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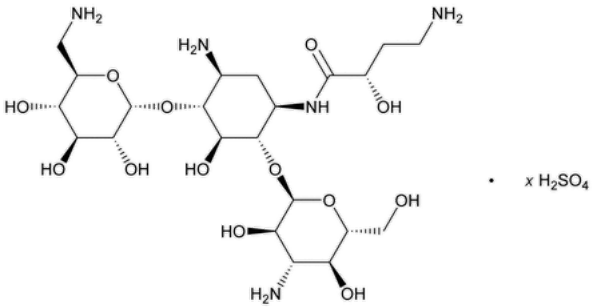
Amikacin Sulfate



$C_{22}H_{43}N_5O_{13} \cdot xH_2SO_4$

D-Streptamine, *O*-3-amino-3-deoxy-α-D-glucopyranosyl-(1→6)-*O*-[6-amino-6-deoxy-α-D-glucopyranosyl-(1→4)]-N^1-(4-amino-2-hydroxy-1-oxobutyl)-2-deoxy-, (*S*)-, sulfate (1:2 or 1:1.8 salt);

O-3-Amino-3-deoxy-α-D-glucopyranosyl-(1→4)-*O*-[6-amino-6-deoxy-α-D-glucopyranosyl-(1→6)]-N^3-(4-amino-L-2-hydroxybutyryl)-2-deoxy-D-streptamine sulfate (1:2 or 1:1.8 salt);

(2*S*)-4-Amino-*N*-{(1*R*,2*S*,3*S*,4*R*,5*S*)-5-amino-2-[(3-amino-3-deoxy-α-D-glucopyranosyl)oxy]-4-[(6-amino-6-deoxy-α-D-glucopyranosyl)oxy]-3-hydroxycyclohexyl}-2-hydroxybutanamide sulfate (1:2 or 1:1.8 salt).

$C_{22}H_{43}N_5O_{13} \cdot 1.8H_2SO_4$ 762.15 CAS RN®: 149022-22-0.

$C_{22}H_{43}N_5O_{13} \cdot 2H_2SO_4$ 781.76 CAS RN®: 39831-55-5; UNII: N6M33094FD.

DEFINITION

Amikacin Sulfate having a molar ratio of amikacin to sulfuric acid (H_2SO_4) of 1:2 contains the equivalent of NLT 674 µg/mg and NMT 786 µg/mg of amikacin ($C_{22}H_{43}N_5O_{13}$), calculated on the dried basis. Amikacin Sulfate having a molar ratio of amikacin to sulfuric acid (H_2SO_4) of 1:1.8 contains the equivalent of NLT 691 µg/mg and NMT 806 µg/mg of amikacin ($C_{22}H_{43}N_5O_{13}$), calculated on the dried basis.

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K or 197A

  Acceptance criteria: The IR absorption spectrum conforms to that of USP Amikacin Sulfate RS, similarly obtained.
- **B.** The retention time of the peak for amikacin of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **C. Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Sulfate*:** Meets the requirements

ASSAY

Change to read:

- **Procedure**

  Mobile phase: 134 mM sodium hydroxide, prepared as follows. Transfer a volume of deionized water to a suitable plastic container, sonicate, degas, and sparge with helium. While stirring, slowly add sodium hydroxide solution of a suitable concentration.

  [Note—Prepare fresh daily. The *Mobile phase* readily absorbs carbon dioxide and produces carbonate that changes the retention time of amikacin. The use of a 50% (w/w), low-carbonate sodium hydroxide solution is recommended.]

  System suitability solution: 0.02 mg/mL of USP Amikacin RS and 0.008 mg/mL of USP Kanamycin Sulfate RS in water

  Standard solution: 0.02 mg/mL of USP Amikacin RS in water

  Sample solution: Equivalent to 0.02 mg/mL of amikacin, from Amikacin Sulfate, in water

  Chromatographic system

  (See *Chromatography ⟨621⟩, System Suitability*.)

  Mode: LC

  Detector: Electrochemical

  Mode: Integrated amperometric

  Electrodes

  Working: Gold

  Reference: Silver–silver chloride

Detector settings: See *Table 1*.

Table 1

Step	Time (s)	Potential (V)	Integration
1	0.00	+0.04	—
2	0.30	+0.04	Begins
3	0.50	+0.04	Ends
4	0.51	+0.80	—
5	0.70	+0.80	—
6	0.71	−0.80	—
7	0.90	−0.80	—

Column: 4-mm × 25-cm; 7.5-µm packing L47

[NOTE—A guard column of packing L47 is recommended.]

Flow rate: 0.5 mL/min

Injection volume: 20 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The relative retention times for kanamycin and amikacin are 0.8 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 3 between kanamycin and amikacin, *System suitability solution*

Tailing factor: NMT 2, *Standard solution*

Relative standard deviation: NMT 3%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the quantity, in µg, of amikacin ($C_{22}H_{43}N_5O_{13}$) in each mg of Amikacin Sulfate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times P \times F$$

r_U = peak response of amikacin from the *Sample solution*

r_S = peak response of amikacin from the *Standard solution*

C_S = concentration of USP Amikacin RS in the *Standard solution* (mg/mL)

C_U = concentration of ▲Amikacin Sulfate▲ (ERR 1-Dec-2023) in the *Sample solution* (mg/mL)

P = potency of amikacin in USP Amikacin RS (mg/mg)

F = conversion factor, 1000 µg/mg

Acceptance criteria: See *Table 2*.

Table 2

Ratio of Amikacin:Sulfuric Acid	Acceptance Criteria (µg/mg)[a]
1:2	674–786
1:1.8	691–806

[a] Calculated on the dried basis.

IMPURITIES

• **RESIDUE ON IGNITION ⟨281⟩:** NMT 1.0%, the charred residue being moistened with 2 mL of nitric acid and 5 drops of sulfuric acid

SPECIFIC TESTS

- **Optical Rotation** ⟨781S⟩, *Procedures, Specific Rotation*

  Sample solution: 20 mg/mL in water

  Acceptance criteria: +76° to +84°

- **Crystallinity** ⟨695⟩**:** Meets the requirements

- **pH** ⟨791⟩

  Sample solution: 10 mg/mL in water

  Acceptance criteria: See *Table 3*.

Table 3

Ratio of Amikacin:Sulfuric Acid	Acceptance Criteria
1:2	2.0–4.0
1:1.8	6.0–7.3

- **Loss on Drying** ⟨731⟩

  Sample: 100 mg

  Analysis: Dry the *Sample* under vacuum at a pressure not exceeding 5 mm of mercury at 110° for 3 h.

  Acceptance criteria: NMT 13.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers.
- **Labeling:** Label it to indicate whether its molar ratio of amikacin to sulfuric acid (H_2SO_4) is 1:2 or 1:1.8.
- **USP Reference Standards** ⟨11⟩

  USP Amikacin RS

  USP Amikacin Sulfate RS

  USP Kanamycin Sulfate RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
AMIKACIN SULFATE	Documentary Standards Support	SM12020 Small Molecules 1
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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