For the use of Registered Medical Practitioner of Hospital or a Laboratory only

Amikacin Injection BP 40mg/ml, 50mg/ml, 125mg/ml & 250mg/ml

COMPOSITION

Each ml contains

Amikacin Sulphate	BP	
Eq. to Amikacin		25mg/50mg/125mg/250mg
Methyl Paraben	BP	0.1%w/v
Propyl Paraben	BP	0.02%w/v
Water for Injection	BP	q.s.

CLINICAL PHARMACOLOGY

Pharmacodynamic properties

Pharmacotherapeutic group: Aminoglycoside antibiotic.

ATC code: J01G B06

Amikacin is a semi-synthetic aminoglycoside antibiotic derived from Kanamycin A. It is active against a broad spectrum of Gram-negative organisms, including *pseudomonas*, *Escherichia coli* and some Gram-positive organisms, e.g. *Staphylococcus aureus*.

Aminoglycoside antibiotics are bactericidal in action. Although the exact mechanism of action has not been fully elucidated, the drugs appear to inhibit protein synthesis in susceptible bacteria by irreversibly binding to 30S ribosomal subunits.

Pharmacokinetic properties

Amikacin is rapidly absorbed after intramuscular injection. Peak plasma concentrations equivalent to about 20 mg/ml are achieved one hour after IM doses of 500 mg, reducing to about 2 µg/ml 10 hours after injections.

Twenty per cent or less is bound to serum protein and serum concentrations remain in the bactericidal range for sensitive organisms for 10 to 12 hours.

Single doses of 500 mg administered as an intravenous infusion over a period of 30 minutes produce a mean peak serum concentration of 38 µg/ml. Repeated infusions do not produce drug accumulation in adults with normal renal function. However, decreased renal function will lead to accumulation.

In adults with normal renal function the plasma elimination half-life of amikacin is usually 2-3 hours. 94 - 98% of a single IM or IV dose of amikacin is excreted unchanged by glomerular filtration within 24 hours. Urine concentrations of amikacin average 563 µg/ml in the first 6 hours following a single 250 mg IM dose and 163 µg/ml over 6-12 hours. Following a single 500 mg IM dose urine concentrations average 832 µg/ml in adults with normal renal function.

Amikacin diffuses readily through extracellular fluids and is excreted in the urine unchanged, primarily by glomerular filtration**.** It has been found in pleural fluid, amniotic fluid and in the peritoneal cavity following parenteral administration.

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% in meningitis.

Intramuscular and intravenous administration

In neonates and particularly in premature babies, the renal elimination of amikacin is reduced.

In a single study in newborns (1-6 days of post natal age) grouped according to birth weights (<2000, 2000-3000 and >3000g). Amikacin was administered intramuscularly and/or intravenously at a dose of 7.5 mg/kg. Clearance in neonates >3000 g was 0.84 ml/min/kg and terminal half-life was about 7 hours. In this group, the initial volume of distribution and volume of distribution at steady state was 0.3 ml/kg and 0.5 mg/kg, respectively. In the groups with lower birth weight clearance/kg was lower and half-life longer. Repeated dosing every 12 hours in all the above groups did not demonstrate accumulation after 5 days.

INDICATION AND USAGE

Amikacin is indicated in the treatment of following infections in adults and pediatric patients including neonates

- Hospital-acquired pneumonia (HAP) including ventilator-associated pneumonia (VAP)
- Complicated Urogenital tract infections including pyelonephritis
- Complicated Intraabdominal infections
- Endocarditis (only in combination with other antibiotics),
- Infected burns

Treatment of patients with bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above.

Amikacin may be used in the management of neutropenic patients with fever that is suspected to be due to a bacterial infection.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

CONTRA-INDICATION

Amikacin sulphate injection 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.

Aminoglycosides may impair neuromuscular transmission, and should not be given to patients with myasthenia gravis.

DRUG INTERACTIONS

Concurrent or serial use with other neurotoxic, ototoxic or nephrotoxic agents, particularly bacitracin, cisplatin, amphotericin B, cyclosporine, tacrolimus, cephaloridine, paromomycin, viomycin, colistimethate/ colistin, vancomycin, or other aminoglycosides should be avoided both systemically and 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.

The risk of ototoxicity is increased when amikacin is used in conjunction with rapidly acting diuretic drugs, particularly when the diuretic is administered intravenously. Diuretics may enhance aminoglycoside toxicity by altering antibiotic concentrations in serum and tissue. Such agents include furosemide and ethacrynic acid which is itself an ototoxic agent. Irreversible deafness may result.

There is an increased risk of nephrotoxicity and possible ototoxicity when aminoglycosides are co-administered with platinum compounds.

The use of amikacin is not recommended in patients receiving anaesthetics or muscle-relaxing drugs (such as volatile anaesthetics, d-tubocurarine, succinylcholine, decamethonium, atracurium, rocuronium, vecuronium) or in patients receiving massive transfusions of citrate-anticoagulated blood) as neuromuscular blockade and consequent respiratory depression may occur. If blockade occurs, calcium salts may reverse this phenomenon.

Indomethacin may increase the plasma concentration of amikacin in neonates.

In patients with severely impaired renal function, a reduction in activity of aminoglycosides may occur with concomitant use of penicillin-type drugs.

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).

There is an increased risk of hypocalcaemia when aminoglycosides are administered with bisphosphonates.

There is an increased risk of nephrotoxicity and possibly of ototoxicity when aminoglycosides are administered with platinum compounds.

Concomitantly administered thiamine (vitamin B1) may be destroyed by the reactive sodium metabisulfite component of the amikacin sulfate formulation.

Sulfite is a very reactive compound. Therefore, mixtures with other medicinal products (other than those indicated.

WARNINGS AND PRECAUTIONS

Allergic reactions

Amikacin contains sodium metabisulfite.

Sodium metabisulfite may rarely cause severe hypersensitivity reactions in susceptible individuals, including anaphylactic symptoms and life- threatening bronchial spasms (bronchospasm).

Sulphite hypersensitivity is generally uncommon and more common in asthmatics than non-asthmatics.

Neuromuscular toxicity

Neuromuscular blockade and respiratory paresis have been reported following parenteral injection, topical lavage (such as orthopedic and abdominal irrigation, or with local empyema treatment) or after oral administration of aminoglycosides. The risk of respiratory paresis when administering aminoglycosides irrespective of the route of administration should be considered, especially in patients receiving anesthetics or neuromuscular blockers Interactions with other medications and other forms of interaction ").

Antidote in neuromuscular blockade: supply of calcium in ionized form (to relieve respiratory paralysis) and neostigmine. Mechanical ventilation may be necessary. In animal studies, neuromuscular blocks and myoparesis were found after administration of high doses of amikacin.

Aminoglycosides should be used with extreme caution in patients with myasthenia gravis as the curare-like effect on the neuromuscular junction may increase myasthenia with the potential for respiratory failure.

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

Nephrotoxicity and Ototoxicity

Amikacin is potentially nephrotoxic and ototoxic; therefore, patients must be carefully monitored clinically. Particular caution should be applied to patients with pre-existing renal insufficiency, or pre-existing hearing or vestibular damage. Safety for treatment periods which are longer than 14 days has not been established.

Precautions regarding the dose should be observed and adequate hydration maintained.

Neurotoxicity occurring in patients treated with aminoglycosides is manifested as vestibular and / or bilateral ototoxicity.

Ototoxicity:

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 over 5-7 days. High frequency deafness usually occurs first and can be detected only by audiometric testing. Vertigo or dizziness may occur and may be evidence of vestibular injury.

Other manifestations of neurotoxicity include numbness, tingling of the skin, muscle twitching and muscle spasms. At the first sign of hearing and / or balance disorders, therapy with amikacin should be discontinued.

The risk of ototoxicity due to aminoglycosides increases with the level of exposure either through consistently high peak serum concentrations or high serum trough concentrations. Patients who develop auditory or vestibular damage may not have any symptoms during therapy that may alert them to 8th nerve damage, and total or partial irreversible bilateral deafness or disabling vertigo may occur after the drug has been discontinued. Aminoglycoside-induced ototoxicity is usually irreversible.

Evidence of ototoxicity (dizziness, vertigo, tinnitus, roaring in the ears and hearing loss) or nephrotoxicity requires discontinuation of the drug or dosage adjustment.

The use of amikacin in patients with a history of allergy to aminoglycosides or in patients who may have subclinical renal or eighth nerve damage induced by prior administration of nephrotoxic and/or ototoxic agents such as streptomycin, dihydrostreptomycin, gentamicin, tobramycin, kanamycin, bekanamycin, neomycin, polymyxin B, colistin, cephaloridine, or viomycin should be considered with caution, as toxicity may be additive.

In these patients amikacin should be used only if, in the opinion of the physician, therapeutic advantages outweigh the potential risks.

Nephrotoxicity:

Aminoglycosides are potentially nephrotoxic. Renal toxicity appears independent of plasma obtained at the peak (C_{max}). The risk of nephrotoxicity is increased in patients with impaired renal function and in patients receiving high doses or prolonged drug therapy.

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 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.

Aminoglycosides may be inactivated by betalactams. Inactivation may continue in samples (serum, cerebrospinal fluid, etc.) taken for laboratory testing and then interfere with aminoglycoside level assays. The samples should therefore be adequately treated after collection (immediate determination, storage in the freezer or addition of beta-lactamase).
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.

Other

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 fields with an aminoglycoside preparation.
- Prolonged antibiotic use may occasionally lead to overgrowth of resistant pathogens. The patient should be constantly monitored in this regard. Should a superinfection occur during therapy, appropriate measures must be taken.
Macular infarction sometimes leading to permanent loss of vision has been reported following intravitreous administration (injection into the eye) of amikacin.
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.
2 ml vial
This medicine contains less than 1 mmol sodium (23mg) per 2ml vial, that is to say essentially 'sodium-free'.
4 ml vial
This medicinal product contains 26.65 mg sodium per 4ml vial, equivalent to 1.33% of the WHO recommended maximum daily intake of 2g sodium for an adult.

SIDE EFFECTS

All aminoglycosides have oto-, nephro- and neurotoxic potential.
The risk of these side effects is greater in patients with already impaired renal function, in patients receiving more than the recommended doses, prolonged therapy and in patients treated with other ototoxic or nephrotoxic drugs.
Frequency is defined using the following convention:
Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); Not known (frequency cannot be estimated from the available data)
Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

MedDRA system organ class	Frequency	Adverse event
Infections and Infestations	Uncommon	Super infection or colonization with resistant bacteria or yeasts [a].
Blood and lymphatic system disorders	Rare	Anemia, eosinophilia, granulocytopenia, thrombocytopenia
Immune system disorders	Not known	Anaphylactic response (anaphylactic reaction, anaphylactic shock and anaphylactic reaction), hypersensitivity
Metabolism and nutrition disorders	Rare	Hypomagnesemia
Nervous system disorders	Rare	Tremor [a], paraesthesia[a], headache, balance disorders
	Not known	paresis[a]
Eye disorders	Rare	Blindness**, retinal infarct[a]
Ear and labyrinth disorders	Common	Tinnitus[a], hypoacusis[a],
	Not known	chochlear damage Deafness [a], sensory deafness [a]
Vascular disorders	Rare	Hypotonia, thrombophlebitis
Cardiac disorders	Rare	Tachycardia and myocarditis
Respiratory, thoracic and mediastinal disorders	Not known	Apnea, bronchospasm
Gastrointestinal disorders	Uncommon	vomiting, nausea
Hepatobiliary disorders	Rare	Elevation of liver enzymes in plasma (SGOT, SGPT, LDH, alkaline phosphatase and bilirubin)
Skin and subcutaneous tissue disorders	Uncommon	Rash
	Rare	Pruritus, urticaria
Musculoskeletal and connective tissue disorders	Rare	Arthralgia, myokymia[a]
Renal and urinary disorders	Common	Nephrotoxicity, oliguria [a]
	Not known	increase in serum creatinine [a], albuminuria [a], azotemia [a], red blood cells in the urine, white blood cells in the urine, cells in the urine Acute renal failure
General disorders and administration site conditions	Rare	Fever
	Not known	Pain in the injection site **

* Changes in renal function are usually reversible at the end of therapy.
** Amikacin is not intended for administration to the vitreous body. When amikacin was injected directly into the eye, maculopathies were observed, occasionally leading to complete loss of vision.
Description of selected adverse reactions
Kidney and urinary tract disorders
Nephrotoxicity is manifested as increased excretion of tubule epithelia, cylindruria, increase in β2-microglobulin excretion, enzyme excretion via urine (e.g. alanine aminopeptidase, glutamine transferase, β-galactosidase, N-acetyl-glucosaminidase), azotemia, decrease in urine osmolarity, increase in blood urea nitrogen and serum creatinine, decrease in creatinine clearance. In case of minor irritations (albumin, erythrocytes, leukocytes or cylinders in urine) the fluid intake should be increased. After discontinuation of the drug, renal impairment is usually reversible.
As with all aminoglycosides, there have been reports of nephrotoxicity and acute renal failure following approval of amikacin.
Disorders of the ear and the labyrinth
Ototoxic reactions involving the 8th cranial nerve occur in approximately 0.5 - 5% of the treated patients. This may involve vestibular or cochlear function.
When treating with amikacin, special attention should be paid to cochlear damage. These are manifested as tinnitus, pressure in the ears and initially merely as audiometrically detectable decrease of acoustic perceptions in the high frequency range (> 4000 Hertz) above the speech range. However, hearing loss can develop to complete, irreversible deafness despite discontinuation of the aminoglycoside. Vestibular disorders manifest in initial symptoms such as dizziness, nausea, and vomiting. In the clinical examination usually a nystagmus is detected. At the first sign of hearing or balance disorders, amikacin therapy should be discontinued.
Disorder of the nervous system
Neuromuscular blockades:
Specific risks are very rare when taking aminoglycosides. The occurrence of neuromuscular blockade, which can lead to respiratory arrest, can occur especially with intrapleural or intraperitoneal administration. The neuromuscular blocking properties of the aminoglycosides are enhanced by inhalation narcotics or muscle relaxants or curare-like drugs. Particularly at risk are patients with myasthenia gravis. Respiratory paresis requires artificial respiration. In addition, the application of potassium salts may be considered as a countermeasure.
Immune system disorders
Due to the content of sulfite it can lead to hypersensitivity reactions that may manifest as vomiting, diarrhea, wheezing, acute asthma attack, disturbance of consciousness or shock in individual cases, especially in bronchial asthma. These reactions can vary widely individually and can lead to life-threatening conditions

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

No studies on the effects on the ability to drive and use machines have been performed. Due to the occurrence of some adverse reactions the ability to drive and use machines may be impaired.

OVERDOSE

In case of overdosage there is a general risk for nephro-, oto- and neurotoxic (neuromuscular blockage) reactions. Neuromuscular blockage with respiratory arrest needs appropriate treatment including application of ionic calcium (e.g. as gluconat or lactobionat in 10-20% solution). In the event of overdosage or toxic reaction, peritoneal dialysis or haemodialysis 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 & MODE OF ADMINISTRATION

Posology
Adults and adolescents over 12 years:
The recommended intramuscular or intravenous dose for adults and adolescents with normal renal function (creatinine clearance ≥50 mg/min) is 15mg/kg/day given either as a single daily dose or as several equal doses (e.g. 7.5mg/kg all 12 hours, or 5mg/kg every 8 hours).
The total daily dose should not exceed 1.5g. For endocarditis and febrile neutropenic patients, dosing should be done twice a day, as there is insufficient data for once-daily dosing.
Children from 4 weeks to 12 years:
The recommended intramuscular or intravenous (slow intravenous infusion) dosage for children with normal renal function is 15-20mg/kg/day, given either as a single daily dose of 15-20mg/kg or divided into two doses of 7.5 mg/kg every 12 hours.
For endocarditis and febrile neutropenic patients, dosing should be done twice a day, as there is insufficient data for once-daily dosing.
Neonates:
An initial dose of 10mg/kg, then 7.5mg/kg every 12 hours.
Preterm infants:
The recommended dose for preterm infants is 7.5mg/kg every 12 hours.
Dosage in elderly patients (≥ 65 years):
Renal function should be taken into account in elderly patients.
Life-threatening infections and/or those caused by Pseudomonas
The adult dose may be increased to 500 mg every eight hours but should neither exceed 1.5 g/day nor be administered for a period longer than 10 days. A maximum total adult dose of 1.5 g should not be exceeded.
Urinary tract infections (other than pseudomonal infections):
7.5 mg/kg/day in two equally divided doses (equivalent to 250 mg twice daily in adults). As the activity of amikacin is enhanced by increasing the pH, a urinary alkalizing agent may be administered concurrently.
Other routes of administration
Amikacin in concentrations of 0.25% (2.5 mg/ml) may be used satisfactorily as an irrigating solution in abscess cavities, the pleural space, the peritoneum and the cerebral ventricles.
Intraperitoneal use
Following exploration for established peritonitis, or after peritoneal contamination due to faecal spill during surgery, Amikacin may be used as an irrigant after recovery from anaesthesia in concentrations of 0.25% (2.5 mg/mL). If instillation is desired in adults, a single dose of 500 mg is diluted in 20 mL of sterile distilled water and may be instilled through a polyethylene catheter sutured into the wound at closure. If possible, instillation should be postponed until the patient has fully recovered from the effects of anaesthesia and muscle-relaxing drugs.
Monitoring
The renal function status should be evaluated by measuring the serum creatinine concentration or preferably by estimation of creatinine clearance. Blood urea nitrogen (BUN) is far less reliable for this purpose. Assessment of renal function should be performed at the start of therapy and should be re-evaluated at regular intervals during treatment.
Amikacin concentrations in serum should be measured in all patients receiving parenteral amikacin and must be measured in obesity, if high doses are being given, the elderly and in cystic fibrosis. Both peak and trough serum concentrations should be measured intermittently

during therapy to ensure adequate but not excessive serum levels. In patients receiving multiple daily dosing peak concentrations (30-90 minutes after injection) of above 35µg/ml and trough concentrations (just before the next dose) of above 10µg/ml should be avoided.
In patients receiving once daily (or extended interval) dosing pre-dose ('trough') concentration should be less than 5 mcg/ml. Peak concentrations (approximately 60 minutes after administration) may exceed 35 mcg/ml.
If the pre-dose ('trough') concentration is high, the interval between doses must be increased. If the post-dose ('peak') concentration is high, the dose must be decreased.
Auditory and vestibular function should also be monitored during treatment, in particular if longer treatment duration (>7-10 days) is considered.
c) Dosage in renal impairment:
NOTE: In patients with impaired renal function (creatinine clearance <50ml/min) the recommended dose has to be decreased and adjusted to the renal function. This can be achieved by increasing the dose interval and/or reducing the dose.
In all patients with renal impairment, serum amikacin peak and trough concentration and renal function must be monitored regularly and the dose regimen altered as necessary (see below).
Once daily/extended interval dosing
Patients with renal impairment in whom once daily dosing would be considered appropriate if their renal function were normal may receive extended interval dosing. The initial dose may be the same as in normal renal function. The dose interval should be at least 24 hours and extended according to the degree of renal impairment and the results of serum amikacin level measurements (see Monitoring Advice).
In severe renal impairment, the initial dose may have to reduced in addition.
Once daily or extended interval dosing should be avoided in patients with a creatinine clearance less than 20 ml/minute.
A once daily/extended interval dose regimen should be avoided in children over 1 month of age with a creatinine clearance less than 20 ml/minute/1.73 m^2.
Reduced dose at fixed intervals:
If patients with renal impairment are given amikacin at fixed time intervals, the dose must be reduced. In these patients, the serum amikacin concentration should be measured to ensure accurate administration and to avoid excessive serum concentrations. If a determination of serum concentration is not possible and the patient's condition is stable, serum creatinine and creatinine clearance rates are the most readily available indicators of the extent of renal dysfunction and the consequent reduction in dose.
As renal function may alter appreciably during therapy, the serum creatinine should be checked frequently and the dosage regimen modified as necessary.
Multiple daily dosing
In patients with renal impairment in whom multiple *daily dosing at fixed intervals* would be considered appropriate if their renal function were normal, the dose must be reduced while the dose interval is maintained. Serum amikacin concentrations should be measured and creatinine clearance should be estimated regularly (see Monitoring Advice).
Treatment should be initiated 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 initially determine the size of maintenance doses administered after 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)
Subsequent doses should be determined based on amikacin serum concentrations (see Monitoring Advice).
Treatment duration
At recommended dosages, infections caused by susceptible pathogens should respond to therapy within 24-48 hours. If clinical response does not occur within 3-5 days, therapy should be discontinued and the antibiotic susceptibility pattern of the invading organism should be rechecked. If necessary, alternative therapy should be considered. Failure of therapy may be due to the resistance of the organism or to septic locus requiring surgical drainage.
The average duration of treatment is 7-10 days. For all routes of administration, the maximum daily dose should not exceed 15-20mg/kg/day. If prolonged treatment is required, it should be carried out after reviewing the necessity of using amikacin, determination of serum amikacin concentrations and additionally monitoring of renal, auditory and vestibular functions as closely as possible daily.
Method of administration
IM use or IV use after dilution.
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.
In paediatric patients the amount of diluents used will depend on the amount of amikacin tolerated by the patient. The solution should normally be infused 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.

PREGNANCY AND LACTATION
There are limited data on use of aminoglycosides in pregnancy. Amnioglycosides can cause foetal harm. Aminoglycosides cross the placenta and there have been reports of total, irreversible, bilateral congenital deafness in children whose mothers received streptomycin during pregnancy. Although adverse effects on the foetus or newborns have not been reported in pregnant women treated with other aminoglycosides, the potential for harm exists. In reproduction toxicity studies in mice and rats no effects on fertility or foetal toxicity were reported. If amikacin 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 foetus.
It is not known whether amikacin is excreted in human milk. A decision should be made whether to discontinue breast-feeding or to discontinue therapy.
Amikacin should be administered to pregnant women and neonatal infants only when clearly needed and under medical supervision.
The safety of amikacin in pregnancy has not yet been established.

STORAGE CONDITION
Store in cool & dark place

KEEP OUT OF REACH OF CHILDREN

PRESENTATION
1ml ampoules & 2ml Vial packed in cardboard carton along with pack insert.

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