Indicated for the treatment of serious bacterial infections caused by susceptible strains of the designated microorganisms in the diseases listed below:

- Septicemia in the pediatric patient and adult caused by P. aeruginosa, E. coli, and Klebsiella spp.
- Lower respiratory tract infections caused by P. aeruginosa, Klebsiella spp, Enterobacter spp, Serratia spp, E. coli, and S. aureus (penicillinase- and non-penicillinase-producing strains).
- Serious central-nervous-system infections (meningitis) caused by susceptible organisms.
- Intra-abdominal infections, including peritonitis, caused by E. coli, Klebsiella spp, and Enterobacter spp.
- Skin, bone, and skin structure infections caused by P. aeruginosa, Proteus spp, E. coli, Klebsiella spp, Enterobacter spp, and S. aureus.
- Complicated and recurrent urinary tract infections caused by P. aeruginosa, Proteus spp, (indole-positive and indole-negative), E. coli, Klebsiella spp, Enterobacter spp, Serratia spp, S. aureus, Providencia spp, and Citrobacter spp.

A hypersensitivity to any aminoglycoside is a contraindication to the use of tobramycin. A history of hypersensitivity or serious toxic reactions to aminoglycosides may also contraindicate the use of any other aminoglycoside because of the known cross-sensitivity of patients to drugs in this class.
Tobramycin Injection, USP

Rx only

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Tobramycin Injection, USP and other antibacterial drugs, Tobramycin Injection, USP should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

WARNINGS

Patients treated with tobramycin injection and other aminoglycosides should be under close clinical observation, because these drugs have an inherent potential for causing ototoxicity and nephrotoxicity.

Neurotoxicity, manifested as both auditory and vestibular ototoxicity, can occur. The auditory changes are irreversible, are usually bilateral, and may be partial or total. Eighteenth-nerve impairment and nephrotoxicity may develop, primarily in patients having preexisting renal damage and in those with normal renal function to whom aminoglycosides are administered for longer periods or in higher doses than recommended. Other manifestations of neurotoxicity may include numbness, skin tingling, muscle twitching, and convulsions. The risk of aminoglycoside-induced hearing loss increases with the degree of exposure to either high peak or high trough serum concentrations. Patients who develop cochlear damage may not have symptoms during therapy to warn them of eighth-nerve toxicity, and partial or total irreversible bilateral deafness may continue to develop after the drug has been discontinued.

Rarely, nephrotoxicity may not become apparent until the first few days after cessation of therapy. Aminoglycoside-induced nephrotoxicity usually is reversible.

Renal and eighth-nerve function should be closely monitored in patients with known or suspected renal impairment and also in those whose renal function is initially normal but who develop signs of renal dysfunction during therapy. Peak and trough serum concentrations of aminoglycosides should be monitored periodically during therapy to assure adequate levels and to avoid potentially toxic levels. Prolonged serum concentrations above 12 mcg/mL should be avoided. Rising trough levels (above 2 mcg/mL) may indicate tissue accumulation. Such accumulation, excessive peak concentrations, advanced age, and cumulative dose may contribute to ototoxicity and nephrotoxicity (see PRECAUTIONS). Urine should be examined for decreased specific gravity and increased excretion of protein, cells, and casts.

Blood urea nitrogen, serum creatinine, and creatinine clearance should be measured periodically. When feasible, it is recommended that serial audiograms be obtained in patients old enough to be tested, particularly high-risk patients. Evidence of impairment of renal, vestibular, or auditory function requires discontinuation of the drug or dosage adjustment.

Tobramycin injection should be used with caution in premature and neonatal infants because of their renal immaturity and the resulting prolongation of serum half-life of the drug.

Concurrent and sequential use of other neurotoxic and/or nephrotoxic antibiotics, particularly other aminoglycosides (e.g., amikacin, streptomycin, neomycin, kanamycin, gentamicin, and paromomycin) cephaloridine, viomycin, polymyxin B, colistin, cefotaxim, and vancomycin, should be avoided. Other factors that may increase patient risk are advanced age and dehydration.

Aminoglycosides should not be given concurrently with potent diuretics, such as ethacrynic acid and furosemide. Some diuretics themselves cause ototoxicity, and intravenously administered diuretics enhance aminoglycoside toxicity by altering serum levels.

SERUM CONCENTRATIONS AND CLEARANCE

The serum half-life in normal individuals is 2 hours. An inverse relationship exists between serum levels and the resulting prolongation of serum half-life of the drug.

MIXED BACTERIAL SPECIES

Aminoglycosides are generally not active against most gram-positive organisms, including Streptococcus pyogenes, Streptococcus pneumoniae, and enterococci. Cross-resistance between aminoglycosides may occur.

Interactions with Other Antibacterial Drugs

In vitro studies have shown that an aminoglycoside combined with an antibiotic that interferes with cell-wall synthesis affects some enterococcal strains synergistically. The combination of penicillin G and tobramycin results in a synergistic bactericidal effect in vitro against certain strains of Enterococcus faecalis. However, this combination is not synergistic against other closely related organisms, e.g., Enterococcus faecium. Species-level identification of enterococci alone cannot be used to predict susceptibility. Susceptibility testing and tests for antibiotic synergism must be performed.

Tobramycin has been shown to be active against most strains of the following bacteria in vitro and in clinical infections as described in INDICATIONS AND USAGE section (1):

- Aerobic Gram-positive bacteria
  - Staphylococcus aureus
  - Aerobic Gram-negative bacteria
  - Citrobacter species
  - Enterobacter species
  - Escherichia coli
  - Klebsiella species
  - Morganella morganii
  - Pseudomonas aeruginosa
  - Proteus mirabilis
  - Proteus vulgaris
  - Providencia species
  - Serratia species

Aminoglycosides are generally not active against most gram-positive bacteria, including Streptococcus pyogenes, Streptococcus pneumoniae, and enterococci.

SPLINTING TECHNIQUES

Quantitative methods are used to determine antimicrobial minimum inhibitory concentrations (MICs). These MICs provide estimates of the susceptibility of bacteria to antibacterial compounds. The MICs should be determined by using a standardized test method.
method. Standardized procedures are based on a dilution method (broth or agar) or equivalent with standardized inoculum concentrations and standardized concentrations of tobramycin powder. The MIC values should be interpreted according to the criteria in Table 1.

**Diffusion Techniques**

Quantitative methods that require measurement of zone diameters also provide reproducible estimates of susceptibility of bacteria to antimicrobial compound. One such standardized procedure requires the use of standardized inoculum concentrations and paper disk impregnated with 10 mcg of tobramycin. The disk diffusion values should be interpreted according to the criteria provided in Table 1.

**Table 1: Susceptibility Interpretive Criteria for Tobramycin**

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Minimum Inhibitory Concentrations (mcg/mL)</th>
<th>Disk Diffusion Zone Diameter Pathogen (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus (includes methicillin-susceptible and methicillin resistant isolates)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enterobacteriaceae</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

S=susceptible, I=intermediate, R=resistant

For *Salmonella spp* and *Shigella spp.*, tobramycin may appear active in vitro but is not effective clinically and should not be reported as susceptible.

A report of “Susceptible” indicates that the antimicrobial is likely to inhibit growth of the pathogen if the antimicrobial compound reaches the concentration at the infection site necessary to inhibit growth of the pathogen. 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.

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 reaches the concentrations usually achievable at the infection site; other therapy should be selected.

**Quality Control**

Standardized susceptibility test procedures require the use of laboratory control to monitor and ensure the accuracy and precision of supplies and reagents used in the assay. Standard tobramycin powder should provide the following range of MIC values provided in Table 2. For the diffusion technique using the 10 mcg tobramycin disk, the criteria provided in Table 2 should be achieved.

**Table 2: Acceptable Quality Control Ranges for Susceptibility Testing**

<table>
<thead>
<tr>
<th>Quality Control Organism</th>
<th>Minimum Inhibitory Concentrations (mcg/mL)</th>
<th>Disk Diffusion (zone diameter in mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichia coli ATCC 25922</td>
<td>0.25 to 1</td>
<td>18 to 26</td>
</tr>
<tr>
<td>Staphylococcus aureus ATCC 25923</td>
<td>Not applicable</td>
<td>19 to 29</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa ATCC 27853</td>
<td>0.25 to 1</td>
<td>20 to 26</td>
</tr>
<tr>
<td>Staphylococcus aureus ATCC 29213</td>
<td>0.12 to 1</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Enterococcus faecalis ATCC 29212</td>
<td>8 to 32</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

**INDICATIONS AND USAGE**

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Tobramycin Injection, USP and other antibacterial drugs, Tobramycin Injection, USP should be used only to treat or prevent infections that are proven or strongly 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.

Tobramycin injection, USP is indicated for the treatment of serious bacterial infections caused by susceptible strains of the designated microorganisms in the diseases listed below:

- Septicemia in the pediatric patient and adult caused by *P. aeruginosa*, *E. coli*, and *Klebsiella spp.*
- Lower respiratory tract infections caused by *P. aeruginosa*, *Klebsiella spp.*, *Enterobacter spp.*, *Serratia spp.*, *E. coli*, and *S. aureus* (penicillinase- and non-penicillinase-producing strains).
- Serious central-nervous-system infections (meningitis) caused by susceptible organisms.
- Intra-abdominal infections, including peritonitis, caused by *E. coli*, *Klebsiella spp.*, and *Enterobacter spp.*
- Skin, bone, and skin structure infections caused by *P. aeruginosa*, *Proteus spp.*, *E. coli*, *Klebsiella spp.*, and *S. aureus*.

**WARNINGS**

See WARNINGS box above.

Tobramycin injection contains sodium metabisulfite, a sulfite 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 sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

Serious allergic reactions including anaphylaxis and dermatologic reactions including exfoliative dermatitis, toxic epidermal necrolysis, erythema multiforme, and Stevens-Johnson Syndrome have been reported rarely in patients on tobramycin therapy. Although rare, fatalities have been reported (see CONTRAINDICATIONS).

If an allergic reaction occurs, the drug should be discontinued and appropriate therapy instituted.

**Clostridium difficile** associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including Tobramycin Injection, USP, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile*.

*Clostridium difficile* produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colostomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated.

**PRECAUTIONS**

General

Prescribing tobramycin injection in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Serum and urine specimens for examination should be collected during therapy, as recommended in the WARNINGS box. Serum calcium, magnesium, and sodium should be monitored.

Peak and trough serum levels should be measured periodically during therapy. Prolonged concentrations above 12 mcg/mL should be avoided. Rising trough levels (above 2 mcg/mL) may indicate tissue accumulation. Such accumulation, advanced age, and cumulative dosage may contribute to ototoxicity and nephrotoxicity. It is particularly important to monitor serum levels in patients with known renal impairment or in patients who require hydration with solutions containing high concentrations of potassium.

A useful guideline would be to perform serum level assays after 2 or 3 doses, so that the dosage could be adjusted if necessary, and at 3- to 4-day intervals during therapy. In the event of changing renal function, more frequent serum levels should be obtained and the dosage or dosage interval adjusted according to the guidelines provided in DOSAGE AND ADMINISTRATION.

In order to measure the peak level, a serum sample should be drawn about 30 minutes following intravenous infusion or 1 hour after an intramuscular injection. Trough levels are measured by obtaining serum samples at 8 hours or just prior to the next dose of tobramycin. These suggested time intervals are intended only as guidelines and may vary according to institutional practices. It is important, however, that there be consistency within the individual patient program unless computerized pharmacokinetic dosing programs are available in the institution. These serum-level assays may be especially useful for monitoring the treatment of severe illness patients with changing renal function or of those infected with less susceptible organisms or those receiving maximum dosage.

Neuromuscular blockade and respiratory paralysis have been reported in cats receiving very high doses of tobramycin (40 mg/kg). The possibility of prolonged or secondary apnea should be considered if tobramycin is administered to anesthetized patients who are also receiving neuromuscular blocking agents, such as succinylcholine, tubocurarine, or decamethonium, or to patients receiving massive transfusions of citrated blood.
If neuromuscular blockade occurs, it may be reversed by the administration of calcium salts.

Cross-allergenicity among aminoglycosides has been demonstrated.

In patients with extensive burns or cystic fibrosis, altered pharmacokinetics may result in reduced serum levels of aminoglycosides. In such patients treated with tobramycin measurement of serum concentration is especially important as a basis for determination of appropriate dosage.

Elderly patients may have reduced renal function that 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. Monitoring of renal function during treatment with aminoglycosides is particularly important in the elderly (see PRECAUTIONS).

An increased incidence of nephrotoxicity has been reported following concomitant administration of aminoglycoside antibiotics and cephalosporins.

Aminoglycosides should be used with caution in patients with muscular disorders, such as myasthenia gravis or parkinsonism, since these drugs may aggravate muscle weakness because of their potential curare-like effect on neuromuscular function.

Aminoglycosides may be absorbed in significant quantities from body surfaces after local irrigation or application and may cause neurotoxicity and nephrotoxicity.

Aminoglycosides have not been approved for intraocular and/or subconjunctival use. Physicians are advised that macular necrosis has been reported following administration of aminoglycosides, including tobramycin, by these routes. See WARNINGS box regarding concurrent use of potent diuretics and concurrent and sequential use of other neurotoxic or nephrotoxic drugs.

The inactivation of tobramycin and other aminoglycosides by β-lactam-type antibiotics (pencillins or cephalosporins) has been demonstrated in vitro and in patients with severe renal impairment. Such inactivation has not been found in patients with normal renal function who have been given the drugs by separate routes of administration.

Therapy with tobramycin may result in overgrowth of nonsusceptible organisms. If overgrowth of nonsusceptible organisms occurs, appropriate therapy should be initiated.

Information for Patients

Patients should be counseled that antibacterial drugs including tobramycin injection should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When tobramycin injection is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken for the entire length of treatment, even if signs and symptoms of infection improve before the full course of therapy has been completed. Ineffective or inadequate therapy may result in the selection of bacteria less susceptible to tobramycin or other antibacterial drugs in the future.

Diarrhea is a common problem caused by antibiotics which usually ends when the antibacterial is discontinued. Sometimes after starting treatment with antibiotics, patients may be develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months after having taken the last dose of the antibiotic. If this occurs, patients should contact their physician as soon as possible.

Pregnancy Category D

Aminoglycosides can cause fetal harm when administered to a pregnant woman. Aminoglycoside antibiotics cross the placenta, and there have been several reports of total irreversible bilateral congenital deafness in children whose mothers received streptomycin during pregnancy. Serious side effects to mother, fetus, or newborn have not been reported in the treatment of pregnant women with other aminoglycosides. If tobramycin is used during pregnancy or if the patient becomes pregnant while taking tobramycin, she should be apprised of the potential hazard to the fetus.

Pediatric Use

See INDICATIONS AND USAGE and DOSAGE AND ADMINISTRATION.

Geriatric Use

Elderly patients may be at a higher risk of developing nephrotoxicity and otoxicity while receiving tobramycin (see WARNINGS, PRECAUTIONS, and OVERDOSAGE). Other factors that may contribute to nephrotoxicity and otoxicity are rising trough levels, excessive peak concentrations, dehydration, concomitant use of other neurotoxic or nephrotoxic drugs, and cumulative dose.

Peak and trough serum levels should be measured periodically during therapy to assure adequate levels and to avoid potentially toxic levels (see WARNINGS and PRECAUTIONS).

Tobramycin is known to be substantially excreted by the kidney, and use of tobramycin may require dosage adjustment in patients with impaired renal function. Dose reduction is required for patients with impaired renal function (see DOSAGE AND ADMINISTRATION). Elderly patients may have reduced renal function that 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. Monitoring of renal function during treatment with aminoglycosides is particularly important in the elderly (see PRECAUTIONS).

Tobramycin 80 mg/2 mL vial contains 1.573 mg (0.0684 mEq) of sodium.

Tobramycin 1200 mg/30 mL vial contains 23.599 mg (0.1261 mEq) of sodium.

ADVERSE REACTIONS

Neurotoxicity

Adverse effects on both the vestibular and auditory branches of the eighth nerve have been noted, especially in patients receiving high doses or prolonged therapy, in those given previous courses of therapy with an ototoxic, and in cases of dehydration. Symptoms include dizziness, vertigo, tinnitus, roaring in the ears, and hearing loss. Hearing loss is usually irreversible and is manifested initially by diminution of high-tone acuity. Tobramycin and gentamicin sulfaesates closely parallel each other in regard to ototoxic potential.

Nephrotoxicity

Renal function changes, as shown by rising BUN, NPN, and serum creatinine and by oliguria, cylindria, and increased proteinuria, have been reported, especially in patients with a history of renal impairment who are treated for longer periods or with higher doses than those recommended. Adverse renal effects can occur in patients with initially normal renal function.

Clinical studies and studies in experimental animals have been conducted to compare the nephrotoxic potential of tobramycin and gentamicin. In some of the clinical studies and in the animal studies, tobramycin causes nephrotoxicity significantly less frequently than gentamicin. In some other clinical studies, no significant difference in the incidence of nephrotoxicity between tobramycin and gentamicin was found.

Other reported adverse reactions possibly related to tobramycin include anemia, granulocytopenia, and thrombocytopenia; and fever, rash, exfoliative dermatitis, itching, urticaria, nausea, vomiting, diarrhea, headache, lethargy, pain at the injection site, mental confusion, and disorientation. Laboratory abnormalities possibly related to tobramycin include increased serum transaminases (AST, ALT); increased serum LDH and bilirubin; decreased serum calcium, magnesium, sodium, and potassium; and leukocytosis, and eosinophilia.

OVERDOSAGE

Signs and Symptoms

The severity of the signs and symptoms following a tobramycin overdose are dependent on the dose administered, the patient's renal function, state of hydration, and age and whether or not other medications with similar toxicities are being administered concurrently. Toxicity may occur in patients treated more than 10 days, in adults given more than 5 mg/kg/day, in pediatric patients given more than 7.5 mg/kg/day, or in patients with reduced renal function where dose has not been appropriately adjusted.

Nephrotoxicity following the parenteral administration of an aminoglycoside is most closely related to the area under the curve of the serum concentration versus time graph. Nephrotoxicity is more likely if trough blood concentrations fail to fall below 2 mg/L, and is also proportional to the average blood concentration. Patients who are elderly, have abnormal renal function, are receiving other nephrotoxic drugs, or are volume depleted are at greater risk for developing acute tubular necrosis. Auditory and vestibular toxicities have been associated with aminoglycoside overdose. These toxicities occur in patients treated longer than 10 days, in patients with abnormal renal function, in dehydrated patients, or in patients receiving medications with additive auditory toxicity.

These patients may not have signs or symptoms or may experience dizziness, tinnitus, vertigo, and a loss of high-tone acuity as ototoxicity progresses. Otoxicity signs and symptoms may not begin to occur until long after the drug has been discontinued.

Neuromuscular blockade or respiratory paralysis may occur following administration of aminoglycosides. Neuromuscular blockade, respiratory failure, and prolonged respiratory paralysis may occur more commonly in patients with myasthenia gravis or Parkinson's disease. Prolonged respiratory paralysis may also occur in patients receiving decamethonium, tubocurarine, or succinylcholine. If neuromuscular blockade occurs, it may be reversed by the administration of calcium salts but mechanical assistance may be necessary.

If tobramycin were ingested, toxicity would be less likely because aminoglycosides are poorly absorbed from an intact gastrointestinal tract.

Treatment

In all cases of suspected overdosage, call your Regional Poison Control Center to obtain the most up-to-date information about the treatment of overdose. This recommendation is made because, in general, information regarding the treatment of overdosage may change more rapidly than the package insert. In managing overdosage, consider the possibility of multiple drug overdoses, interaction among drugs, and unusual drug kinetics in your patient.

The initial intervention in a tobramycin overdose is to establish an airway and ensure oxygenation and ventilation. Resuscitative measures should be initiated promptly if respiratory paralysis occurs.

Patients who have received an overdose of tobramycin and who have normal renal function should be adequately hydrated to maintain a urine output of 3 to 5 mL/kg/hr. Fluid balance, creatinine clearance, and tobramycin plasma levels should be carefully monitored until the serum tobramycin level falls below 2 mcg/mL.

Patients in whom the elimination half-life is greater than 2 hours or whose renal function is abnormal may require more aggressive therapy. In such patients, hemodialysis may be beneficial.

DOSAGE AND ADMINISTRATION

Tobramycin may be given intramuscularly or intravenously. Recommended dosages are the same for both routes. The patient’s pretreatment body weight should be obtained for calculation of correct dosage. It is desirable to measure both peak and trough serum concentrations (see WARNINGS box and PRECAUTIONS).

Administration for Patients with Normal Renal Function

Adults with Serious Infections: 3 mg/kg/day in 3 equal doses every 8 hours (see Table 3).

Adults With Life-Threatening Infections: Up to 5 mg/kg/day may be administered in 3 or 4 equal doses (see Table 3). The dosage should be reduced to 3 mg/kg/day as soon as clinically indicated. To prevent increased toxicity due to excessive blood levels, dosage should not exceed 5 mg/kg/day unless serum levels are monitored (see WARNINGS box and PRECAUTIONS).
**Table 3**

DOSAGE SCHEDULE GUIDE FOR ADULT WITH NORMAL RENAL FUNCTION (Dosage at 8-Hour Intervals)

<table>
<thead>
<tr>
<th>For Patient Weighing</th>
<th>Usual Dose for Serious Infections 1 mg/kg q8h (Total, 3 mg/kg/day)</th>
<th>q8h</th>
<th>mL/dose *</th>
</tr>
</thead>
<tbody>
<tr>
<td>kg</td>
<td>lb</td>
<td>mg/dose</td>
<td>mL/dose *</td>
</tr>
<tr>
<td>120</td>
<td>264</td>
<td>120 mg</td>
<td>3 mL</td>
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<tr>
<td>115</td>
<td>253</td>
<td>115 mg</td>
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</tr>
<tr>
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<tr>
<td>105</td>
<td>231</td>
<td>105 mg</td>
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<td>220</td>
<td>100 mg</td>
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<td>95</td>
<td>210</td>
<td>95 mg</td>
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</tr>
<tr>
<td>40</td>
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<td>40 mg</td>
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*DOSAGE SCHEDULE GUIDE FOR ADULT WITH NORMAL RENAL FUNCTION (continued)/Dosage at 8-Hour Intervals*

<table>
<thead>
<tr>
<th>For Patient Weighing</th>
<th>Maximum Dose for Life-Threatening Infections (Reduce as soon as possible) 1.66 mg/kg q8h (Total 5 mg/kg/day)</th>
<th>q8h</th>
<th>mL/dose *</th>
</tr>
</thead>
<tbody>
<tr>
<td>kg</td>
<td>lb</td>
<td>mg/dose</td>
<td>mL/dose *</td>
</tr>
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<td>1.6 mL</td>
</tr>
</tbody>
</table>

*Applicable to all product forms except Tobramycin Injection Pediatric, 10 mg/mL.

Pediatric Patients (greater than 1 week of age): 6 to 7.5 mg/kg/day in 3 or 4 equally divided doses (2 to 2.5 mg/kg every 8 hours or 1.5 to 1.89 mg/kg every 6 hours).

Premature or Full-Term Neonates 1 Week of Age or Less: Up to 4 mg/kg/day may be administered in 2 equal doses every 12 hours.

It is desirable to limit treatment to a short term. The usual duration of treatment is 7 to 10 days. A longer course of therapy may be necessary in difficult and complicated infections. In such cases, monitoring of renal, auditory, and vestibular functions is advised, because neurotoxicity is more likely to occur when treatment is extended longer than 10 days.

**Dosage in Patients with Cystic Fibrosis**

In patients with cystic fibrosis, altered pharmacokinetics may result in reduced serum concentrations of aminoglycosides. Measurement of tobramycin serum concentration during treatment is especially important as a basis for determining appropriate dose. In patients with severe cystic fibrosis, an initial dosing regimen of 10 mg/kg/day in 4 equally divided doses is recommended. This dosing regimen is suggested only as a guide. The serum levels of tobramycin should be measured directly during treatment due to wide interpatient variability.

**Administration for Patients with Impaired Renal Function**

Whenever possible, serum tobramycin concentrations should be monitored during therapy.

Following a loading dose of 1 mg/kg, subsequent dosage in these patients must be adjusted, either with reduced doses administered at 8-hour intervals or with normal doses given at prolonged intervals. Both of these methods are suggested as guides to be used when dialysis is being performed.

Reduced dosage at 8-hour intervals: When the creatinine clearance rate is 70 mL or less per minute or when the serum creatinine value is known, the amount of the reduced dose can be determined by multiplying the normal dose from Table 3 by the percent of normal dose from the accompanying nomogram.

Normal dosage at prolonged intervals: If the creatinine clearance rate is not available and the patient’s condition is stable, a dosage frequency in hours for the dosage given in Table 3 can be determined by multiplying the patient’s serum creatinine by 6.

**Dosage in Obese Patients**

The appropriate dose may be calculated by using the patient’s estimated lean body weight plus 40% of the excess as the basic weight on which to figure mg/kg.

**Intramuscular Administration**

Tobramycin may be administered by withdrawing the appropriate dose directly from a vial.

**Intravenous Administration**

For intravenous administration, the usual volume of diluent (0.9% Sodium Chloride Injection or 5% Dextrose Injection) is 50 to 100 mL for adult doses. For pediatric patients, the volume of diluent should be proportionately less than that for adults. The diluted solution usually should be infused over a period of 20 to 60 minutes. Infusion periods of less than 20 minutes are not recommended because peak serum levels may exceed 12 mcg/mL (see WARNINGS box).

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

Prior to administration, parenteral drug products should be inspected visually for particulate matter and discoloration whenever solution and container permit.

**HOW SUPPLIED**

Tobramycin Injection, USP, in multiple dose vials, is supplied as follows:

- NDC 17478-114-02 40 mg/mL 2 mL in a 2 mL vial, packaged in 25
- NDC 17478-114-30 40 mg/mL 30 mL in a 30 mL vial, packaged in 1

Each vial of Tobramycin Injection contains tobramycin sulfate equivalent to 80 mg/2 mL or 1200 mg/30 mL of tobramycin and each mL contains tobramycin sulfate equivalent to 40 mg tobramycin, phenol 5 mg; sodium metabisulfite 3.2 mg; edetate disodium 0.1 mg and water for injection, q.s. sulfuric acid and/or sodium hydroxide may have been added to adjust the pH (3.0 to 6.5).

**Storage:** Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

This container closure is not made with natural rubber latex.

**REFERENCES**


**Akorn**

Manufactured by: Akorn, Inc.

Lake Forest, IL 60045

TDB00N Rev. 08/14
To order products call 800-932-5676
or fax 800-943-3694

www.akorn.com

NOT FOR PRESCRIBING PURPOSES. PLEASE REFER TO PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION INCLUDING BOXED WARNING.