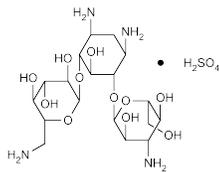


Kanamycin Sulfate



$C_{18}H_{36}N_4O_{11} \cdot H_2SO_4$ 582.58
 D-Streptamine, O-3-amino-3-deoxy- α -D-glucopyranosyl-(1 \rightarrow 6)-
 O-[6-amino-6-deoxy- α -D-glucopyranosyl(1 \rightarrow 4)]-2-deoxy-, sul-
 fate (1:1) (salt).
 Kanamycin sulfate (1:1) (salt) [133-92-6; 25389-94-0].

» Kanamycin Sulfate has a potency equivalent to not less than 750 μ g of kanamycin ($C_{18}H_{36}N_4O_{11}$) per mg, calculated on the dried basis.

Packaging and storage—Preserve in tight containers.

Labeling—Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms.

USP Reference standards <11>—

USP Amikacin RS
 USP Endotoxin RS
 USP Kanamycin Sulfate RS

Identification—

A: Dissolve about 10 mg in 1 mL of water, add 1 mL of a solution of ninhydrin in butyl alcohol (1 in 500), and add 0.5 mL of pyridine. Heat in a steam bath for 5 minutes, and add 10 mL of water: a deep purple color is produced.

B: It meets the requirements of the tests for *Sulfate* <191>.

C: The retention time of the peak for kanamycin in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation*, as obtained in the *Assay*.

Crystallinity <695>: meets the requirements.

pH <791>: between 6.5 and 8.5, in a solution (1 in 100).

Loss on drying <731>—Dry about 100 mg, accurately weighed, in a capillary-stoppered bottle in vacuum at a pressure not exceeding 5 mm of mercury at 60° for 3 hours: it loses not more than 4.0% of its weight.

Residue on ignition <281>: not more than 1.0%, the charred residue being moistened with 2 mL of nitric acid and 5 drops of sulfuric acid.

Chromatographic purity—Dissolve a quantity of Kanamycin Sulfate in water to obtain a test solution having a concentration of 30 mg per mL. Dissolve a suitable quantity of USP Kanamycin Sulfate RS in water to obtain a Standard solution having a known concentration of 30 mg per mL. Dilute a portion of this solution quantitatively with water to obtain a *Diluted standard solution* having a concentration of 0.90 mg per mL. Apply separate 1- μ L portions of the three solutions to the starting line of a suitable thin-layer chromatographic plate (see *Chromatography* <621>) coated with a 0.25-mm layer of chromatographic silica gel and heated at 110° for 1 hour and cooled immediately before use. Allow the spots to dry, and develop the chromatogram in a suitable chamber, previously equilibrated for 90 minutes with a developing solvent of monobasic potassium phosphate solution (7.5 in 100), until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the chamber, and air-dry. Spray the plate with a solution of ninhydrin in butyl alcohol (1 in 100). Dry the plate at 110° for 10 minutes, and examine the chromatograms: the chromatograms show principal spots at about

the same R_f value, and no secondary spot, if present in the chromatogram from the test solution, is more intense than the principal spot obtained from the *Diluted standard solution*.

Other requirements—Where the label states that Kanamycin Sulfate is sterile, it meets the requirements for *Sterility* and *Bacterial endotoxins* under *Kanamycin Injection*. Where the label states that *Kanamycin Sulfate* must be subjected to further processing during the preparation of injectable dosage forms, it meets the requirements for *Bacterial endotoxins* under *Kanamycin Injection*.

Assay—

Mobile phase—Use a 0.115 N sodium hydroxide solution. Make adjustments if necessary (see *System Suitability* under *Chromatography* <621>).

Resolution solution—Prepare a solution in water containing about 0.02 mg of USP Amikacin RS per mL and 0.008 mg of USP Kanamycin Sulfate RS per mL.

Standard preparation—Quantitatively dissolve an accurately weighed quantity of USP Kanamycin Sulfate RS in water to obtain a solution having a known concentration of about 0.008 mg per mL.

Assay preparation—Transfer about 40 mg of Kanamycin Sulfate, accurately weighed, to a 250-mL volumetric flask, dilute with water to volume, and mix. Transfer 5.0 mL of this solution to a 100-mL volumetric flask, dilute with water to volume, and mix.

Chromatographic system (see *Chromatography* <621>)—The liquid chromatograph is equipped with an electrochemical detector, a gold working electrode, a pH silver-silver chloride reference electrode, a guard column that contains packing L47, and a 4-mm \times 25-cm analytical column that contains packing L47. The electrochemical detector is used in the integrated amperometric mode with a range of 300 nC and an output of 1 V full-scale. The potential is programmed as follows.

Time (seconds)	Potential (V)	Integration
0.00	+0.04	
0.30	+0.04	begins
0.50	+0.04	ends
0.51	+0.80	
0.70	+0.80	
0.71	-0.80	
0.90	-0.80	

The flow rate is about 0.5 mL per minute. Chromatograph the *Resolution solution*, and record the peak responses as directed for *Procedure*: the relative retention times are about 1.0 for kanamycin and 1.3 for amikacin; and the resolution, R , between kanamycin and amikacin is not less than 3. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure*: the tailing factor is not more than 2; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 20 μ L) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the quantity, in μ g, of kanamycin ($C_{18}H_{36}N_4O_{11}$) in each mg of Kanamycin Sulfate taken by the formula:

$$5000(CP/W)(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Kanamycin Sulfate RS in the *Standard preparation*; P is the designated content, in μ g per mg, of kanamycin in USP Kanamycin Sulfate RS; W is the weight, in mg, of Kanamycin Sulfate taken to prepare the *Assay preparation*; and r_U and r_S are the kanamycin peak areas obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Kanamycin Sulfate Capsules

» Kanamycin Sulfate Capsules contain the equivalent of not less than 90.0 percent and not more than 115.0 percent of the labeled amount of kanamycin ($C_{18}H_{36}N_4O_{11}$).

Packaging and storage—Preserve in tight containers.

USP Reference standards (11)—

USP Amikacin RS
USP Kanamycin Sulfate RS

Identification—

A: *Thin-Layer Chromatographic Identification Test* (201)—

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture, heated at 110° for 1 hour and cooled immediately before use.

Test solution—Dissolve a suitable quantity of Capsule contents in water to obtain a solution having a concentration of about 1 mg of kanamycin per mL.

Developing solvent system: monobasic potassium phosphate solution (15 in 100).

Procedure—Proceed as directed in the chapter. Allow the spots to dry, and develop the chromatogram in a suitable chamber, previously equilibrated for 18 hours with *Developing solvent system*. Remove the plate from the chamber, and air-dry. Spray the plate with a solution of ninhydrin in butyl alcohol (1 in 100). Dry the plate at 110° for 10 minutes, and examine the chromatograms.

B: The retention time of the peak for kanamycin in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation*, as obtained in the *Assay*.

Dissolution, Procedure for a Pooled Sample (711)—

Medium: 0.01 N hydrochloric acid; 900 mL.

Apparatus 1: 100 rpm.

Time: 45 minutes.

Procedure—Determine the amount of kanamycin ($C_{18}H_{36}N_4O_{11}$) dissolved by employing the procedure set forth in the *Assay*, making any necessary modifications.

Tolerances—Not less than 75% (Q) of the labeled amount of $C_{18}H_{36}N_4O_{11}$ is dissolved in 45 minutes.

Loss on drying (731)—Dry about 100 mg in a capillary-stoppered bottle in vacuum at 60° for 3 hours: it loses not more than 4.0% of its weight.

Assay—

Mobile phase, Resolution solution, Standard preparation, and Chromatographic system—Proceed as directed in the *Assay under Kanamycin Sulfate*.

Assay preparation—Remove, as completely as possible, the contents of not fewer than 10 Capsules, and mix. Transfer an accurately weighed quantity of the mixed contents, equivalent to about 80 mg of kanamycin, to a 250-mL volumetric flask, add about 50 mL of water, and swirl to dissolve. Dilute with water to volume, and mix. Transfer 5.0 mL of this solution to a second 250-mL volumetric flask, dilute with water to volume, and mix.

Procedure—Proceed as directed in the *Assay under Kanamycin Sulfate*. Calculate the quantity, in mg, of kanamycin ($C_{18}H_{36}N_4O_{11}$) in the portion of Capsules taken by the formula:

$$125CP(r_u / r_s)$$

in which the terms are as defined therein.

Kanamycin Injection

» Kanamycin Injection contains an amount of Kanamycin Sulfate equivalent to not less than 90.0 percent and not more than 115.0 percent of the labeled amount of kanamycin ($C_{18}H_{36}N_4O_{11}$). It contains suitable buffers and preservatives.

Packaging and storage—Preserve in single-dose or in multiple-dose containers, preferably of Type I or Type III glass.

USP Reference standards (11)—

USP Amikacin RS
USP Endotoxin RS
USP Kanamycin Sulfate RS

Identification—

A: Dilute a suitable volume of Injection with water to obtain a test solution having a concentration of about 1 mg of kanamycin per mL. This solution meets the requirements of *Identification test A* under *Kanamycin Sulfate Capsules*.

B: The retention time of the peak for kanamycin in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation*, as obtained in the *Assay*.

Bacterial endotoxins (85)—It contains not more than 0.67 USP Endotoxin Unit per mg of kanamycin.

Sterility (71)—It meets the requirements when tested as directed for *Membrane Filtration* under *Test for Sterility of the Product to be Examined*.

pH (791): between 3.5 and 5.0.

Particulate matter (788): meets the requirements for small-volume injections.

Other requirements—It meets the requirements under *Injections* (1).

Assay—

Mobile phase, Resolution solution, Standard preparation, and Chromatographic system—Proceed as directed in the *Assay under Kanamycin Sulfate*.

Assay preparation—Dilute an accurately measured volume of Injection quantitatively, and stepwise if necessary, with water to obtain a solution having a concentration of about 0.006 mg of kanamycin per mL.

Procedure—Proceed as directed in the *Assay under Kanamycin Sulfate*. Calculate the quantity, in mg, of kanamycin ($C_{18}H_{36}N_4O_{11}$) in each mL of the Injection taken by the formula:

$$(L / D)(CP / 1000)(r_u / r_s)$$

in which *L* is the labeled quantity, in mg, of kanamycin in each mL of the Injection; *D* is the concentration, in mg per mL, of kanamycin in the *Assay preparation*, on the basis of the labeled quantity per mL and the extent of dilution; and the other terms are as defined therein.

Kaolin

» Kaolin is a native hydrated aluminum silicate, powdered and freed from gritty particles by elutriation.

Packaging and storage—Preserve in well-closed containers.

Identification—Mix 1 g with 10 mL of water and 5 mL of sulfuric acid in a porcelain dish. Evaporate the mixture until the excess water is removed, and continue heating the residue until dense, white fumes of sulfur trioxide appear. Cool, cautiously