Tobramycin Mylan

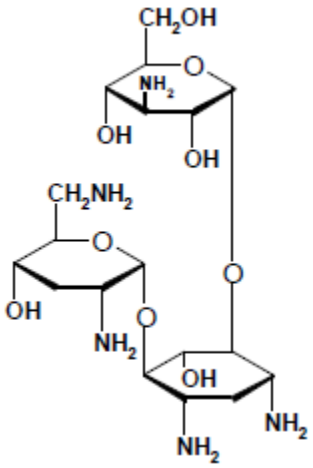
Tobramycin Solution for Injection

PRODUCT INFORMATION

NAME OF THE MEDICINE

Active ingredient	:	Tobramycin
Chemical name	:	D-Streptamine, *O*-3-amino-3-deoxy-α-D-glucopyranosyl-(1→6)-O-[2,6-diamino-2,3,6-trideoxy- α-D-*ribo*-hexopyranosyl-(1→4)]-2-deoxy.

Structural formula :



Molecular formula	:	$C_{18}H_{37}N_5O_9$	Molecular weight	:	467.51
			CAS Registry no.	:	32986-56-4

DESCRIPTION

Tobramycin is an aminoglycoside antibiotic obtained from cultures of *Streptomyces tenebrarius*. Tobramycin is a white to almost white hygroscopic powder. It is freely soluble in water and very slightly soluble in 96% ethanol.

Tobramycin Mylan is a clear, colourless solution. Each vial contains 80 mg tobramycin as active ingredient. The vials also contain disodium edetate 0.2 mg, sodium bisulfite 6.4 mg, sulfuric acid 44.14 mg and water for injections. Additionally sodium hydroxide may have been added to adjust the pH. The pH of the solution is approximately 6.0.

PHARMACOLOGY

Pharmacokinetics

Following intramuscular administration of a single dose of tobramycin 1 mg/kg in adults with normal renal function, peak plasma tobramycin concentrations averaging 4 to 6 micrograms per mL are obtained within 30 to 90 minutes; plasma concentrations of the drug are 1 microgram per mL or less at 8 hours. Following intravenous infusion of the same dose over 30 to 60 minutes, similar plasma concentrations of the drug are obtained. Tobramycin is poorly absorbed from the gastrointestinal tract. After injection tobramycin has been detected in body fluids but concentrations in the cerebrospinal fluid are low even when there is meningeal inflammation.

The major route of elimination is renal and the drug is eliminated almost entirely by glomerular filtration. Protein binding of tobramycin has been reported as zero. The plasma elimination half-life of tobramycin is usually 2 to

3 hours in adults with normal renal function and is reported to range from 5 to 70 hours in adults with impaired renal function. In full-term infants the plasma elimination half-life is reported to average 4.6 hours and in low birth-weight infants it averages 8.7 hours.

Peak urine concentrations ranging from 75 to 100 micrograms per mL have been observed after the intramuscular injection of a single dose of 1 mg/kg. After several days of treatment, the amount of tobramycin excreted in the urine approaches the daily amount administered. When renal function is impaired, excretion of tobramycin is slowed, and accumulation of the drug may cause toxic blood levels. In patients undergoing dialysis, 25 to 70% of the administered dose may be removed, depending on the duration and type of dialysis.

Microbiology

Tobramycin is bactericidal in activity. It enters the cells via a complex active transport mechanism and exerts its activity primarily on the 30S ribosomal subunit, interfering with initial and subsequent steps in protein synthesis. It also acts to induce misreading of the genetic code of the mRNA template, resulting in incorporation of incorrect amino acids.

Tobramycin, in common with all other aminoglycosides, is primarily antibacterial against aerobic gram-negative bacilli. Tobramycin is considered more active than most other aminoglycosides against *Pseudomonas aeruginosa*.

Tobramycin is usually active against most strains of the following organisms:

- *Pseudomonas aeruginosa*
- *Proteus* species (indole-positive and indole-negative) including: *Pr. mirabilis*;
- *Pr. morganii*; *Pr. rettgeri* and *Pr. vulgaris*
- *Escherichia coli*
- *Klebsiella, Enterobacter, Serratia* species
- *Citrobacter* species
- *Providencia* species
- *Staphylococci*, including *Staph. aureus* (coagulase-positive and coagulase-negative).

Aminoglycosides have a low order of activity against most gram-positive organisms, including *Streptococcus pyogenes*, *S. Pneumoniae* and *enterococci*.

Some strains of Group D *streptococci* are susceptible *in vitro* although most strains of *enterococci* show resistance. *In vitro* studies have shown that an aminoglycoside combined with an antibiotic which interferes with cell wall synthesis affects some group D streptococcal strains synergistically. The combination of benzylpenicillin and tobramycin results in a synergistic bactericidal effect *in vitro* against certain strains of *S. faecalis*. However, this combination is not synergistic against other closely related organisms, e.g. *S. faecium*. Specification of group D *streptococci* alone cannot, therefore, be used to predict susceptibility. Susceptibility testing and tests for antibiotic synergism are emphasised.

Cross resistance between aminoglycosides occurs and depends largely on inactivation by bacterial enzymes.

INDICATIONS

Tobramycin is indicated in the treatment of the following serious infections caused by susceptible micro-organisms:

- central nervous system infections, including meningitis;

- septicaemia and neonatal sepsis;
- gastro-intestinal infections, including peritonitis;
- complicated and recurrent urinary tract infections such as pyelonephritis and cystitis;
- lower respiratory tract infections, including pneumonia, bronchopneumonia and acute bronchitis;
- bone, skin and skin structure infections, including burns.

Tobramycin may be considered in serious staphylococcal infections for which penicillin or other less potentially toxic drugs are contraindicated and when bacterial susceptibility testing and clinical judgement indicate its use. Aminoglycosides, including tobramycin, are not indicated in uncomplicated initial episodes or urinary tract infections unless the causative organisms are not susceptible to antibiotics having less potential toxicity.

Bacterial cultures should be obtained prior to and during treatment to isolate and identify aetiologic organisms and to test their susceptibility to tobramycin. If susceptibility tests show that the causative organism is resistant to tobramycin, other appropriate therapy should be instituted. In patients in whom gram negative septicaemia, neonatal sepsis, or meningitis is suspected, including those in whom concurrent therapy with a penicillin or cephalosporin and an aminoglycoside may be indicated, tobramycin therapy may be initiated before results of susceptibility studies are obtained. The decision to continue tobramycin therapy should be based upon the results of susceptibility studies, severity of the infection, and the important additional concepts discussed under **PRECAUTIONS**.

CONTRAINDICATIONS

Patients with a history of previous hypersensitivity to tobramycin or to any of the components of Tobramycin Mylan.

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.

PRECAUTIONS

Bacterial cultures should be obtained before and during treatment to isolate and identify aetiologic organisms and to test their susceptibility to tobramycin. If the organisms are resistant other appropriate therapy should be instituted. In patients in whom gram negative septicaemia, neonatal sepsis or meningitis is suspected, including those in whom concurrent therapy with a penicillin or cephalosporin and an aminoglycoside may be indicated, tobramycin therapy may be initiated before results of susceptibility studies are obtained.

Cross-allergenicity among aminoglycosides has been known to occur.

Serum and urine should be monitored during therapy, including peak and trough drug levels; serum creatinine and creatinine clearance; serum calcium, magnesium and sodium; urinary specific gravity excretion of protein, cells and casts.

Patients treated with aminoglycoside antibiotics should be under close clinical observation because these drugs have the inherent potential for causing ototoxicity and nephrotoxicity. Tobramycin has an inherent potential for causing ototoxicity and nephrotoxicity, particularly if patients have pre-existing renal damage or if the drug is administered for longer periods or at higher doses than those recommended.

Both vestibular and auditory ototoxicity can occur. The auditory changes are irreversible, usually bilateral, and may be partial or total. Aminoglycoside induced nephrotoxicity is usually reversible. Eighth nerve impairment may develop in patients with pre-existing renal damage and if tobramycin is administered for longer periods or in higher doses than those 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 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 manifest until the first few days after cessation of therapy. Tobramycin is potentially nephrotoxic; therefore, renal and eighth nerve function should be closely monitored, particularly 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. 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 in renal, vestibular, and/or auditory function requires discontinuation of the drug, (or dosage adjustment, if continuation of therapy is considered essential).

Peak and trough serum levels should be measured periodically during therapy, and prolonged concentrations above 12 micrograms/mL should be avoided. Rising trough levels (above 2 micrograms/mL) may indicate tissue accumulation. Such accumulation, excessive peak concentrations, advanced age, dehydration, and cumulative dose may contribute to ototoxicity and nephrotoxicity. Urine should be examined for decreased specific gravity and increased excretion of protein, cells, and casts. Experience with gentamicin suggests that ototoxicity may develop at peak levels below 12 micrograms/mL. Care should be taken to avoid trough levels in excess of approximately 3 micrograms/mL in conjunction with a degree of renal failure and a treatment period beyond 10 to 14 days. It is particularly important to monitor serum levels closely in patients with known renal impairment.

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 also 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 (see **DOSAGE AND ADMINISTRATION**).

In order to measure the peak level, a serum sample should be drawn about 30 minutes after completion of the intravenous infusion or 1 hour after an intramuscular injection. Trough levels are measured by obtaining serum samples 8 hours after the dose 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.

Renal and eighth nerve function should be closely monitored in patients in whom renal impairment is known or who develop signs of dysfunction during therapy. Evidence of impairment in renal, vestibular and/or auditory function requires discontinuation of the drug or dosage adjusted.

Elderly patients may have reduced renal function that may not be evident in the results of routine screening tests, such as serum urea or serum creatinine. A creatinine clearance determination may be more useful. Monitoring of renal function during treatment with aminoglycosides is particularly important in such patients.

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

Tobramycin 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.

In patients with extensive burns, altered pharmacokinetics may result in reduced serum drug levels. Dosage must be based on measured serum levels in these patients.

Absorption from body surfaces after local irrigation or application may be significant and may lead to neurotoxicity or nephrotoxicity.

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

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.

If overgrowth of nonsusceptible organisms occurs, appropriate therapy should be initiated.

Tobramycin Mylan contains sodium bisulfite which may cause allergic type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people.

Use in pregnancy (Category D)

Tobramycin and other aminoglycosides are known to cross the placenta. There is evidence of selective uptake of aminoglycosides by the foetal kidney resulting in cellular damage (probably reversible) to immature nephrons. Eighth cranial nerve damage has also been reported following *in utero* exposure to some of the aminoglycosides. Because of their chemical similarity, aminoglycosides must be considered potentially nephrotoxic and ototoxic to the foetus. It should also be noted that therapeutic blood levels in the mother do not equate with safety for the foetus.

Aminoglycosides, including tobramycin, cross the placental membrane producing foetal serum levels 25 to 50% of those found in maternal serum.

Australian categorisation definition of:
Category D: Drugs which have caused, are suspected to have caused or may be expected to cause, an increased incidence of human foetal malformations or irreversible damage. These drugs may also have adverse pharmacological effects. Accompanying text above should be consulted for further details.

Use in lactation

Tobramycin is excreted in milk with concentrations of 0.60 and 0.85 micrograms/mL at one and eight hours after an IM dose of 80 mg. It is not known whether it is harmful to the newborn.

INTERACTIONS WITH OTHER MEDICINES

Potent diuretics: If possible, do not give tobramycin in conjunction with ethacrynic acid, frusemide or other potent diuretics which may themselves cause ototoxicity or enhance aminoglycoside toxicity by altering antibiotic concentrations in serum and tissue.

Other neurotoxic and/or nephrotoxic agents: If possible, avoid concurrent or sequential use of other neurotoxic and/or nephrotoxic antibiotics, particularly other aminoglycosides, cephaloridine, polymyxin B, colistin, cisplatin and vancomycin.

Neuromuscular blocking agents or other medications with neuromuscular blocking activity: Care is required if other drugs with a neuromuscular blocking action are given concomitantly with aminoglycosides (see **PRECAUTIONS**, use in anaesthetic practice). The neuromuscular blocking properties of aminoglycosides may be sufficient to provoke severe respiratory depression in patients receiving general anaesthetics or opioids.

Amphotericin B: May produce synergistic renal toxicity.

Methoxyflurane: May produce additive or synergistic nephrotoxicity. Renal impairment may appear at lower than usual dosage levels of the drug.

Beta lactam antibiotics: Since aminoglycosides have been shown to be incompatible with some beta lactams *in vitro,* these antibiotics should be administered separately if both are required. Antagonism *in vivo* has been reported only in a few patients with severe renal impairment, in whom aminoglycoside activity was diminished.

ADVERSE EFFECTS

Tobramycin ototoxicity presents as vestibular dysfunction with or without high frequency hearing loss, similar to that of other aminoglycosides. In addition it may produce transient cochlear toxicity, perhaps due to a metabolic block.

Ototoxic damage may progress in some patients even after the drug is discontinued. Factors associated with increased incidence of ototoxicity include advanced age, underlying renal disease, previous auditory damage, duration of treatment; elevated body temperature, low haematocrit, severity of illness and total dose of drug.

Genito-Urinary: Renal function changes, as shown by rising serum urea, NPN, and serum creatinine and by oliguria, cylindruria, 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.

Musculoskeletal: The aminoglycosides are known to possess neuromuscular blocking effects and to be capable of exacerbating impairment of neuromuscular transmission in clinical conditions such as myasthenia gravis or severe hypocalcaemia, or when used in conjunction with nondepolarising neuromuscular relaxants such as d-tubocurarine.

Neuromuscular blockade may result in weakness of skeletal muscles and respiratory depression especially in patients with myasthenia gravis, severe hypocalcaemia or who have recently received other neuromuscular blocking agents. Peritoneal lavage with tobramycin could precipitate apnoea because high concentrations of drug come in contact with the diaphragm. Rarely blockade has been observed following intramuscular or intravenous injection. Tobramycin is usually safely used prior to surgery if given in recommended single doses.

Biochemical abnormalities: Some patients with malignant diseases have developed a complex metabolic syndrome of 2 to 8 weeks duration after administration of tobramycin, including hypocalcaemia, hypomagnesaemia, hypokalaemia, hypo-albuminaemia, hypophosphataemia and hypouricaemia.

Other reported abnormalities include increased AST, ALT, serum bilirubin and alkaline phosphatase.

Dermatological: Maculopapular rash, urticaria, itching; pain after intramuscular use and thrombophlebitis after intravenous use.

Gastrointestinal: Nausea and vomiting.

Haematological and reticulo-endothelial: Anaemia, granulocytopenia and thrombocytopenia; eosinophilia, decreased platelet and white cell counts.

Immunological: Fever, rash, itching, urticaria. Adverse effects on the immune response via inhibition of chemotaxis and microbicidal activity of phagocytes have been reported. Angioedema, exfoliative dermatitis, stomatitis and anaphylaxis are hypersensitivity reactions reported with aminoglycosides in general.

Nervous system: Lethargy. Acute brain syndrome has been reported in an elderly patient after four days of therapy with tobramycin. The delirium was reversed after drug discontinuance.

DOSAGE AND ADMINISTRATION

Contains no antimicrobial agent. Product is for single use in one patient only. Discard any residue.

Adult

Tobramycin may be given intramuscularly or intravenously (see below) and the dosage is the same for either route of administration. It is desirable to measure both peak and trough serum concentrations (see **PRECAUTIONS**). The patient's pretreatment body weight should be obtained for calculation of correct dosage. In obese patients, the appropriate dose may be calculated by using the patient's estimated lean body weight plus 40 percent of the excess as the basic weight on which to figure mg/kg.

Intramuscular administration

Dosage for patients with normal renal function:

a. Serious infections: 3 mg/kg/day in three equal doses every eight hours.

b. Mild to moderate urinary tract infections: 2 to 3 mg/kg/day in two or three equally divided doses.

c. Life threatening infections: Dosages up to 5 mg/kg/day in 3 or 4 equal doses with reduction to 3 mg/kg/day as soon as clinically indicated. Dosage should not exceed 5 mg/kg/day unless serum levels are monitored.

The following table may be used as a guide:

DOSAGE SCHEDULE GUIDE FOR ADULTS WITH NORMAL RENAL FUNCTION (Dosage at eight-hour intervals)

Patient bodyweight (kg)	Usual dose for serious infections 1 mg/kg every 8 hours (total 3 mg/kg/day)		Maximum dose for life-threatening infections 1.66 mg/kg every 8 hours (total 5 mg/kg/day with reduction to 3mg/kg/day as soon as clinically indicated)	
	Dose every eight hours			
	mg/dose	mL/dose	mg/dose	mL/dose
120	120	3.0	200	5.0
110	110	2.75	183	4.5
100	100	2.5	166	4.2
90	90	2.25	150	3.75
80	80	2.0	133	3.3
70	70	1.75	116	2.9
60	60	1.5	100	2.5
50	50	1.25	83	2.1
40	40	1.0	66	1.6

The usual duration of treatment is seven to ten days. A longer course may be necessary in difficult 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 ten days.

Dosage 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 must be adjusted either with lower doses at 8 hour intervals or with normal doses at prolonged intervals. Both methods are only guides to be used when serum levels of drug cannot be monitored. They are based on creatinine clearance or serum creatinine levels, because these values correlate with the half-life of tobramycin. Neither regimen should be used when dialysis is being performed.

Reduced Dosage at eight hour intervals (Regimen I):

An appropriate reduced dosage range can be found in the accompanying table for any patient for whom the creatinine clearance or serum creatinine values are known. The choice of dose within the indicated range should be based on the severity of the infection, the susceptibility of the pathogen, and individual patient considerations, especially renal function. An alternate rough guide for determining reduced dosage at eight hour intervals (for patients whose steady state serum creatinine values are known) is to divide the normally recommended dose by the patient's serum creatinine expressed as mg percent.

Prolonged intervals between fixed doses (Regimen II):

Recommended intervals between doses are given in the accompanying table. As a general rule, the dosage frequency in hours can be determined by multiplying the patient's serum creatinine level expressed as mg percent by six.

The dosage schedule derived from either method should be used in conjunction with careful clinical and laboratory observations of the patient and should be modified as necessary.

TWO MAINTENANCE REGIMENS BASED ON RENAL FUNCTION AND BODY WEIGHT FOLLOWING A LOADING DOSE OF 1 mg/kg*

Renal Function†			**REGIMEN I** Adjusted doses at 8 hour intervals		**REGIMEN II** Adjusted intervals between fixed dose	
Serum Creatinine		Creatinine Clearance	50 – 60 kg	60 – 80 kg	Fixed dose for 50 – 60 kg = 60 mg	Fixed dose for 60 – 80 kg = 80 mg
mg %	mmol/L	mL/min				
< 1.4	< 0.12	> 69	60 mg	80 mg	8 h	
1.4 – 1.9	0.12 – 0.17	69 – 40	30 – 60 mg	50 – 80 mg	12 h	
2.0 – 3.3	0.18 – 0.29	39 – 20	20 – 25 mg	30 – 45 mg	18 h	
3.4 – 5.3	0.30 – 0.46	19 – 10	10 – 18 mg	15 – 24 mg	24 h	
5.4 – 7.5	0.47 – 0.66	9 – 5	5 – 9 mg	7 – 12 mg		
> 7.5	> 0.66	< 5	2.5 – 4.5 mg	3.5 – 6 mg		

*For life threatening infections, dosages 50 percent above those recommended may be used. The dosages should be reduced as soon as possible after improvement is noted.

†If used to estimate degree of renal impairment, serum creatinine concentrations should reflect a steady state of renal azotaemia.

Intravenous use

Tobramycin may be further diluted for infusion in Sodium Chloride Intravenous Infusion 0.9% or Glucose Intravenous Infusion 5%. To reduce microbiological hazard, use as soon as practicable after preparation. If storage is necessary, hold at 2 to 8°C for not more than 24 hours.

The intravenous dose is the same as the intramuscular dose. The usual volume of diluent for adult doses is 50 to 100 mL. For children, the volume of diluent should be proportionately less than for adults. The diluted solution should usually be infused over a period of 20 to 30 minutes. Infusion periods of less than 20 minutes may cause peak serum levels to exceed 12 micrograms/mL (see **PRECAUTIONS**).

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

Paediatric

Tobramycin may be given intramuscularly or intravenously. For intravenous administration, the volume of diluent should be proportionately less than for adults.

1. Children and older infants: 6 to 7.5 mg/kg/day in 3 or 4 equally divided doses (2 to 2.5 mg/kg every eight hours, or 1.5 to 1.89 mg/kg every six hours.

2. Neonates (one week of age or less): Up to 4 mg/kg per day may be administered in two equal doses every 12 hours.

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

OVERDOSAGE

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, given more than 5 mg/kg/day, children given more than 7.5 mg/kg/day, or patients with reduced renal function whose 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 to below 2 micrograms/mL 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 toxicities. These patients may not have signs or symptoms or may experience dizziness, tinnitus, vertigo, and loss of high-tone acuity as ototoxicity progresses. Ototoxicity 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, prolonged respiratory paralysis and respiratory failure 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 suxamethonium. If neuromuscular blockade occurs, it may be reversed by the administration of calcium salts but controlled or assisted ventilation may be necessary.

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

Treatment

In managing overdosage, consider the possibility of multiple drug overdoses, interaction among drugs, and unusual drug kinetics in the 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 that have received an overdose of tobramycin and 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 micrograms/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, haemodialysis may be beneficial.

For information on the management of overdosage, contact the Poison Information Centre on 13 11 26 (Australia).

PRESENTATION AND STORAGE CONDITIONS

Tobramycin Mylan : It is a clear, colorless sterile liquid available in 2 mL glass vials in cartons of 1, 5 and 10 vials.

Tobramycin Mylan should be stored below 25°C. Protect from light.

Some pack sizes may not be marketed.

NAME AND ADDRESS OF SPONSOR

Alphapharm Pty Limited

Level 1, 30 The Bond

30-34 Hickson Road

Millers Point NSW 2000

ABN 93 002 359 739

www.mylan.com.au

POISON SCHEDULE OF THE MEDICINE

S4 (Prescription Only Medicine)

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (the ARTG)

25 February 2016

DATE OF MOST RECENT AMENDMENT

9 February 2017