# WHO-PQ RECOMMENDED SUMMARY OF PRODUCT CHARACTERISTICS

*This summary of product characteristics focuses on uses of the medicine covered by WHO's Prequalification Team - Medicines. The recommendations for use are based on WHO guidelines and on information from stringent regulatory authorities.*[*]

*The medicine may be authorised for additional or different uses by national medicines regulatory authorities.*

[*]https://extranet.who.int/pqweb/sites/default/files/documents/75%20SRA%20clarification_Feb2017_newtempl.pdf

# 1. NAME OF THE MEDICINAL PRODUCT

[TB319 trade name]†

# 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ampoule of 2 mL of solution for injection contains amikacin (as sulfate) equivalent to 500 mg amikacin.

*Excipients with known effects:*

Each ampoule contains 13.2 mg of sodium metabisulfite.

For a full list of excipients see 6.1

# 3. PHARMACEUTICAL FORM

Solution for injection.

A clear, colourless to slightly yellow liquid.

# 4. CLINICAL PARTICULARS

## 4.1 Therapeutic indications

[TB319 trade name] is indicated in combination with other antituberculosis agents for the treatment of multi-drug resistant tuberculosis (MDR-TB) caused by amikacin-sensitive strains of *Mycobacterium tuberculosis*.

Amikacin is only indicated as a second-line antimycobacterial agent when first-line medicines cannot be used because of resistance or intolerance.

Consideration should be given to current official treatment guidelines for tuberculosis (e.g., those of the WHO).

## 4.2 Posology and method of administration

**Posology**

[TB319 trade name] is always given in combination with other anti-tuberculosis medicines for the treatment of MDR-TB.

The duration of amikacin therapy is based on individual response and drug susceptibility (please refer to official treatment guidelines for tuberculosis).

*Dosing recommendations for patients 15 years and older*

The recommended dose is 15-20 mg/kg body weight, taken once daily, up to a maximum dose of 1 g per day.

| Weight-based daily dose | Weight bands in patients 15 years old or older | | | | |
|---|---|---|---|---|---|
| | 30-35 kg | 36-45 kg | 46-55 kg | 56-70 kg | >70 kg |
| Volume of 500 mg/2 mL solution for injection, ampoule* | 2.5 mL | 3 mL | 3-4 mL | 4 mL | 4 mL |

* The weight-based daily dose is for 6 or 7 days/week administration (M/W/F scheduling may permit higher dosing). Volumes shown may differ by preparation. For iv use, the volume may be increased.

† Trade names are not prequalified by WHO. This is the national medicines regulatory agency's responsibility.

*Children younger than 15 years*

The dose is 15-20 mg/kg body weight, taken once daily, up to a maximum dose of 1 g per day.

| Weight-based daily dose | Weight bands in patients under 15 years old | | | | | | |
|---|---|---|---|---|---|---|---|
| | 5-6 kg | 7-9 kg | 10-15 kg | 16-23 kg | 24-30 kg | 31-34 kg | > 34 kg |
| Volume of 500 mg/2 mL solution for injection, ampoule* | 0.4 mL | 0.6 mL | 0.8-1.0 mL | 1.2-1.5 mL | 2.0 mL | (> 14 years) | (> 14 years) |

* Weight-based daily dose is for 6 or 7 days/week administration (M/W/F scheduling may permit higher dosing). Volumes shown may differ by preparation. Dosing closer to the upper limit of the mg/kg/day is more desirable. For iv use, the volume may be increased.

***Special populations***

*Renal impairment*

[TB319 trade name] should be used with caution in patients with renal disease because of the increased risk of both ototoxicity and nephrotoxicity, and plasma-drug concentrations should be monitored. In patients with $CL_{CR}$ < 50 mL/min the dose should be decreased and/or the interval between doses increased, based on plasma drug concentrations.

As renal function may change during therapy, serum creatinine should be checked frequently, and the dosage regimen modified as necessary.

In patients with severe renal impairment ($CL_{CR}$ < 30 ml/min or on dialysis) and those on haemodialysis, the dose should be adjusted to 12–15 mg/kg once daily, 2–3 times each week at roughly equal intervals throughout the week (see sections 4.4 and 5.2). In patients on haemodialysis, the dose should be given after the dialysis on the day of haemodialysis.

*Hepatic impairment*

No dose adjustment is necessary.

*Paediatric population*

The use of injectable agents, such as amikacin, in children should be exceptional and limited to salvage therapy because of the risk of serious toxicities (i.e. ototoxicity and nephrotoxicity), and given the profound impact that hearing loss can have on the acquisition of language and the ability to learn at school. [TB319 trade name] should only be used in children under strict monitoring to ensure early detection of ototoxicity.

**Method of administration**

Amikacin may be given intramuscularly or intravenously.

*Intramuscular injection*

Adults: The preferred site is the mid-lateral thigh or the upper outer quadrant of the buttock. The deltoid area (at the upper third of upper arm) should be used only if well-developed such as in certain adults and older children.

Children: It is recommended that intramuscular injections be given preferably in the mid-lateral muscles of the thigh.

*Intravenous injection or infusion*

See section 6.6 for advice on reconstitution of injection.

## 4.3 Contraindications

Hypersensitivity to amikacin or to any of the excipients listed in section 6.1.

Clinically significant hypersensitivity to other aminoglycosides may contraindicate the use of amikacin because of the known cross-sensitivity of patients to medicines in this class.

## 4.4 Special warnings and precautions for use

***Warnings***

Amikacin should only be used to treat tuberculosis if susceptibility to amikacin is confirmed and if high-quality audiometry monitoring for hearing loss can be ensured.

*Neuro/ototoxicity*

The use of aminoglycosides, including amikacin, is associated with a risk of hearing impairment and renal injury resulting from its toxic effects on the auditory and vestibular branches of the eighth cranial nerve and the renal tubules. Patients with impaired renal function and those with normal renal function who receive high doses or prolonged therapy (as for the treatment of tuberculosis) are at increased risk of severe neurotoxic (mainly ototoxic) and nephrotoxic reactions. The risk of these toxic effects should be carefully weighed against the potential benefits of treatment. The use of amikacin in patients with renal insufficiency or auditory impairment must be undertaken with great caution.

Neurotoxicity is manifested by bilateral auditory toxicity and sometimes by vestibular ototoxicity, both of which may be permanent. Loss of high frequency perception usually occurs before there is noticeable clinical hearing loss and can be detected by audiometric testing. There may not be clinical symptoms to warn of developing cochlear damage. Vertigo may occur and there may be evidence of vestibular injury. Other manifestations of neurotoxicity may include numbness, skin tingling, muscle twitching, and convulsions. The risk of hearing loss increases with the degree of exposure to either high peak or high trough serum concentrations and continues to progress after drug withdrawal.

Because of the risk of hearing impairment, the use of amikacin in children, especially in very young children and children with mild disease as determined by the absence of malnutrition, serious forms of extrapulmonary disease, cavitation on chest radiography or HIV infection should be avoided. Hearing loss can have a permanent impact on the acquisition of language and the ability to learn at school. If amikacin is used in children, regular audiometry is critical.

Amikacin should be avoided in patients who may have subclinical renal or eighth nerve damage induced by prior use of nephrotoxic and/or ototoxic agents such as amphotericin B, streptomycin, dihydrostreptomycin, gentamicin, tobramycin, kanamycin, neomycin, polymyxin B, colistin, cephaloridine, vancomycin or viomycin, as toxicity may be additive. If its use is unavoidable, these patients should be monitored closely for neurotoxic and nephrotoxic reactions.

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 medicines.

*Neuromuscular toxicity*

Neuromuscular blockade and respiratory paralysis have been reported following aminoglycoside use. The possibility of respiratory paralysis should be considered if aminoglycosides are administered by any route, especially in patients receiving anaesthetics or neuromuscular blocking agents or in patients receiving massive transfusions of citrate-anticoagulated blood (see section 4.5). If neuromuscular blockade occurs, mechanical respiratory assistance may be necessary.

Amikacin should be used with caution in conditions characterised by muscular weakness, since it may aggravate muscle weakness because of its potential curare-like effect on the neuromuscular junction.

*Resistance*

Amikacin must be used in conjunction with adequate doses of other antituberculous drugs. The use of amikacin alone allows rapid development of strains resistant to it.

As with other antibiotics, the use of amikacin may result in overgrowth of non-susceptible organisms. If this occurs, appropriate therapy should be instituted.

***Precautions***

As amikacin is potentially ototoxic, hearing (e.g. by audiometry) and vestibular function should be assessed before starting treatment and at monthly intervals during treatment.

In case of clinically significant ototoxicity or if early symptoms of vestibular toxicity appear, the dosing frequency should be decreased to 2–3 times a week. If symptoms worsen despite dose adjustment, amikacin should be stopped and, if possible, additional anti-TB medicines should be added to reinforce the regimen. Hearing loss and vestibular dysfunction are generally not reversible upon discontinuation of therapy.

Patients should be well hydrated during treatment. Renal function should be tested at least monthly throughout treatment, and the dose should be reduced in patients with known or suspected renal impairment (see section 4.2). If serum creatinine continues to rise, amikacin should be stopped.

If feasible, therapeutic drug monitoring should be conducted in patients with renal impairment. Peak and trough plasma-amikacin concentration should be measured at the start of treatment, and plasma-amikacin concentrations should be measured throughout treatment. Peak concentrations (30 to 90 minutes after injection) >35 μg/mL and trough concentrations (just prior to the next dose) >10 μg/mL should be avoided because of the associated risk of toxicities (for therapeutic drug concentrations see section 5.2).

Elderly patients may have reduced renal function. Monitoring of renal function in elderly patients during treatment with aminoglycosides is particularly important.

Changes in hepatic function may occur and liver function should be tested periodically.

***Excipients***

Each ampoule contains 13.2 mg of sodium metabisulfite (E223), a sulfite that may rarely cause severe hypersensitivity reactions and bronchospasm. Sulfite sensitivity in the general population is generally uncommon and is seen more frequently in asthmatic than in non-asthmatic subjects.

It is important to consider the contribution of excipients from all the medicines that the patient is taking.

## 4.5 Interaction with other medicinal products and other forms of interaction

Simultaneous administration of other antituberculous medicines which also have ototoxic and nephrotoxic potential (e.g. streptomycin, kanamycin) is not recommended. Also, other neurotoxic, ototoxic or nephrotoxic medicines should not be administered to patients receiving amikacin. These include other aminoglycoside antibiotics, polymyxin B, colistin, cephalosporins, amphotericin B, ciclosporin, cisplatin, methoxyflurane and diuretics (e.g. furosemide, etacrynic acid, mannitol). Where this is not possible, neurotoxic, ototoxic or nephrotoxic effects should be carefully monitored for.

Neuromuscular blockade and respiratory paralysis may occur from administration of aminoglycosides to patients under the influence of anaesthetics or muscle-relaxing medicines (including ether, halothane, d-tubocurarine, succinylcholine, decamethonium, atracurium, rocuronium, vecuronium or in patients receiving massive transfusions of citrate-anticoagulated blood).

Concurrent use of the botulinum toxin and aminoglycoside antibiotics may increase the risk of toxicity due to enhanced neuromuscular block.

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).

Indomethacin may increase the plasma concentration of amikacin in neonates. Indomethacin and other non-steroidal anti-inflammatory drugs (NSAIDs) may also enhance the nephrotoxicity of amikacin.

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

A reduction in the effect of neostigmine or pyridostigmine occurs with concomitant administration of aminoglycoside antibiotics.

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

## 4.6 Fertility, pregnancy and breastfeeding

*Pregnancy*

Studies in animals have shown reproductive toxicity (see section 5.3).

The safety of amikacin in pregnancy has not yet been established. Amikacin should be administered to pregnant women and neonatal infants only when clearly needed and under medical supervision (see section 4.4).

There are limited data on the use of aminoglycosides in pregnancy. Aminoglycosides can cause fetal harm. Aminoglycosides cross the placenta and there have been reports of total, irreversible, bilateral congenital deafness in children whose mother received streptomycin during pregnancy. Adverse effects on the fetus or newborns have been reported in pregnant women treated with other aminoglycosides, therefore the potential for harm exists. If amikacin is used during pregnancy or if the patient becomes pregnant while taking this medicine, the patient should be appraised of the potential hazard to the fetus.

*Breastfeeding*

Amikacin appeared in human milk in low concentrations. Milk:plasma ratios ranging between 0.05 and 0.40 have been reported. The small dose derived from breastfeeding and the poor gastrointestinal absorption of [TB319 trade name] make it unlikely that neonatal toxicity would appear from milk exposure.

Amikacin can be used under caution during breastfeeding.

*Fertility*

There are no data on the effects of amikacin on human male or female fertility. Animal studies indicate no effects of amikacin on male or female fertility (see section 5.3).

## 4.7 Effects on ability to drive and use machines

Patients should be warned about the potential for symptoms of vestibular toxicity while taking amikacin (see sections 4.4 and 4.8) and should be advised not to drive or operate machines if any of these symptoms occur.

## 4.8 Undesirable effects

The majority of available safety data on amikacin has been generated in patients with other conditions than tuberculosis in studies using shorter treatment durations (mostly up to 10 days) than recommended for tuberculosis treatment.

The major toxic effects associated with amikacin therapy are ototoxicity and nephrotoxicity. The risks are higher for patients with renal impairment or a history of renal impairment, for those receiving concomitant or sequential treatment with other ototoxic or nephrotoxic drugs or rapid acting diuretic agents given intravenously, and for patients treated for longer periods and/or with higher doses than recommended.

The adverse reactions are listed below by body system organ class and frequency. Frequencies are defined as follows: 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). Note that the frequencies relate to short-term therapy (<1 month).

**Infections and infestations**

| | |
|---|---|
| Uncommon | superinfections or colonization with resistant bacteria or yeast |

**Blood and lymphatic system disorders**

| | |
|---|---|
| Rare | anaemia, eosinophilia, thrombocytopenia, granulocytopenia |

**Immune system disorders**

| | |
|---|---|
| Frequency not known | hypersensitivity reactions, anaphylactic reaction, anaphylactic shock, anaphylactoid reaction |

**Metabolism and nutrition disorders**

| | |
|---|---|
| Rare | hypomagnesaemia |

**Nervous system disorders**

| | |
|---|---|
| Common | vertigo |
| Rare | paresthesia, tremor, balance disorders, headache |
| Frequency not known | paralysis |

**Ear and labyrinth disorders**

| | |
|---|---|
| Common | hearing loss, tinnitus |
| Frequency not known | deafness, sensory deafness |

**Vascular disorders**

| | |
|---|---|
| Rare | hypotension |

**Cardiac disorders**

| | |
|---|---|
| Rare | tachycardia and myocarditis |

**Respiratory, thoracic and mediastinal disorders**

| | |
|---|---|
| Frequency not known | apnoea, bronchospasm |

**Gastrointestinal disorders**

| | |
|---|---|
| Uncommon | nausea, vomiting |

**Hepatobiliary disorders**

| | |
|---|---|
| Rare | elevated transaminases |

**Skin and subcutaneous tissue disorders**

| | |
|---|---|
| Uncommon | rash |
| Rare | urticaria, pruritus |

**Musculoskeletal, connective tissue and bone disorders**

| | |
|---|---|
| Rare | arthralgia, muscle twitching |

**Renal and urinary disorders**

| | |
|---|---|
| Common | nephrotoxicity, oliguria |
| Frequency not known | increased serum creatinine, albuminuria, azotaemia, haematuria, acute renal failure |

**General disorders and administration site conditions**

| | |
|---|---|
| Rare | pyrexia |

### *Reporting of suspected adverse reactions*

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Health care providers are asked to report any suspected adverse reactions to the marketing authorisation holder, or, if available, via the national reporting system.

### 4.9 Overdose

*Symptoms*

In case of overdosage there is a general risk of nephro-, oto- and neurotoxic (neuromuscular blockade and respiratory paralysis) reactions (see section 4.4).

*Treatment*

Symptomatic and supportive therapy is recommended. Neuromuscular blockade with respiratory arrest needs appropriate treatment. Artificial respiration may be required in the event of respiratory paralysis.

Fluid balance, electrolytes and creatinine clearance should be monitored. Haemodialysis or peritoneal dialysis is effective in the removal of amikacin from the blood. In the newborn infant, exchange transfusion may also be considered.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Aminoglycoside antibacterials; ATC Code J01GB06.

*Mode of action*

Amikacin is a semi-synthetic aminoglycoside antibiotic derived from kanamycin A. It is a bactericidal agent, most likely acting through inhibition of protein synthesis by binding to the 30S ribosomal subunits.

*Mechanisms of resistance*

Various mechanisms may underlie resistance against aminoglycosides. The most common mechanism is inactivation of aminoglycosides by aminoglycoside-modifying enzymes (acetyltransferases, phosphotransferases or nucleotidyltransferases). Resistance can also be caused by modification of the ribosome target through mutations or by ribosomal methyltransferase enzymes. In addition, decreased permeability of the bacterial cell wall and active expulsion of aminoglycosides out of the cell by efflux pumps contribute to resistance.

There is partial cross-resistance of amikacin with other aminoglycoside antibiotics.

### 5.2 Pharmacokinetic properties

No pharmacokinetic data are available for [TB319 trade name] since a biowaver applies.

| **Absorption** | |
|---|---|
| Absorption | Rapid absorption after intramuscular injection.<br>Peak serum levels of approximately 11 mg/L and 23 mg/L are reached one hour after intramuscular doses of 250 mg and 500 mg respectively.<br>Peak serum concentration of 38 mg/L are reached at the end of a 30-min intravenous infusion of 500 mg. |
| Oral Bioavailability | ~100% |
| Food effect | Not applicable |
| $T_{max}$ | 1–2 hours |
| **Distribution** | |
| Volume of distribution (mean) | 24 L |
| Plasma protein binding *in vitro* | <20% |
| Tissue distribution | Amikacin has been found in cerebrospinal fluid, pleural fluid, amniotic fluid and in the peritoneal cavity following parenteral administration. It accumulates in the renal cortex and inner ear fluid |

| | |
|---|---|
| | and is only slowly eliminated from these deep compartments.<br>Amikacin passes the placental barrier and is excreted in human milk. Concentrations reaching 20% of those in the mother have been found in fetal blood and in the amniotic fluid. |
| **Metabolism** | |
| | Amikacin is not metabolised. |
| Active metabolites | Not applicable |
| **Elimination** | |
| Plasma half-life | 2 to 3 hours. Elimination is via the kidneys, mainly by glomerular filtration, as unchanged drug. |
| Mean serum clearance | 100 mL/min |
| Mean renal clearance | 94 mL/min (in subjects with normal renal function) |
| % of dose excreted in urine | 94–98% |

**Special populations**

*Renal impairment*

Amikacin is excreted primarily by glomerular filtration. Elimination is decreased in patients with impaired renal function, resulting in an increased elimination-half-life. This may lead to accumulation of amikacin.

*Hepatic impairment*

Drug concentrations are not affected by hepatic disease.

*Paediatric patients*

Data from dosing studies on a daily basis show that levels in CSF in normal children are around 10 to 20% of serum concentrations and may reach 50% in meningitis.

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 >3000 g). 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.

## 5.3 Preclinical safety data

Neuromuscular blockade and muscular paralysis have been demonstrated in laboratory animals given high doses of amikacin.

In repeat-dose toxicity studies, the main effects were nephrotoxicity and ototoxicity.

Amikacin has been tested for mutagenicity. The tests indicate that amikacin is not an in vivo mutagen. No carcinogenicity studies have been performed.

In studies on reproduction toxicity, amikacin caused dose-related nephrotoxicity in pregnant rats and their fetuses. Reproductive toxicity studies in offspring of mice, rats and rabbits revealed increased fetal death rates. Intravitreal dosages of 200 mg/kg/day in pregnant rats and pregnant guinea pigs led to hearing impairment in the offspring.

# 6. PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

Sodium metabisulfite

Sodium citrate dihydrate

Sulfuric acid (for pH adjustment)

Water for injection

## 6.2 Incompatibilities

Amikacin is incompatible with some penicillins and cephalosporins, amphotericin, chlorothiazide sodium, erythromycin, gluceptate, heparin, nitrofurantoin sodium, phenytoin sodium, thiopentone sodium and warfarin sodium, and depending on the composition and strength of the vehicle, tetracyclines, vitamin B, vitamin C, and potassium chloride.

If concomitant use with other antibacterial agents is indicated, amikacin should not be mixed with other medicines, but must be administered separately.

## 6.3 Shelf life

18 months

## 6.4 Special precautions for storage

Store below 30°C. Avoid excursions above 30°C.

Following dilution with the infusion solutions, chemical and physical in-use stability has been demonstrated for 24 hours at 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 at 2 to 8ºC, unless dilution has taken place in controlled and validated aseptic conditions.

## 6.5 Nature and contents of container

2 ml colourless type I glass ampoules.

Pack size: Carton of 10 ampoules.

## 6.6 Special precautions for disposal and other handling

Single use only.

Amikacin solution should be checked for particulate matter and discoloration before use. Solutions that show discoloration, haziness, visible particulate matter or precipitation should not be used.

Amikacin solution for injection can be mixed with D5W or other solutions for intravenous infusion. Adult doses should be administered over 30–60 minutes.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

# 7. SUPPLIER

Qilu Pharmaceutical Co., Ltd.
No. 23999 Gong Ye Bei Road
Jinan, Shandong Province,

250100
P. R. China

## 8. WHO REFERENCE NUMBER (WHO Prequalification Programme)

TB319

## 9. DATE OF PREQUALIFICATION

11 May 2018

## 10. DATE OF REVISION OF THE TEXT

November 2021
Section 7 was updated in February 2024

***References***

WHO Consolidated Guidelines on Tuberculosis, Module 4: Treatment - Drug-Resistant Tuberculosis Treatment. 15 June 2020.
https://www.who.int/publications/i/item/9789240007048

WHO Operational Handbook on Tuberculosis, Module 4: Treatment - Drug-Resistant Tuberculosis Treatment. 15 June 2020.
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Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis. WHO 2014.
https://apps.who.int/iris/bitstream/handle/10665/130918/9789241548809_eng.pdf

Label Amikacin Sulfate: https://www.drugs.com/pro/amikacin.html [Accessed November 2021]

Fachinformation Amikacin B. Braun Infusionslösung:
https://www.fachinfo.de/pdf/014273#view=FitH&pagemode=none&toolbar=1&statusbar=0&messages=0&navpanes=0 [Accessed November 2021]

UK SmPC Amikacin 250 mg/ml Solution for Injection/Infusion:
https://www.medicines.org.uk/emc/product/11189/smpc [Accessed November 2021]

UK SmPC Amikacin 250 mg/ml Injection:
https://www.medicines.org.uk/emc/product/3784/smpc [Accessed November 2021]

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Garneau-Tsodikovaa S. and Labby KJ. Mechanisms of Resistance to Aminoglycoside Antibiotics: Overview and Perspectives. Medchemcomm. 2016 Jan 1; 7(1): 11–27.

Section 4.6 and 5.3
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*Detailed information on this medicine is available on the World Health Organization (WHO) website: https://extranet.who.int/pqweb/medicines*