SCHEDULING STATUS S4

1. NAME OF THE MEDICINE

AMIKACIN 500 mg/2 ml PHARMA-Q solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each single dose 2 ml vial contains: 500 mg amikacin (as amikacin sulphate).

Sugar content: Sugar free

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Clear, colorless to pale yellow solution for injection practically free from particles.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

AMIKACIN 500 mg/2 ml PHARMA-Q is indicated for the treatment of serious nosocomial gram-negative bacillary infections.

AMIKACIN 500 mg/2 ml PHARMA-Q is not indicated in the treatment of uncomplicated urinary tract infection unless the causative organisms are not susceptible to antibiotics having less potential toxicity. In these cases, reduced dosage may be prescribed (see section 4.2).

Concomitant therapy with a β-lactam antibiotic may be indicated in certain severe infections.

4.2 Posology and method of administration

Posology

Should clinical response not occur in 3 to 5 days, alternate therapy should be considered.

Treatment should preferably not continue for longer than 7 to 10 days and the total dosage in adults should not exceed 15 g. Because the risk of side effects is increased at high plasma concentrations it is desirable to determine dosage requirements by individual monitoring by means of serum concentrations and creatinine clearance. This is especially important in patients receiving high doses of prolonged courses, in infants and the elderly and in patients with impaired renal function in whom it is crucial to reduce maintenance dosage. The patient's pre-treatment body weight should be obtained for calculation of correct dosage.

Serum concentrations should be monitored, in patients without renal function impairment, and especially in patients with impaired renal function to ensure adequate concentrations and to avoid potentially toxic concentrations. Therapeutic concentration for amikacin should be in line with local laboratory practices.

Prolonged peak (post-distributional) concentrations (measured 15 to 30 minutes after injection) and trough concentrations (measured immediately prior to the next dose) greater than 30 µg/ml and 10 µg/ml respectively should be avoided.
Dosage adjustments should be individualised and based on peak and trough serum concentrations.

Renal Impairment:

The status of renal function should be estimated by measurement of the serum creatinine concentration or calculation of endogenous creatinine clearance rate. Reassessment of renal function should be made periodically during therapy. The patients should be well hydrated.

Adults and children (with impaired renal function):

Doses may be adjusted in patients with impaired renal function either by administering normal doses at prolonged intervals or by administering reduced doses at a fixed interval.

Both methods are based on the patient's creatinine clearance or serum creatinine values since these have been found to correlate with aminoglycoside half-lives including AMIKACIN 500 mg/2 ml PHARMA-Q in patients with diminished renal function. Neither method should be used when dialysis is being performed.

Normal dosage at prolonged intervals:

If the creatinine clearance rate is not available and the patient's condition is stable, dosage interval (in hours) = serum creatinine concentration in mmol/l (mg/ml) x 9 e.g., if the serum creatinine concentration is 0,176 mmol/l (2 mg/100 ml), the recommended single dose (7,5 mg/kg) should be administered every 18 hours.

Reduced dosage at fixed time intervals:

When renal function is impaired and it is desirable to administer AMIKACIN 500 mg/2 ml PHARMA-Q at a fixed time interval, dosage must be reduced. In these patients serum amikacin concentrations should be measured to assure accurate administration and to avoid concentration above local laboratory practices value. If serum assay determinations are not available and the patient's condition is stable, 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 dose, calculated for a patient with a normal renal function, 7,5 mg/kg, as a loading dose then calculate:

Maintenance doses*

$$= \frac{\text{observed CrCL in ml/min}}{\text{Normal CrCL in ml/min}} \times \text{calculated loading dose in mg}$$

*administered every 12 hours CrCL =creatinine clearance rate

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.

Adults and children (with normal renal function):

15 mg per kg lean body mass daily in divided doses every 8 to 12 hours to a maximum of 1,5 g daily in adults. Cystic fibrosis and burn patients may require larger doses, but because they eliminate the AMIKACIN 500 mg/2 ml PHARMA-Q faster than average, the dosing interval may need to be decreased too.

Neonates:

A loading dose of 10 mg per kg lean body mass followed by 15 mg per kg in two divided doses.

Preterm neonates:

9 mg per kg intravenously every 18 hours in infants under 30 weeks post conceptional age and every 12 hours in those over 30 weeks.

If a dose of AMIKACIN 500 mg/2 ml PHARMA-Q 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.

Method of administration

It is recommended that a needle not larger than 21 gauge is used to reduce fragmentation of the rubber stopper.

AMIKACIN 500 mg/2 ml PHARMA-Q may be given intramuscularly or intravenously.

Intravenous injections should be slow over 2 to 3 minutes or by infusion (0,25 %) over 30 to 60 minutes in adults or 1 to 2 hours in infants.

AMIKACIN 500 mg/2 ml PHARMA-Q may be diluted with 200 ml diluent to achieve a concentration of 0,25 % (2,5 mg/ml).

For instructions on dilution of the medicine before administration, see section 6.6.

4.3 Contraindications

- Hypersensitivity to amikacin or other aminoglycoside antibiotics or to any ingredients of AMIKACIN 500 mg/2 ml PHARMA-Q listed in section 6.1;
- Pregnancy and lactation;
- Patients with myasthenia gravis;
- Severe renal function impairment;
- Hearing impairment.

4.4 Special warnings and precautions for use

Since AMIKACIN 500 mg/2 ml PHARMA-Q forms complexes with a number of medicines, leading to incompatibilities and loss of activity, extemporaneous admixtures with AMIKACIN 500 mg/2 ml PHARMA-Q are not recommended. Each medicine should be administered separately.

Patients should be well hydrated during AMIKACIN 500 mg/2 ml PHARMA-Q therapy.

Caution should be applied to patients with pre-existing renal insufficiency, pre-existing hearing or vestibular damage and diminished glomerular filtration. 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.

If therapy is expected to last seven days or more in patients with renal impairment, or 10 days in other patients, a pre-treatment audiogram should be obtained and repeated during therapy.

Renal Toxicity

Aminoglycosides are potentially nephrotoxic. Renal toxicity is independent of plasma obtained at the peak (C_{max}). The risk of nephrotoxicity is greater in patients with impaired renal function, and in those who receive higher doses, or in those whose therapy is prolonged.

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.

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.

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 medicine or dosage adjustment.

Concurrent and/or sequential, oral, or topical use of other neurotoxic or nephrotoxic medicines, 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.

Patients suffering from pre-existing renal insufficiency should be assessed by the usual methods prior to therapy and periodically during therapy. Daily doses should be reduced and/or the interval between doses lengthened in accordance with serum creatinine

concentrations to avoid accumulation of abnormally high blood levels and to minimize the risk of ototoxicity. Regular monitoring of serum medicine concentration and of renal function is particularly important in elderly patients, who may have reduced renal function that may not be evident in the results of routine screening tests i.e. blood urea and serum creatinine.

Neuro/Ototoxicity

Neurotoxicity, manifested as vestibular and/or bilateral ototoxicity, can occur in patients treated with aminoglycosides such as AMIKACIN 500 mg/2 ml PHARMA-Q. 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 of treatment, even in healthy patients. 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 medicine has been discontinued. Aminoglycoside-induced ototoxicity is usually irreversible.

Neuromuscular Toxicity

Neuromuscular blockade and respiratory paralysis have been reported following parenteral injection, topical instillation (as in orthopaedic 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 anaesthetics, neuromuscular blocking medicines such as tubocurarine, succinylcholine, decamethonium, atracurium, rocuronium, vecuronium or in patients receiving massive transfusions of citrate-anticoagulated blood. If neuromuscular blockade occurs,

calcium salts may reverse respiratory paralysis, but mechanical respiratory assistance may be necessary. Neuromuscular blockade and muscular paralysis have been demonstrated in laboratory animals given high doses of amikacin.

AMIKACIN 500 mg/2 ml PHARMA-Q must not be used in patients with myasthenia gravis. AMIKACIN 500 mg/2 ml PHARMA-Q should be used with caution in patients with muscular disorders such as Parkinsonism since these medicines may aggravate muscle weakness because of their potential curare-like effect on the neuromuscular junction.

Allergic reactions

The use of AMIKACIN 500 mg/2 ml PHARMA-Q 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 medicines such as streptomycin, dihydrostreptomycin**,** gentamicin, tobramycin, kanamycin, neomycin, polymyxin B, colistin, cephaloridine or viomycin should be considered with caution, as toxicity may be additive.

Large doses of AMIKACIN 500 mg/2 ml PHARMA-Q administered during surgery have been responsible for a transient myasthenic syndrome.

AMIKACIN 500 mg/2 ml PHARMA-Q in vials 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. Sulfite sensitivity is seen more frequently in asthmatic than in non-asthmatic subjects.

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.

The use of AMIKACIN 500 mg/2 ml PHARMA-Q may result in overgrowth of non-susceptible organisms. If this occurs, appropriate therapy should be instituted.

Inventrious use

Macular infarction sometimes leading to permanent loss of vision has been reported following intravitreous administration (injection into the eye) of amikacin.

Paediatric population

AMIKACIN 500 mg/2 ml PHARMA-Q 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 medicines.

4.5 Interactions with other medicines and other forms of interaction

The concurrent or serial use of other neurotoxic, ototoxic or nephrotoxic medicines, particularly bacitracin, cisplatin, amphotericin B, ciclosporin, tacrolimus, cephaloridine, paromomycin, viomycin, polymyxin B, colistin, vancomycin, or other aminoglycosides should be avoided either systemically or topically because of the potential for additive effects. Where this is not possible, monitor carefully.

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 concurrent use of AMIKACIN 500 mg/2 ml PHARMA-Q 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.

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 medicine 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 bisulfite component of the amikacin sulfate formulation.

The intraperitoneal use of amikacin is not recommended in patients under the influence of anaesthetics or muscle-relaxing medicines (including ether, halothane, d-tubocurarine, succinylcholine and decamethonium) as neuromuscular blockade and consequent respiratory depression may occur.

Paediatric population

Indomethacin may increase the plasma concentration of AMIKACIN 500 mg/2 ml PHARMA-Q in neonates.

4.6 Fertility, pregnancy and lactation

Safety in pregnancy and breastfeeding has not been established

Pregnancy

AMIKACIN 500 mg/2 ml PHARMA-Q is contraindicated during pregnancy (see section 4.3).

Use of AMIKACIN 500 mg/2 ml PHARMA-Q during pregnancy may damage the 8th cranial nerve of the foetus.

If the patient becomes pregnant while receiving AMIKACIN 500 mg/2 ml PHARMA-Q, the patient should be apprised of potential hazard to the foetus**.**

Lactation

AMIKACIN 500 mg/2 ml PHARMA-Q is contraindicated in lactation (see section 4.3).

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.

Fertility

In reproduction toxicity studies in mice and rats no effects on fertility or foetal toxicity were reported.

4.7 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 (see section 4.8) the ability to drive and use machines may be impaired.

4.8 Undesirable effects

a. Summary of the safety profile

All aminoglycosides have the potential to induce ototoxicity, renal toxicity, and neuromuscular blockade. These toxicities occur more frequently in patients with renal impairment, in patients treated with other ototoxic or nephrotoxic medicines, and in patients treated for longer periods and/or with higher doses than recommended (see section 4.4)

b. Tabulated summary of adverse reactions

Infections and Infestations

Less frequent: Superinfections or colonisation with resistant bacteria or yeast.

Blood and lymphatic system disorders

Frequency not known: Hypocalcaemia and hypokalaemia have occurred in association with antineoplastic medicines. Anaemia, purpura may occur, eosinophilia.

Immune system disorders

Frequency not known: Hypersensitivity (skin itching, redness, rash or swelling) to AMIKACIN 500 mg/2 ml PHARMA-Q and cross allergy among aminoglycosides has been demonstrated. Increased serum aminotransferase values and increased serum billrubin concentrations have been reported.

Metabolism and nutrition disorders

Less frequent: Hypomagnesaemia.

Nervous system disorders

Less frequent: Tremor, paraesthesia, headache, balance disorder.

Frequency not known: Paralysis, neurotoxicity (numbness, skin tingling, muscle twitching and convulsions).

Eye disorders

Less frequent: Retinal infarction, blindness.

Frequency not known: Visual disturbances.

Ear and labyrinth disorders

Frequency not known: Irreversible ototoxicity (auditory with loss of hearing, ringing or buzzing, a feeling of fullness in the ears and vestibular with clumsiness, dizziness, nausea, vomiting, unsteadiness) as well as reversible nephrotoxicity may occur.

Vascular disorders

Less frequent: Hypotension

Respiratory, thoracic and mediastinal disorders

Frequency not known: Apnoea, bronchospasm.

Gastro-intestinal disorders

Less frequent: Nausea, vomiting

Frequency not known: Pseudomembranous colitis may occur

Skin and subcutaneous tissue disorders

Less frequent: Rash, pruritus, urticarial.

Musculoskeletal, connective tissue and bone disorders

Frequency not known: AMIKACIN 500 mg/2 ml PHARMA-Q possesses a neuromuscular blocking action and respiratory depression and muscular paralysis have been reported.

Renal and urinary disorders

Less frequent: Oliguria, blood creatinine increased, albuminuria, azotemia, red blood cells urine, white blood cells urine.

Frequency not known: Acute renal failure may occur. When patients are well hydrated and kidney function is normal, risk of nephrotoxic reactions with AMIKACIN 500 mg/2 ml PHARMA-Q is low if the dosage recommendations (see section 4.2) are not exceeded. Volume depletion or hypotension, liver disease or females have been reported as additional risk factors for nephrotoxicity. Because of the high concentrations of amikacin in the urine and kidney, patients should be well hydrated to prevent or minimize chemical irritation of the renal tubules.

General disorders and administration site conditions

Less frequent: Pyrexia

c. Description of selected adverse reactions

Renal function changes are usually reversible when the medicine is discontinued.

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 (see section 4.4).

Macular infarction sometimes leading to permanent loss of vision has been reported following intravitreous administration (injection into the eye) of amikacin.

When the recommended precautions and dosages are followed the incidence of toxic reactions, such as tinnitus, vertigo, and partial reversible deafness, skin rash, medicine fever, headache, paraesthesia, nausea and vomiting is low. Urinary signs of renal irritation (albumin, casts, and red or white cells), azotaemia and oliguria have been reported although they are rare.

d. Paediatric population

AMIKACIN 500 mg/2 ml PHARMA-Q 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 medicines.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the “6.04 Adverse Drug Reaction Reporting Form”, found online under SAHPRA’s publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

In case of overdosage there is a general risk for nephro-, oto- and neurotoxic (neuromuscular blockage) reactions. Since there is no specific antidote, treatment of AMIKACIN 500 mg/2 ml PHARMA-Q overdose or toxic reactions should be symptomatic and supportive.

In the event of overdosage or toxic reaction, peritoneal dialysis or haemodialysis will aid in the removal of AMIKACIN 500 mg/2 ml PHARMA-Q from the blood. AMIKACIN 500 mg/2 ml PHARMA-Q levels are also reduced during continuous arteriovenous hemofiltration. In the new-born infant, exchange transfusion may also be considered.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group and ATC code: J01G B06

Pharmacodynamic effects

Amikacin is a semi-synthetic aminoglycoside with a broad antimicrobial activity and exhibits resistance to aminoglycoside-inactivating enzymes.

Aminoglycosides inhibit protein synthesis in susceptible bacteria by binding to the 30S ribosomal unit.

5.2 Pharmacokinetic properties

Amikacin is bactericidal and is effective *in vitro* against many species of Gram-negative bacteria including species of: *Citrobacter*, *Escherichia, Enterobacter, Klebsiella, Proteus, Providencia, Pseudomonas* and *Serratia.* It is effective against most strains of *Staphylococcus aureus, Listereria monocytogenes* and some *Staphylococcus epidermidis* may also be sensitive. *In vitro* activity does not necessarily imply *in vivo* efficacy.

Distribution

It is largely excluded from most cells, from the central nervous system and eye. Penetration into respiratory secretions is poor. Diffusion into pleural and synovial fluid is relatively slow, but concentrations that approximate those in the plasma may be achieved after repeated administration.

High concentrations are found in the renal cortex and in the endolymph and perilymph of the inner ear. Inflammation increases its penetration into peritoneal and pericardial cavities.

Inadequate concentrations for the treatment of meningitis are achieved in the cerebrospinal fluid in adults.

Absorption

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.

Elimination

Elimination of amikacin is almost entirely by glomerular filtration. Amikacin has a half-life of 2-3 hours, most of the dose being excreted within 24 hours.

Paediatric population

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 (< 2 000, 2 000-3 000 and > 3000 g). Amikacin was administered intramuscularly and/or intravenously at a dose of 7,5 mg/kg. Clearance in neonates > 3 000 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.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium meta bisulfite, sodium citrate (dihydrate), sulfuric Acid 10 %, water for Injections.

6.2 Incompatibilities

AMIKACIN 500 mg/2 ml PHARMA-Q is incompatible (*in-vitro*) with beta-lactam antibacterial (penicillin and cephalosporin), aminophyllin, amphotericin, hydrochlorothiazide, dexamethasone, sodium phosphate, erythromycin, heparin, phenytoin sodium, potassium chloride, tetracyclines, sodium thiopentone, Vitamin B and C complex and warfarin sodium. Since AMIKACIN 500 mg/2 ml PHARMA-Q forms complexes with a number of medicines, leading to incompatibilities and loss of activity, extemporaneous admixtures with AMIKACIN 500 mg/2 ml PHARMA-Q are not recommended. Each medicine should be administered separately.

6.3 Shelf life

Before mixing: 24 months

After mixing: Following dilution in 5 % glucose solution or 5 % glucose and 0,45 % sodium chloride solutions chemical and physical in-use stability has been demonstrated for 24 hours when stored at or below 25 °C

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours. Any unused portion must be discarded.

6.4 Special precautions for storage

Store at or below 25 °C

KEEP OUT OF REACH OF CHILDREN.

For storage conditions after first opening of the medicine, see section 6.3.

6.5 Nature and contents of container

2 ml in 2 ml flint glass USP type-I 13 mm neck vial stoppered with 13 mm grey chlorobutyl rubber stopper (RFU) and sealed with 13 mm blue color flip off aluminium seal in a single carton.

6.6 Special precautions for disposal and other handling

AMIKACIN 500 mg/2 ml PHARMA-Q should be diluted with 5 % glucose solution or 5 % glucose and 0,45 % sodium chloride solutions.

AMIKACIN 500 mg/2 ml PHARMA-Q may be diluted with 200 ml diluent to achieve a concentration of 0,25 % (2,5 mg/ml).

Discard any unused portion.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Pharma-Q Holdings (Pty) Ltd

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Industria-West

2093

Johannesburg

Tel: +27 11 247 1600

8. REGISTRATION NUMBER

51/20.1.1/1065

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

20 July 2021

10. DATE OF REVISION OF THE TEXT

23 March 2026