustment), Water for Injection

Gentamicin(e) comes in the following dosage forms:
Gentamicin(e) comes as a sterile solution (liquid). It is supplied as:
- Gentamicin(e) [Gentamicin (as sulfate) in 0.9% sodium chloride injection] 1.0 mg/mL
- Gentamicin(e) [Gentamicin (as sulfate) in 0.9% sodium chloride injection] 1.6 mg/mL

Do not use Gentamicin(e) if you have an allergy to:
- gentamicin
- any other aminoglycoside antibiotics such as amikacin, kanamycin, parmomycin, streptomycin, tobramycin
- any of the nonmedicinal ingredients in Gentamicin(e) (see "What the important nonmedicinal ingredients are:").

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Gentamicin(e). Talk about any health conditions or problems you may have, including if you:
- Have kidney problems
- Have hearing problems or if you have been treated with medications that affect hearing in the past (see "Interactions with this medication" section below)
- Have muscle problems (such as myasthenia gravis or Parkinson's disease)
- Have nerve problems
- Have diabetes
- Have liver problems
- Have problems with balance
- Suffer from heart failure
- Are pregnant or intend to become pregnant. This medication is not usually given to pregnant women because it can harm the baby.
- Are breastfeeding or plan to breast feed

Other warnings you should know about:
- People that are dehydrated and adults over the age of 65 may be at greater risk for side effects. Drink plenty of water while you are receiving this medicine. Talk with your healthcare professional about this.
- This medication may make you dizzy. Do not drive or operate machinery unless you are fully alert.
- If you develop severe diarrhoea (very loose or watery stool), tell your healthcare professional right away. Do this even if it occurs several weeks after you stopped taking Gentamicin(e). Diarrhoea may mean that you have a serious condition affecting your bowel (colitis). You may need urgent medical care. Do not try to treat loose stools without first checking with your healthcare professional (see the "Serious side effects and what to do about them" table below).

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Gentamicin(e):

- Other antibiotics such as:
  - Aminoglycosides (e.g. amikacin, kanamycin, parmomycin, streptomycin tobramycin)
  - Cephalosporins like cefazolin, cefixime or cephalexin
  - Clindamycin
  - piperacillin
  - polymixin B, colistin
  - vancomycin
- Amphotericin B, an anti-fungal medicine
- Anti-cancer drugs, such as cisplatin and carboplatin
- Diuretics “water pills” such as ethacrynic acid or furosemide
- Medicines used to suppress the immune system, such as cyclosporine and tacrolimus
- Medications used to reduce fever and inflammation (nonsteroidal anti-inflammatory) such as indomethacin
- Zalcitabine, an HIV medication
- Mannitol
- Magnesium
- Medications given during surgery to relax the muscles such as tubocurarine and and succinylcholine
- Medicines used to treat myasthenia gravis such as neostigmine and pyridostigmine
- Live typhoid vaccine

The above medicines may:

- harm your nervous system, kidneys or hearing
- affect the way Gentamicin(e) works or be affected by Gentamicin(e). You may need different amounts of your medicine, or you may need to take a different medicine.

Many other medications that do not appear on this list may also harm your nervous system, kidneys or hearing. If you are not sure if your medicines might interact with Gentamicin(e), ask your pharmacist or healthcare professional. Always keep a list of your medicines and show it to your healthcare professional when you get a new medicine.

How to take Gentamicin(e):
Your healthcare professional will give **Gentamicin(e)** as a slow drip through a needle into a vein (infusion).

Usual dose:
Your healthcare professional will work out the right dose for you. This will depend on your age, weight, type of infection and how well your kidneys are working.

Your healthcare professional will also tell you how long to use **Gentamicin(e).**

Ask your healthcare professional if you have any questions about how many doses of **Gentamicin(e)** you will need or when you will receive them.

Overdose:

If you think you have taken too much Gentamicin(e), contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:
Gentamicin(e) is administered by a healthcare professional. If you think you have missed a dose talk to your healthcare professional.

What are possible side effects from using Gentamicin(e)?

These are not all the possible side effects you may feel when taking Gentamicin(e). If you experience any side effects not listed here, contact your healthcare professional. Ask your healthcare professional any questions that you may have. Please also see "To help avoid side effects and ensure proper use…" sections.

Side effects may include:
- nausea, vomiting
- lack of appetite (anorexia)
- increased salivation
- weight loss
- pain in the area where you had Gentamicin(e) shot.
- weakness or tiredness
- headache
- joint pain
- fever

Call your healthcare professional or get medical help if any of these side effects bother you or do not go away.

Tell your doctor if you experience any additional side effects.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
COMMON **Kidney problems**: •swelling in the arms or legs •dark-coloured urine •unable to pass urine •change in the amount of urine you passing •unusual tiredness or weakness			✓
Ears and hearing problems: •dizziness, •problems with balance,			✓

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
•sensation of spinning •change in hearing •complete hearing loss			
UNKNOWN FREQUENCY **Nervous System Problems:** •poor coordination, unsteady walk, •dizziness, •tingling, numbing, nerve pain, or change in skin sensation •muscle twitching •seizure (fits)			✓
Allergic reactions (hyper-sensitivity) •severe rash, hives, itching •swelling of face, lips, mouth, throat or tongue •wheezing, tightness in the chest or throat •difficulty breathing or talking			✓
Serious life-threatening skin reactions •(Stevens-Johnson syndrome, Toxic Epidermal Necrolysis) •unexplained widespread skin pain •flu-like symptoms (fever, sore mouth and throat, cough, fatigue, burning eyes etc.) •painful red or purplish rash that spreads and blisters on mouth, nose, eyes and genitals •shedding of your skin within days after blisters form			✓
Decreased of cells in the blood that help the blood clot (Platelets): •easy bruising, •abnormal bleeding, bleeding when you brush your teeth, •Pinpoint red spots on the skin		✓	
Decreased White Blood Cells: more likely to develop infections, fatigue, fever, aches, pains and flu-like symptoms		✓	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Bowel infection (Clostridium difficile colitis): Diarrhea (very loose stool) that does not go away (bloody or watery) with or without fever or stomach cramps			✓
Changes in vision (blurred vision).			✓
Any breathing difficulties			✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:
Store between 15°- 25°C.

Keep out of reach and sight of children.

If you want more information about Gentamicin(e):

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (https://health-products.canada.ca/dpd-bdpp/index-eng.jsp); the manufacturer's website (http://www.baxter.ca), or by calling 1-888-719-9955.

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