Zomacin

(Amikacin Sulphate) USP

INJECTION

DESCRIPTION

Amikacin sulfate is a semisynthetic aminoglycoside antibiotic derived from kanamycin. ZOMACIN is supplied as a sterile, clear, colorless solution.

COMPOSITION

ZOMACIN 100mg

Each 2ml contains: Amikacin as Sulphate (USP).....100mg

ZOMACIN 250mg

Each 2ml contains: Amikacin as Sulphate (USP).....250mg

ZOMACIN 500mg

Each 2ml contains: Amikacin as Sulphate (USP).....500mg

ACTION

CLINICAL PHARMACOLOGY: INTRAMUSCULAR ADMINISTRATION

ZOMACIN is rapidly absorbed and is well tolerated locally after intramuscular administration. In normal adult volunteers, average peak serum concentrations of about 12, 16 and 21mcg/mL are obtained 1 hour after intramuscular administration of 250mg (3.7mg/kg) 375mg (5mg/kg), and 500mg (7.5 mg/kg) single doses, respectively. At 10 hours, serum levels are about 0.3mcg/mL, 1.2mcg/mL and 2.1mcg/mL respectively. There is no evidence of drug accumulation with repeated dosing for 10 days when administered in recommended doses.

With normal renal function 91.9% of an intramuscular dose is excreted unchanged in the urine in the first 8 hours, and 98.2% within 24 hours. Mean urine concentrations for 6 hours are 563mcg/mL following a 250mg dose, 697mcg/mL following a 375mg dose and 832mcg/mL following a 500mg dose.

Studies in newborns of different weights (less than 1.5 kg, 1.5 to 2.0 kg, over 2.0 kg) given ZOMACIN intramuscularly at a dose of 7.5 mg/kg revealed that, as is the case with other aminoglycosides, serum half-life values correlated inversely with post-natal age and renal clearances of amikacin.

The volume of distribution indicates that amikacin, like other aminoglycosides, remains primarily in the extracellular fluid space of neonates. Repeated dosing every 12 hours in all the above groups did not demonstrate accumulation after 5 days.

CLINICAL PHARMACOLOGY: INTRAVENOUS ADMINISTRATION

Single doses of 500mg (7.5 mg/kg) administered to normal adults as an infusion over a period of 30 minutes produced a mean peak serum concentration of 38mcg/mL at the end of the infusion, and levels of 24mcg/mL 18mcg/mL, and 0.75mcg/mL at 30 minutes, 1 hour, and 10 hours post-infusion, respectively. Eighty-four percent of the administered dose was excreted in the urine in 9 hours and 94 percent within 24 hours. Repeated infusions of 7.5 mg/kg every 12 hours in normal adults were well tolerated and caused no drug accumulation.

Single doses of 15mg/kg administered intravenously over 30 minutes to adult volunteers with normal renal function resulted in mean peak serum concentrations, of 77mcg/mL and levels of 47mcg/mL and 1mcg/mL at 1 and 12 hours, respectively, following the infusion. A mean peak serum concentration of 55mcg/mL after a 30-minute infusion of 15 mg/kg is seen in elderly patients (mean creatinine clearance of 64mL/min) with serum concentrations of 5.4mcg/mL at 12 hours and 1.3mcg/mL at 24 hours following the infusion. In multiple dose studies, no accumulation was noted in patients with normal renal function receiving once daily-doses of 15 to 20mg/kg.

GENERAL

In normal adult subjects, the mean serum half-life is slightly over 2 hours with a mean total apparent volume of distribution of 24 liters, approximately 28 percent of body weight. Serum protein binding ranges from 0 to 11 percent. The mean serum clearance rate is about 100mL/min and the renal clearance rate is 94mL/min in subjects with normal renal function. Amikacin is excreted primarily by way of glomerular filtration. Patients with impaired renal function or diminished glomerular filtration excrete the drug much more slowly, prolonging the serum half-life. Therefore, renal function should be monitored carefully and dosage adjusted accordingly (see suggested dosage schedule under Dosage and Administration). Following administration at recommended doses, therapeutic levels are found in bone, heart, gallbladder, and lung tissue in addition to significant concentrations in urine, bile, sputum, bronchial secretions, interstitial, pleural, and synovial fluids.

Data from multiple daily dose trials show that spinal fluid levels in normal infants are approximately 10 to 20% of the serum concentrations and may reach 50% when the meninges are inflamed. ZOMACIN has been demonstrated to cross the placental barrier and yield significant concentrations in amniotic fluid. The peak fetal serum concentration is about 16% of the peak maternal serum concentration and maternal and fetal serum half-life values are about 2 and 3.7 hours, respectively.

MICROBIOLOGY

Gram-negative Amikacin is active in vitro against Pseudomonas species. Escherichia coli, Proteus species (indole-positive and indole-negative), Providencia species, Klebsiella Enterobacter-Serratia species, Acinetobacter (formerly Mima- Herellea) species and Citrobacter freundii. When strains of the above organisms are found to be resistant to other aminoglycosides, including gentamicin, tobramycin, and kanamycin, many are susceptible to amikacin in vitro. Amikacin resists degradation by most aminoglycoside inactivating enzymes known to affect gentamicin, tobramycin, and kanamycin.

In vitro studies have shown that ZOMACIN, combined with a beta-lactam antibiotic, acts synergistically against many clinically important gram-negative organisms. Persistent suppression of bacterial growth of many gram-negative organisms after in vitro exposure (post-antibiotic effect) to ZOMACIN occurs. Gram-positive Amikacin is active in vitro against penicillinase and non-penicillinase producing Staphylococcus species including methicillin-resistant strains. Methicillin-resistant Staphylococcus aureus (MRSA) may not be completely sensitive to amikacin. Aminoglycosides in general have been shown to have a low order of activity against other gram-positive organisms; viz, Streptococcus pyogenes, enterococci and Streptococcus pneumoniae.

DISC SUSCEPTIBILITY TESTS

Quantitative methods that require measurement of zone diameters give precise estimates of antibiotic susceptibility. One such procedure has been recommended for use with discs to test susceptibility to amikacin. Interpretation involves correlation of the diameters obtained in the disc test with MIC values for amikacin. When the causative organism is tested by the Kirby-Bauer method of disc susceptibility, a 30mcg amikacin disc should give a zone of 17 mm or greater to indicate susceptibility. Zone sizes of 14 mm or less indicate resistance. Zone sizes of 15 to 16 mm indicate intermediate susceptibility. With this procedure, a report from the laboratory of “susceptible" indicates that the infecting organism is likely to respond to therapy. A report of “resistant" indicates that the infecting organism is not likely to respond to therapy. A report of “intermediate susceptibility" suggests that the organism would be susceptible if the infection were confined to tissues and fluids (e.g., urine), in which high antibiotic levels were attained.

CONTRAINDICATIONS

ZOMACIN is contraindicated in patients with known allergy to amikacin or any component of the formulation. A history of hypersensitivity or serious toxic reactions to aminoglycosides may contraindicate the use of any aminoglycoside because of the known cross sensitivities of patients to drugs in this class.

WARNINGS

Patients treated with parenteral aminoglycosides should be under close clinical observation because of the potential ototoxicity and nephrotoxicity associated with their use. Safety for treatment periods which are longer than 14 days has not been established.Neurotoxicity, manifested as vestibular and/or bilateral auditory ototoxicity, can occur in patients treated with aminoglycosides. The risk of aminoglycoside-induced ototoxicity is greater in patients with impaired renal function, and in those who receive high doses, or in those whose therapy is prolonged. High frequency deafness usually occurs first and can be detected only by audiometric testing. Vertigo may occur and may be evidence of vestibular injury. Other manifestations of neurotoxicity may include numbness, skin tingling, muscle twitching and convulsions. The risk of ototoxicity due to aminoglycosides increases with the degree of exposure to either persistently high peak or high trough serum concentrations. Patients developing cochlear or vestibular damage may not have symptoms during therapy to warn them of developing eighth nerve toxicity, and total or partial irreversible bilateral deafness or disabling vertigo may occur after the drug has been discontinued. Aminoglycoside-induced ototoxicity is usually irreversible.

Aminoglycosides are potentially nephrotoxic. The risk of nephrotoxicity is greater in patients with impaired renal function, and in those who receive high doses, or in those whose therapy is prolonged.

Renal and eighth-cranial nerve function should be closely monitored especially in patients with known or suspected renal impairment at the onset of therapy, and also in those whose renal function is initially normal but who develop signs of renal dysfunction during therapy. Serum concentrations of amikacin should be monitored when feasible to assure adequate levels and to avoid potentially toxic levels. Urine should be examined for decreased specific gravity, increased excretion of proteins, and the presence of cells or casts. Blood urea nitrogen, serum creatinine, or creatinine clearance should be measured periodically. Serial audiograms should be obtained where feasible in patients old enough to be tested, particularly high risk patients. Evidence of ototoxicity (dizziness, vertigo, tinnitus, roaring in the ears, and hearing loss) or nephrotoxicity requires discontinuation of the drug or dosage adjustment.

Concurrent and/or sequential systemic, oral, or topical use of other neurotoxic or nephrotoxic products, particularly bacitracin, cisplatin, amphotericin B, cephaloridine, paromomycin, viomycin, polymyxin B, colistin, vancomycin, or other aminoglycosides should be avoided. Other factors that may increase risk of toxicity are advanced age and dehydration.

The concurrent use of ZOMACIN with potent diuretics (ethacrynic acid,- or furosemide) should be avoided since diuretics by themselves may cause ototoxicity. In addition, when administered intravenously, diuretics may enhance aminoglycoside toxicity by altering antibiotic concentrations in serum and tissue.

Neuromuscular blockade and respiratory paralysis have been reported following parenteral injection, topical instillation (as in orthopedic and abdominal irrigation or in local treatment of empyema), and following oral use of aminoglycosides. The possibility of respiratory paralysis should be considered if aminoglycosides are administered by any route, especially in patients receiving anesthetics, neuromuscular blocking agents such as tubocurarine, succinylcholine, decamethonium, or in patients receiving massive transfusions of citrate-anti-coagulated blood. If neuromuscular blockade occurs, calcium salts may reverse respiratory paralysis, but mechanical respiratory assistance may be necessary.

ZOMACIN contains sodium bisulfite, 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 uncommon and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in non-asthmatic subjects.

INDICATIONS

ZOMACIN is indicated in the short-term treatment of serious infections due to susceptible strains of gram-negative bacteria, including Pseudomonas species, Escherichia coli, species of indole-positive and indole-negative Proteus, Providencia species, Klebsiella-Enterobacter-Serratia species, and Acinetobacter (Mima-Herellea) species.

Clinical studies have shown ZOMACIN to be effective in bacteremia and septicemia (including neonatal sepsis); in serious infections of the respiratory tract, bones and joints, central nervous system (including meningitis) and skin and soft tissue; intra-abdominal infections (including peritonitis); and in burns and post-operative infections (including post-vascular surgery). Clinical studies have shown ZOMACIN also to be effective in serious, complicated, and recurrent urinary tract infections due to these organisms. Aminoglycosides, including ZOMACIN, are not indicated in uncomplicated initial episodes of urinary tract infections unless the causative organisms are not susceptible to antibiotics having less potential toxicity. When amikacin is indicated in the treatment of uncomplicated urinary tract infections, reduced dosage may be prescribed (see Dosage and Administration). Bacteriologic studies should be performed to identify causative organisms and their susceptibilities to amikacin. ZOMACIN may be considered as initial therapy in suspected gram-negative infections and therapy may be instituted before obtaining the results of susceptibility testing. Clinical trials demonstrate that ZOMACIN is effective in infections caused by gentamicin and/or tobramycin resistant strains of gram-negative organisms, particularly Proteus rettgeri, Providencia stuartii, Serratia marcescens, and Pseudomonas aeruginosa. The decision to continue therapy with the drug should be based on results of susceptibility tests, the severity of the infection, the response of the patient, and the important additional considerations contained in the Warnings above. ZOMACIN has also been shown to be effective in staphylococcal infections and may be considered as initial therapy under certain conditions in the treatment of known or suspected staphylococcal disease. Examples include severe infections where the causative organism may be either a gram-negative bacterium or a staphylococcus, infections due to susceptible strains of staphylococci in patients allergic to other antibiotics, and in mixed staphylococcal/gram-negative infections. In certain severe infections such as neonatal sepsis, concomitant therapy with a penicillin-type drug may be indicated because of the possibility of infections due to gram-positive organisms such as streptococci.

PRECAUTIONS

Aminoglycosides are quickly and almost totally absorbed when they are applied topically, except to the urinary bladder, in association with surgical procedures. Irreversible deafness, renal failure and death due to neuromuscular blockade have been reported following irrigation of both small and large surgical fluids with an aminoglycoside preparation.

The concurrent or serial use of other ototoxic or nephrotoxic agents should be avoided either systemically or topically because of the potential for additive effects. Increased nephrotoxicity has been reported following concomitant parenteral administration of aminoglycoside antibiotics and cephalosporins. Concomitant cephalosporin use may spuriously elevate creatinine serum level determinations.

OTOTOXICITY: See Warnings above.

NEPHROTOXICITY

Patients should be well hydrated during treatment and renal function should be assessed by the usual methods prior to starting therapy and daily during the course of treatment A reduction of dosage (see Dosage and Administration) is required if evidence of renal dysfunction occurs such as presence of urinary casts, white or red cells, albuminuria, decreased creatinine clearance, decreased urine specific gravity, increased BUN, serum creatinine, or oliguria.

If azotemia increases, or if a progressive decrease in urinary output occurs, treatment should be stopped.

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

NEUROTOXICITY
Neuromuscular blockade and muscular paralysis have been demonstrated in laboratory animals given high doses of amikacin. The possibility of neuromuscular blockade and respiratory paralysis should be considered when amikacin is administered concomitantly with anesthetic or neuromuscular blocking drugs. If blockade occurs, calcium salts may reverse this phenomenon.
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 the neuromuscular junction.

OTHER
As with other antibiotics, the use of amikacin may result in overgrowth of non-susceptible organisms. If this occurs, appropriate therapy should be instituted. In vitro admixture of aminoglycosides with beta-lactam antibiotics (penicillins or cephalosporins) may result in significant mutual inactivation. A reduction in serum activity may also occur when an aminoglycoside or penicillin-type drug is administered in vivo by separate routes. Inactivation of the aminoglycoside is clinically significant only in patients with severely impaired renal function. Inactivation may continue in specimens of body fluids collected for assay, resulting in inaccurate aminoglycoside readings. Such specimens should be properly handled (assayed promptly, frozen, or treated with beta-lactamase).

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY
Long-term studies in animals to evaluate carcinogenic potential have not been performed, and mutagenicity has not been studied. ZOMACIN administered to rats at doses up to 10 times the human daily dose did not impair male or female fertility.

PREGNANCY
Aminoglycosides can cause fetal harm when administered to a pregnant woman. Aminoglycosides cross the placenta and there have been several reports of total irreversible, bilateral congenital deafness in children whose mothers received streptomycin during pregnancy. Although serious side effects to the fetus or 'newborns' have not been reported in the treatment of pregnant women with other aminoglycosides, the potential for harm exists. Reproduction studies of amikacin have been performed in rats and mice and revealed no evidence of impaired fertility or harm to the fetus due to amikacin. There are no well controlled studies in pregnant women, but investigational experience does not include any positive evidence of adverse effects to the fetus. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

NURSING MOTHERS
It is not known whether this drug is excreted in human milk. As a general rule, nursing should not be undertaken while a patient is receiving any drug, since many drugs are excreted in human milk.

PEDIATRIC USE
Aminoglycosides should be used with caution in premature and neonatal infants because of the renal immaturity of these patients and the resulting prolongation of serum half-life of these drugs.

ADVERSE EVENTS
All aminoglycosides have the potential to induce ototoxicity, renal toxicity and neuromuscular blockade (see Warnings and Precautions). These toxicities occur more frequently in patients with renal impairment, in patients treated with other ototoxic or nephrotoxic drugs, and in patients treated for longer periods and/or with higher doses than recommended.

NEUROTOXICITY-OTOTOXICITY
Toxic effects on the eighth cranial nerve can result in hearing loss, loss of balance, or both. Amikacin primarily affects auditory function. Cochlear damage includes high frequency deafness and usually occurs before clinical hearing loss can be detected by audiometric testing.

NEUROTOXICITY-NEUROMUSCULAR BLOCKAGE
Acute muscular paralysis and apnea can occur following treatment with aminoglycoside drugs.

NEPHROTOXICITY
Elevation of serum creatinine, albuminuria, presence of red cells, white cells or casts in the urine, azotemia and oliguria may occur. Renal function changes are usually reversible when the drug is discontinued. As would be expected with any aminoglycoside, reports of toxic nephropathy and acute renal failure have been received during post-marketing surveillance.

OTHER
Other adverse reactions which have been reported on rare occasions are skin rash, drug fever, headache, paresthesia, tremor, nausea and vomiting, eosinophilia, arthralgia, anemia, hypotension, and hypomagnesemia. Macular infarction sometimes leading to permanent loss of vision has been reported following intravitreous administration (injection into the eye) of amikacin.

OVER-DOSAGE
In the event of over-dosage or toxic reaction, peritoneal dialysis or hemodialysis will aid in the removal of amikacin from the blood. Amikacin levels are also reduced during continuous arteriovenous hemofiltration. In the newborn infant, exchange transfusion may also be considered.

DOSAGE AND ADMINISTRATION
The patient's pretreatment body weight should be obtained for calculation of correct dosage. ZOMACIN may be given intramuscularly or intravenously. The status of renal function should be estimated by measurement of the serum creatinine concentration or calculation of the endogenous creatinine clearance rate. The blood urea nitrogen (BUN) is much less reliable for this purpose. Reassessment of renal function should be made periodically during therapy.
Whenever possible, amikacin concentrations in serum should be measured to assure adequate, but not excessive levels. It is desirable to measure both peak and trough serum concentrations intermittently during therapy. Peak concentrations (30-90 minutes after injection) above 35mcg/mL and trough concentrations (just prior to the next dose) above 10mcg/mL should be avoided. Dosage should be adjusted as indicated. In patients with normal renal function, once-daily dosing may be used; peak concentrations in these cases may exceed 35mcg/mL (see Once-Daily Dosing and Administration in Patients with Impaired Renal Function below).

INTRAMUSCULAR AND INTRAVENOUS ADMINISTRATION IN PATIENTS WITH NORMAL RENAL FUNCTION
The recommended intramuscular or intravenous dosage for adults, children, and older infants with normal renal function is 15 mg/kg/day divided into 2 or 3 equal doses administered at equally-divided intervals; i.e., 7.5 mg/kg q 12 h or 5 mg/kg q 8 h. Treatment of patients with large body mass should not exceed 1.5 g/day. In premature, the recommended dose is 7.5 mg/kg every twelve hours. Newborns should receive 10 mg/kg as a loading dose and 7.5 mg/kg q 12 h thereafter. Infants older than 2 weeks and children should receive 7.5 mg/kg q 12 h or 5 mg/kg q 8 h as noted above.
ONCE-DAILY DOSING: Alternatively, in patients with normal renal function reflected by creatinine clearance is 50mL/min, a single daily intravenous dose of 15 mg/kg/day in adults, or 20 mg/kg/day in children (4 weeks or older) may be considered for bacteremia, septicemia, respiratory tract infections, complicated urinary tract infections, intra-abdominal infections and empiric use in febrile neutropenia. Information on the use of once-daily dosing in patients with other organ system involvement is limited. (See also above regarding monitoring of peak and trough serum amikacin concentrations.)
When ZOMACIN is indicated in uncomplicated urinary tract infections, a total daily dose of 500mg may be administered either in a single dose or in two divided doses (250mg b.i.d.). Care should be taken to calculate the doses accurately and the 50 mg/mL reconstituted solution should be further diluted when necessary to allow administration of accurate doses in the smaller premature Infant. The usual duration of treatment is 7 to 10 days. The total daily dose by all routes of administration should not exceed 15-20mg/kg/day. In difficult and complicated infections where treatment beyond 10 days is considered, the use of ZOMACIN should be reevaluated and, if continued, renal, auditory, vestibular function should be monitored, as well as serum amikacin levels. At the recommended dosage level, uncomplicated infections due to amikacin-sensitive organisms should respond in 24 to 48 hours. If definite clinical response does not occur within 3 to 5 days, therapy should be stopped and the antibiotic susceptibility pattern of the invading organism should be rechecked. Failure of the infection to respond may be due to resistance of the organism or to the presence of septic foci requiring surgical drainage.

ADMINISTRATION IN PATIENTS WITH IMPAIRED RENAL FUNCTION
NOTE: In patients with renal impairment reflected by creatinine clearance <50 mL/min, administration of the total daily dose of amikacin in single daily doses is not desirable since these patients will have protracted exposure to high trough concentrations. See below for dosage recommendations in patients with impaired renal function. For patients with impaired renal function receiving usual twice or three times daily dosing, whenever possible, serum amikacin concentrations should be monitored by appropriate assay procedures. Doses should be adjusted in patients with impaired renal function either by administering normal doses at prolonged intervals or by administering reduced dosage at fixed intervals. Both methods are based on the patient's creatinine clearance or serum creatinine values since these have been found to correlate with aminoglycoside half-life in patients with diminished renal function. These dosage schedules must be used in conjunction with careful clinical and laboratory observations of the patient and should be modified as necessary, including modification when dialysis is being performed.

NORMAL DOSE AT PROLONGED INTERVALS BETWEEN DOSING
If the creatinine clearance rate is not available and the patient's condition is stable, a dosage interval in hours for the normal single dose (that would be given to patients with normal renal function on a BID schedule, 7.5mg/kg) can be calculated by multiplying the patient's serum creatinine by nine; e.g., if the serum creatinine concentration is 2mg/100mL, the recommended single dose (7.5 mg/kg) should be administered q 18 h.

REDUCED DOSE AT FIXED TIME INTERVALS BETWEEN DOSING
When renal function is impaired and it is desirable to administer ZOMACIN at a fixed time interval, dose must be reduced. In these patients serum amikacin concentrations should be measured to assure accurate administration and to avoid excessive serum concentrations. If serum assay determinations are not available, and the patient's condition is stable, serum creatinine and creatinine clearance values are the most readily available indicators of the degree of renal impairment to use as a guide for dosage.
First, initiate therapy by administering a normal dose, 7.5 mg/kg, as a loading dose. This dose is the same as the normally recommended dose which would be calculated for a patient with a normal renal function as described above. To determine the size of maintenance doses administered every 12 hours, the loading dose should be reduced in proportion to the reduction in the patient's creatinine clearance rate:
Maintenance dose every 12 hours-=

$$\frac{\text{observed CrCl in mL/min x calculated loading dose in mg}}{\text{normal CrCl in mL/min}}$$

(CrCl = creatinine clearance rate)
An alternate rough guide for determining reduced dosage at twelve-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. The above dosage schedules are not intended to be rigid recommendations, but are provided as guides to dosage when the measurement of amikacin serum levels is not feasible.

INTRAVENOUS ADMINISTRATION: PREPARATION OF SOLUTIONS
The solution for intravenous use is prepared by adding the desired dose to 100mL or 200mL of sterile diluent such as normal saline or 5% dextrose in water or any other compatible solution. The solution is administered to adults over a 30- to 60-minute period. The total daily dose should not exceed 15-20mg/kg/day. In pediatric patients, the amount of fluid, used will depend on the amount tolerated by the patient. It should be in a sufficient amount to infuse the amikacin over a 30- to 60-minute period. Infants should receive a 1 - to 2-hour infusion. Amikacin should not be physically premixed with other drugs, but should be administered separately according to the recommended dose and route.

STABILITY IN IV FLUIDS
ZOMACIN is stable for 24 hours at room temperature, at concentrations of 0.25 and 5.0 mg/mL in the following solutions:
5% Dextrose Injection
5% Dextrose and 0.2% Sodium Chloride Injection
5% Dextrose and 0.45% Sodium Chloride Injection
0.9% Sodium Chloride Injection Lactated Ringer's Injection
Normosol® M in 5% Dextrose Injection (or Plasma-Lyte 56 Injection in 5% Dextrose in Water)
Normosol® R in 5% Dextrose Injection (or Plasma-Lyte 148 Injection in 5% Dextrose in Water)
In the above solutions with ZOMACIN concentrations of 0.25 and 5.0 mg/mL, solutions aged for 60 days at 4°C and then stored at 25°C had utility times of 24 hours.
At the same concentrations, solutions frozen and aged for 30 days at -15°C, thawed, and stored at 25°C had utility times of 24 hours.
Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever the solution and container permit.
Aminoglycosides administered by any route should not be physically premixed with other drugs but should be administered separately.
Because of the potential toxicity of aminoglycosides, "fixed dosage" recommendations which are not based upon body weight are not advised. Rather, it is essential to calculate the dosage to fit the needs of each patient.

INSTRUCTIONS
Store below 30°C. Protect from heat & light. Keep all medicines out of the reach of children. To be sold on the prescription of a registered medical practitioner only.
Avoid freezing and injection should not be used if vial is leaking, solution is cloudy or contains undissolved particles.

PRESENTATION
ZOMACIN 100mg, 250mg & 500mg packs containing vial of injection.

زوماسِن انجکشن
(ایمیکاسِن سلفیٹ) یو ایس پی

ہدایات: **30°** سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ گرمی اور روشنی سے بچائیں۔ تمام دوائیں بچوں کی پہنچ سے دُور رکھیں۔ صرف مستند ڈاکٹر کے نسخے پر فروخت کریں۔ منجمد ہونے سے بچائیں۔ انجکشن کے لیک ہونے، دھندلا ہونے یا اس میں کوئی غیر حل پذیر شے نظر آنے کی صورت میں ہرگز استعمال نہ کریں۔

Manufactured by:
STANDPHARM PAKISTAN (PVT) LTD.
20 Km Ferozepur Road Lahore, Pakistan.

0661-00