AMINOGLYCOSIDES (Systemic)

Amikacin¾AM300

Indications
Biliary tract infections (treatment)¾Amikacin, gentamicin, kanamycin, netilmicin, and tobramycin are indicated in the treatment of biliary tract infections caused by susceptible organisms.

Bone and joint infections (treatment)¾Amikacin, gentamicin, kanamycin, netilmicin, and tobramycin are indicated in the treatment of bone and joint infections caused by susceptible organisms.

Brucellosis (treatment)¾Streptomycin is indicated in the treatment of brucellosis caused by Brucella species.

Central nervous system infections (including meningitis and ventriculitis) (treatment)¾Amikacin, gentamicin, kanamycin, netilmicin, and tobramycin are indicated in the treatment of central nervous system infections caused by susceptible organisms.

Granuloma inguinale (treatment)¾Streptomycin is indicated in the treatment of granuloma inguinale.

Intra-abdominal infections (including peritonitis)(treatment)¾Amikacin, gentamicin, kanamycin, netilmicin, and tobramycin are indicated in the treatment of intra-abdominal infections caused by susceptible organisms.

Plague (treatment)¾Streptomycin is indicated in the treatment of plague.

Pneumonia, gram-negative, bacterial (treatment)¾Amikacin, gentamicin, kanamycin, netilmicin, and tobramycin are indicated in the treatment of bacterial, gram-negative pneumonia caused by susceptible organisms.

Septicemia, bacterial (treatment)¾Amikacin, gentamicin, kanamycin, netilmicin, and tobramycin are indicated in the treatment of bacterial septicemia caused by susceptible organisms.

Skin and soft tissue infections (including burn wound infections) (treatment)¾Amikacin, gentamicin, kanamycin, netilmicin, and tobramycin are indicated in the treatment of skin and soft tissue infections caused by susceptible organisms.

Tuberculosis (treatment)¾Streptomycin is indicated in the treatment of tuberculosis.

Tularemia (treatment)¾Streptomycin is indicated in the treatment of tularemia.

Urinary tract infections (recurrent complicated)(treatment)¾Amikacin, gentamicin, kanamycin, netilmicin, and tobramycin are indicated in the treatment of recurrent complicated urinary tract infections caused by susceptible organisms.

Not all species or strains of a particular organism may be susceptible to a specific aminoglycoside.

Mechanism of action/Effect:

Actively transported across the bacterial cell membrane, irreversibly binds to one or more specific receptor proteins on the 30 S subunit of bacterial ribosomes, and interferes with an initiation complex between messenger RNA (mRNA) and the 30 S subunit. DNA may be misread, thus producing nonfunctional proteins; polyribosomes are split apart and are unable to synthesize protein. This results in accelerated aminoglycoside transport, increasing the disruption of bacterial cytoplasmic membranes, and eventual cell death. 79

Cross-sensitivity and/or related problems

Patients hypersensitive to one aminoglycoside may be hypersensitive to other aminoglycosides also. 70, 71, 72, 73, 74

Carcinogenicity/Mutagenicity/Tumorigenicity

Amikacin and kanamycin¾Studies on the carcinogenic or mutagenic effects in humans have not been done. 56, 58, 70, 72

Netilmicin¾Lifetime carcinogenicity studies in mice and rats have not shown any netilmicin-related tumors. Mutagenicity studies in mice and rats have shown negative results. 73

Pregnancy/Reproduction

Fertility¾Amikacin: Reproduction studies in rats and mice have not shown that amikacin causes impaired fertility. 56, 70

Gentamicin: Reproduction studies in rats and rabbits have not shown that gentamicin causes impaired fertility. 49, 57

Amikacin: Adequate and well-controlled studies in humans have not been done. Amikacin has not been shown to cause adverse effects on the fetus, even though peak fetal serum concentrations of amikacin average approximately 16% of peak maternal serum concentrations and amikacin may be concentrated in the fetal kidneys. However, since other aminoglycosides have been reported to cause deafness in the fetus, risk-benefit must be carefully considered when this medication is required in life-threatening situations or in serious diseases for which other medications cannot be used or are ineffective. 56, 70

Geriatrics

Because of their toxicity, aminoglycosides should be used with caution in elderly patients, only after less toxic alternatives have been considered and/or found ineffective. Elderly patients are more likely to

have an age-related decrease in renal function. 71 Recommended doses should not be exceeded, and the patient's renal function should be carefully monitored during therapy. Geriatric patients may require smaller daily doses of aminoglycosides in accordance with their increased age, decreased renal function, and, possibly, decreased weight. 61 In addition, loss of hearing may result even in patients with normal renal function.

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):

Note: Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.

>> Aminoglycosides, 2 or more concurrently or

>> Capreomycin 52, 62, 70, 71, 72, 73, 74, 99

(concurrent and/or sequential use of 2 or more aminoglycosides by any route or concurrent use of capreomycin with aminoglycosides should be avoided since the potential for ototoxicity, nephrotoxicity, and neuromuscular blockade may be increased; hearing loss may occur and may progress to deafness even after discontinuation of the drug; loss of hearing may be reversible, but usually is permanent; neuromuscular blockade may result in skeletal muscle weakness and respiratory depression or paralysis [apnea]. Also, concurrent use of 2 or more aminoglycosides may result in reduced bacterial uptake of each one since the medications compete for the same uptake mechanism)

Antimyasthenics 84, 85

(concurrent use of medications with neuromuscular blocking action may antagonize the effect of antimyasthenics on skeletal muscle; temporary dosage adjustments of antimyasthenics may be necessary to control symptoms of myasthenia gravis during and following use of medications with neuromuscular blocking action)

Beta-lactam antibiotics 55, 109, 120

(aminoglycosides can be inactivated by many beta-lactam antibiotics [cephalosporins, penicillins] in vitro and in vivo in patients with significant renal failure. Degradation depends on the concentration of the beta-lactam, storage time, and temperature)

Indomethacin, intravenous 54

(when aminoglycosides are administered concurrently with intravenous indomethacin in the premature neonate, renal clearance of aminoglycosides may be decreased, leading to increased plasma concentrations, elimination half-lives, and risk of aminoglycoside toxicity; dosage adjustment of aminoglycosides based on measurement of plasma concentrations and/or evidence of toxicity may also be required)

>> Methoxyflurane or 102

>> Polymyxins, parenteral 62, 70, 71, 72, 73, 74

(concurrent and/or sequential use of these medications with aminoglycosides should be avoided since the potential for nephrotoxicity and/or neuromuscular blockade may be increased; neuromuscular blockade may result in skeletal muscle weakness and respiratory depression or paralysis [apnea]; caution is also recommended when methoxyflurane or polymyxins are used concurrently with aminoglycosides during surgery or in the postoperative period)

>> Nephrotoxic medications, other(See Appendix II) or

>> Ototoxic medications, other (See Appendix II) 70, 71, 72, 73, 74, 83, 87, 88

(concurrent or sequential use of these medications with aminoglycosides may increase the potential for ototoxicity or nephrotoxicity; hearing loss may occur and may progress to deafness even after discontinuation of the drug and may be reversible, but usually is permanent; serial audiometric function determinations may be required with concurrent or sequential use of other ototoxic antibacterials; renal function determinations may be required)

(vancomycin and aminoglycosides must often be administered concurrently in the prophylaxis of bacterial endocarditis, in the treatment of endocarditis caused by streptococci and Corynebacteria species, in the treatment of resistant staphylococcal infections, or in penicillin-allergic patients; appropriate monitoring will help to reduce the risk of nephrotoxicity or ototoxicity; renal function determinations, serum aminoglycoside and vancomycin concentrations, dosage reductions, and/or dosage interval adjustments, or alternate antibacterials, may be required)

>> Neuromuscular blocking agents or medications with neuromuscular blocking activity, other 3

(concurrent use of medications with neuromuscular blocking activity, including halogenated hydrocarbon inhalation anesthetics, opioid analgesics, and massive transfusions with citrate anticoagulated blood, with aminoglycosides should be carefully monitored since neuromuscular blockade may be enhanced, resulting in skeletal muscle weakness and respiratory depression or paralysis [apnea]; caution is recommended when these medications and aminoglycosides are used concurrently during surgery or in the postoperative period, especially if there is a possibility of incomplete reversal of neuromuscular blockade postoperatively; treatment with anticholinesterase agents or calcium salts may help reverse the blockade)

Laboratory value alterations

The following have been selected on the basis of their potential clinical significance (possible effect in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):

With physiology/laboratory test values¾Alanine aminotransferase (ALT [SGPT]), serum and

Alkaline phosphatase, serum and

Aspartate aminotransferase (AST [SGOT]), serum and

Bilirubin, serum and

Lactate dehydrogenase (LDH), serum

(values may be increased 46, 47, 48, 49, 50, 51, 52, 53, 71)

Blood urea nitrogen (BUN) and

Creatinine, serum

(concentrations may be increased 46, 47, 48, 49, 50, 51, 52, 53, 71)

Calcium, serum and

Magnesium, serum and

Potassium, serum and

Sodium, serum

(concentrations may be decreased 47, 48, 49, 71, 73)

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)¾ not necessarily inclusive (>> = major clinical significance).

Risk-benefit should be considered when the following medical problems exist

>> Botulism, infant or 72

>> Myasthenia gravis or 47, 48, 49, 51, 70, 72, 74, 84

>> Parkinsonism

(aminoglycosides may cause neuromuscular blockade, resulting in further skeletal muscle weakness)

Dehydration or 70

>> Renal function impairment 46, 47, 48, 49, 50, 51, 52, 53, 70, 71, 72, 73, 74

(possible increased risk of toxicity because of elevated serum concentrations; it is recommended that aminoglycosides be administered in a reduced dosage at a fixed interval, or in normal doses at prolonged intervals, to patients with impaired renal function)

>> Eighth-cranial-nerve impairment 46, 47, 48, 49, 50, 51, 52, 53, 70, 72, 74

(aminoglycosides may cause auditory and vestibular toxicity)

>> Previous allergic reaction to aminoglycosides 70, 71, 72, 73, 74

(hypersensitivity reaction to one aminoglycoside may contraindicate the use of other aminoglycosides due to known cross-sensitivity)

Patient monitoring

The following may be especially important in patient monitoring (other tests may be warranted in some patients, depending on condition; >> = major clinical significance):

For all aminoglycosides 70, 71, 72, 73, 74

>> Aminoglycoside concentrations, serum

(aminoglycoside levels should be monitored in all patients, especially neonates and the elderly, even without renal function impairment, to avoid potentially toxic concentrations from accumulation of the drug; peak levels should be drawn 30 minutes after a 30-minute aminoglycoside infusion, to allow for drug distribution, and trough levels, immediately prior to the next dose; see General Dosing Information)

>> Audiograms and

>> Renal function determinations and

>> Vestibular function determinations

(may be required prior to, periodically during, and following treatment in patients with pre-existing renal or eighth-cranial-nerve impairment; twice-weekly or weekly audiometric testing to detect high-frequency hearing loss in patients old enough to be tested and daily renal function determinations may be required in patients on high-dose therapy or therapy continued for longer than 10 days, especially if renal function is changing; renal function determinations may be required to detect nephrotoxicity and to help prevent severe neurotoxic reactions; audiometric testing may also be required with concurrent or sequential administration of other ototoxic antibacterials; if renal, vestibular, or auditory function impairment occurs, reduction in dose or discontinuation of the aminoglycoside may be required)

>> Urinalyses

(may be required prior to treatment and daily during treatment to detect albumin, casts, and cells in the urine, as well as decreased specific gravity 56, 70)

For streptomycin

>> Caloric stimulation tests

(may also be required prior to, periodically during, and following prolonged therapy to detect vestibular toxicity)

Side/Adverse Effects

Note: Leg cramps, skin rash, fever, and seizures have been reported when gentamicin was administered concurrently by the systemic and intrathecal routes.

Endotoxin-like reactions (shaking, chills, and fever) have been reported with once-daily dosing regimens of gentamicin, possibly due to elevated endotoxin levels in certain brands of the drug 126, 127.

Neuromuscular blockade, respiratory paralysis, ototoxicity, and nephrotoxicity may occur following local irrigation and following topical application of aminoglycosides during surgery.

Because of its potential toxicity, use of parenteral neomycin is not recommended.

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)¾not necessarily inclusive:

Those indicating need for medical attention

Incidence more frequent

Nephrotoxicity (greatly increased or decreased frequency of urination or amount of urine; increased thirst; loss of appetite; nausea; vomiting); neurotoxicity (muscle twitching; numbness; seizures; tingling); ototoxicity, auditory (any loss of hearing; ringing or buzzing, or a feeling of fullness in the ears); ototoxicity, vestibular (clumsiness; dizziness; nausea; vomiting; unsteadiness); peripheral neuritis (burning of face or mouth; numbness; tingling)¾ streptomycin only

Incidence less frequent

Hypersensitivity (skin itching, redness, rash, or swelling); optic neuritis (any loss of vision)¾streptomycin only

Incidence rare

Endotoxin-like reaction 126, 127 (shaking; chills; fever)¾gentamicin only; neuromuscular blockade (difficulty in breathing; drowsiness; weakness)

Those indicating possible ototoxicity, vestibular toxicity, or nephrotoxicity and the need for medical attention if they occur and/or progress after medication is discontinued

Any loss of hearing; clumsiness or unsteadiness; dizziness; greatly increased or decreased frequency of urination or amount of urine; increased thirst; loss of appetite; nausea or vomiting; ringing or buzzing or a feeling of fullness in the ears

Overdose

For more informatin on the management of overdose or unintentional ingestion, contact a Poison Control Center (See Poison Control Center Listing).

Treatment of overdose

Specific treatment¾Hemodialysis or peritoneal dialysis to remove aminoglycosides from the blood of patients with impaired renal function. 71, 73

Anticholinesterase agents, calcium salts, or mechanical respiratory assistance to treat neuromuscular blockade, resulting in prolonged skeletal muscle weakness and respiratory depression or paralysis (apnea), that may occur when two or more aminoglycosides are given concurrently. 74

Supportive care¾Since there is no specific antidote, treatment of aminoglycoside overdose or toxic reactions should be symptomatic and supportive. Patients in whom intentional overdose is known or suspected should be referred for psychiatric consultation.

Patient Consultation

As an aid to patient consultation, refer to Advice for the Patient, Aminoglycosides (Systemic) .

In providing consultation, consider emphasizing the following selected information (>> = major clinical significance):

Before using this medication

>> Conditions affecting use, especially:

Hypersensitivity to aminoglycosides

Pregnancy¾May be nephrotoxic in the fetus or cause irreversible deafness in children whose mothers received aminoglycosides during pregnancy

Use in children¾Premature infants and neonates may be more susceptible to renal toxicity because of their immature renal capability

Use in the elderly¾Geriatric patients may be at risk of renal toxicity because of an age-related decrease in renal function

Other medications, especially 2 or more aminoglycosides used together, capreomycin, other nephrotoxic or ototoxic medications, or other neuromuscular blocking agents

Other medical problems, especially eighth-cranial-nerve impairment, infant botulism, myasthenia gravis, parkinsonism, or renal function impairment

Proper use of this medication

>> Importance of receiving medication for full course of therapy and on regular schedule

>> Proper dosing

Side/adverse effects

Signs of potential side effects, especially hypersensitivity, shaking, chills, fever, optic neuritis, neuromuscular blockade, nephrotoxicity, neurotoxicity, auditory and vestibular ototoxicity, and peripheral neuritis, which are more likely to occur in children and the elderly

General Dosing Information

Because of the low therapeutic index of aminoglycosides, it is best to base dosage calculations on ideal body weight (IBW) as follows:
IBW (males) = 50 kg + (2.3 kg ´ inches over 5 feet)
IBW (females) = 45 kg + (2.3 kg ´ inches over 5 feet)

Serum concentrations should be monitored, especially in neonates and the elderly, even without renal function impairment, and in patients with impaired renal function to ensure adequate concentrations and to avoid potentially toxic concentrations. Therapeutic concentrations are shown in the table below. Prolonged peak (post-distributional) concentrations(measured 15 to 30 minutes after injection) and trough concentrations (measured immediately prior to the next dose) 56, 70 greater than those shown below should be avoided 62, 70, 71, 72, 73.

Drug	Therapeutic Concentration (mcg/mL)	Maximum Peak Concentration (mcg/mL)	Maximum Trough Concentration (mcg/mL)
Amikacin	15-25	35	5
Gentamicin	4-10	10	2
Kanamycin	15-30	30-35	5
Netilmicin	6-12	16	2
Streptomycin	-	20-25 a	-
Tobramycin	4-10	10	2

a In patients with renal damage. Peak concentrations greater than 50 mcg per mL are associated with increased risk of toxicity.

Because of their larger volume of distribution and reduced renal development, infants may require larger doses, given at less frequent intervals, for achievement of therapeutic serum concentrations. Cystic fibrosis patients and burn patients may also require larger doses, but because they eliminate the aminoglycoside faster than average, the dosing interval may need to be decreased too.

Serum concentrations should be used whenever possible to monitor aminoglycoside therapy. Creatinine clearance may be used to help monitor therapy, in conjunction with serum levels. Creatinine clearance (in mL per minute) may be calculated as follows: 73

Adult males: Creatinine clearance

= [(140 - age) ´ (ideal body weight in kg)]/[72 ´ serum creatinine (mg per dL)]

Adult females: Creatinine clearance

= [(140 - age) ´ (ideal body weight in kg)]/[72 ´ serum creatinine (mg per dL)] ´ 0.85

Creatinine clearance may also be calculated in SI units (as mL per second) as follows:

Adult males: Creatinine clearance

= [(140 - age) ´ (ideal body weight in kg)]/[50 ´ serum creatinine (micromoles per L)]

Adult females: Creatinine clearance

= [(140 - age) ´ (ideal body weight in kg)]/[50 ´ serum creatinine (micromoles per L)] ´ 0.85

The following dosing chart by Sarubbi and Hull (Ann Intern Med 1978; 89: 612-8) may be used to provide the clinician with an initial loading dose and maintenance dosage regimen in adult patients. Further dosage adjustments should be individualized and based on peak and trough serum concentrations, which should be drawn after the third maintenance dose.

1. Select loading dose based on the patient's ideal body weight (in mg per kg of body weight [mg/kg]) to provide peak serum concentration in the range listed below for the desired aminoglycoside.

Aminoglycoside	Usual Loading Dose (mg/kg)	Expected Peak Serum Concentrations (mcg/mL)
Gentamicin Tobramycin	1.5 to 2	4 to 10
Amikacin Kanamycin	5 to 7.5	15 to 30
Netilmicin	1.3 to 3.25	4 to 12

2. Select maintenance dose (as percentage of chosen loading dose) to maintain peak serum concentrations indicated above according to desired dosing interval and the patient's corrected creatinine clearance. This chart is not applicable to neonates and children.

CrCl (mL/min)/ (mL/sec)	Half-life (hours)	Percentage of Loading Dose Required for Dosage Interval Selected		
		8 hours	12 hours	24 hours
90/1.50	3.1	84%	-	-
80/1.33	3.4	80	91%	-
70/1.17	3.9	76	88	-
60/1.00	4.5	71	84	-
50/0.83	5.3	65	79	-
40/0.67	6.5	57	72	92%
30/0.50	8.4	48	63	86
25/0.42	9.9	43	57	81
20/0.33	11.9	37	50	75
17/0.28	13.6	33	46	70
15/0.25	15.1	31	42	67
12/0.20	17.9	27	37	61
10 a/0.17 a	20.4	24	34	56
7/0.12	25.9	19	28	47
5/0.08	31.5	16	23	41
2/0.03	46.8	11	16	30
0/0	69.3	8	11	21

a Dosing for patients with CrCl <10 mL/min (<0.17 mL/sec) should be assisted by measured serum levels.

After an initial full therapeutic loading dose, neonates or patients with impaired renal, vestibular, or auditory function may require (1) a reduction in the maintenance dose administered either (a) by administration of the usual dose at prolonged intervals or (b) by administration of reduced dose at fixed intervals or (2) discontinuation of the aminoglycoside. Since aminoglycosides are not metabolized and are excreted primarily in the urine, toxic concentrations may accumulate in patients with impaired renal function. 71, 74

Because of the high concentrations of aminoglycosides in the urine and excretory system, patients should be well hydrated to prevent or minimize chemical irritation of the renal tubules. 73 Therapeutic serum aminoglycoside levels are usually not needed to effectively treat urinary tract infections.

If a dose of this medication is missed, give it as soon as possible. However, if it is almost time for the next dose, skip the missed dose and go back to the regular dosing schedule. Do not double doses.

AMIKACIN

Additional Dosing Information

For initial dosing guidelines for patients with renal function impairment, see the Sarubbi and Hull nomogram in General Dosing Information.

Burn and certain other patients may require a dose of 5 to 7.5 mg per kg of body weight (mg/kg) every four to six hours because of the shorter half-life (1 to 1.5 hours) in these patients.

Amikacin sulfate injection may also be administered as an aerosol nebulization.

Parenteral Dosage Forms

AMIKACIN SULFATE INJECTION USP

Usual adult and adolescent dose

Antibacterial(systemic)¾Intramuscular or intravenous infusion, 5 mg per kg of body weight every eight hours; or 7.5 mg per kg of body weight every twelve hours for seven to ten days. 56

Note: Urinary tract infections, bacterial (uncomplicated)¾Intramuscular or intravenous infusion, 250 mg every twelve hours. 56

Following hemodialysis, a supplemental dose of 3 to 5 mg per kg of body weight may be administered.

Usual adult prescribing limits

Up to 15 mg per kg of body weight daily, but not to exceed 1.5 grams daily for more than ten days.

Usual pediatric dose

Antibacterial(systemic):¾Intramuscular or intravenous infusion¾ Premature neonates:
¾Initially, 10 mg per kg of body weight, then 7.5 mg per kg of body weight every eighteen to twenty-four hours for seven to ten days.

Neonates:
¾Initially, 10 mg per kg of body weight, then 7.5 mg per kg of body weight every twelve hours for seven to ten days.

Older infants and children:
See Usual adult and adolescent dose. 56

Strength(s) usually available

U.S.¾50 mg per mL (Rx)[Amikin (sodium bisulfite 0.13%)] [Generic]

250 mg per mL (Rx)[Amikin (sodium bisulfite 0.66%)] [Generic]

Canada¾250 mg per mL (Rx)[Amikin (sodium bisulfite 0.66%)]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from freezing.

Preparation of dosage form:

To prepare initial dilution for intravenous use, add the contents of each 500-mg vial to 100 to 200 mL of 0.9% sodium chloride injection, 5% dextrose injection, or other suitable diluent. The resulting solution should be administered slowly over a 30- to 60-minute period to help avoid neuromuscular blockade. Pediatric patients may require a proportionately smaller volume of diluent. 70

Stability:

Intravenous infusions of amikacin retain their potency for 24 hours at room temperature at concentrations of 0.25 and 5 mg per mL in dextrose injection, dextrose and sodium chloride injection, 0.9% sodium chloride injection, lactated Ringer's injection, and other electrolyte-containing solutions (see manufacturer's package insert). 70

Intravenous infusions of amikacin retain their potency for 60 days at 4 °C (39 °F) at concentrations of 0.25 and 5 mg per mL in the above-listed diluents. When these solutions are then stored at 25 °C (77 °F), they retain their potency for 24 hours. 56, 70

Intravenous infusions of amikacin retain their potency for 30 days when frozen at -15 °C (5 °F) at concentrations of 0.25 and 5 mg per mL in the above-listed diluents. When these solutions are thawed and stored at 25 °C (77 °F), they retain their potency for 24 hours. 56, 70

Solutions may vary in color from colorless to light straw or very pale yellow; this variation does not affect their potency. Discard dark-colored solutions.

Incompatibilities:

Extemporaneous admixtures of beta-lactam antibacterials (penicillins and cephalosporins) and aminoglycosides may result in substantial mutual inactivation. If these groups of antibacterials are administered concurrently, they should be administered in separate sites. Do not mix them in the same intravenous bag or bottle. 70, 91

Amikacin is incompatible with amphotericin B, cephalothin sodium, nitrofurantoin sodium, sulfadiazine sodium, and tetracyclines (in some solutions).

Since complexes form with a number of other drugs also, extemporaneous admixtures with Amikacin Sulfate Injection USP are not recommended. 70