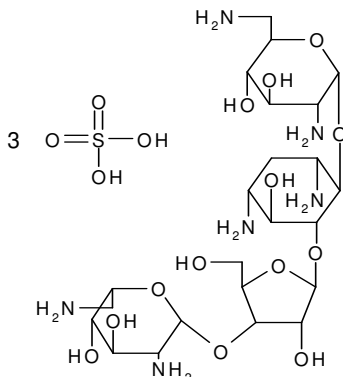


# Neomycin Sulfate USP

## Neomycin Sulfate USP Micronized



$C_{23}H_{46}N_6O_{13} \cdot 3H_2SO_4$

MW 909.89

### NOMENCLATURE

Neomycin Sulphate (EP nomenclature)

Neomycins Sulfate

Sulfate of 2-Deoxy-4-*O*-(2,6-diamino-2,6-dideoxy- $\alpha$ -D-glucopyranosyl)-5-*O*-[3-*O*-(2,6-diamino-2,6-dideoxy- $\beta$ -L-idopyranosyl)]- $\beta$ -D-ribofuranosyl]-D-streptamine

CAS 1405-10-3

Antibacterial

Laboratory Code: PNU-4567

USAN, INN, BAN: Neomycin Sulfate

JAN: Fradiomycin Sulfate

### DESCRIPTION

Neomycin Sulfate from Pfizer is a white to slightly yellow powder, or cryodesiccated solid. It is odorless or practically so and is hygroscopic. Its solutions are dextrorotatory. It is freely soluble in water, very slightly soluble in alcohol, insoluble in acetone, in chloroform, and in ether.

### USP SPECIFICATIONS

	<u>Test</u>	<u>Specification</u>
Identification		
	A. Thin-Layer Chromatography	Positive
	B. Color	Positive
	C. Sulfate	Meets Test

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pH

5.0 to 7.5

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### USP SPECIFICATIONS (continued)

	<u>Test</u>	<u>Specification</u>
Loss on Drying		Not More Than 8.0%
Assay (Dried Basis)		Not Less Than 600 µg of Neomycin per mg
Endotoxins		Not More Than 1.30 EU/MG
Pathogens		Absence
Microcount Bacteria		Not More Than 500 CFU/G
Microcount Fungi		Not More Than 50 CFU/G

In addition to the US Registration Specifications, the following apply to Neomycin Sulfate from Pfizer labeled “EP”.

### CHARACTERS

Neomycin Sulfate from Pfizer is a white or a yellowish-white powder. It is hygroscopic. It is very soluble in water; very slightly soluble in alcohol; practically insoluble in acetone.

### EP SPECIFICATIONS

	<u>Test</u>	<u>Specification</u>
Identification		
A. Liquid Chromatography		Positive
B. Sulfates		Positive
pH		5.0 to 7.5
Special Optical Rotation (Dried Basis)		+53.5° to +59.0°
Related Substances		
Neamine		Not More Than 2%
Neomycin C		3% to 15%
Any Other Individual Impurity		Not More Than 5%
Total of Other Impurities		Not More Than 15%
Sulfate (Dried Basis)		27.0% to 31.0%
Loss on Drying		Not More Than 8.0%
Sulfated Ash		Not More Than 1.0%
Assay (Dried Basis)		Not Less Than 680 IU of Neomycin per mg

### Particle Size for Micronized Grades

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<u>Parameter</u>	<u>Target</u>	<u>Method</u>
Less Than 20 microns	Not Less Than 99%	Celloscope
Less Than 10 microns	Not Less Than 75%	Celloscope

### Regulatory Filings:

See Neomycin sulfate under Regulatory

### Organic Volatile Impurities

Of the solvents targeted in USP 26 General Chapter <467>, only methylene chloride may appear in bulk pharmaceutical products manufactured by Pfizer at the Kalamazoo plant. For those products where OVI testing is required, our material will meet the compendial limits for methylene chloride and other solvents that may be added to the target list in the future.

Neomycin Sulfate from Pfizer meets the requirements of USP 26 General Chapter <467>.

### ICH Residual Solvents – Aqueous Nature of Process

Pfizer produces Neomycin Sulfate using water as the only solvent, in equipment dedicated to its production. Therefore, all lots of Neomycin Sulfate will meet the ICH residual solvent guidance.

### ICH Residual Metals

Pfizer is currently developing a strategy to assess the detection and quantitation of ICH residual metals in Pfizer's active pharmaceutical ingredients. Currently, no residual metals are known to be present in Neomycin Sulfate from Pfizer.

### Chemical Certificate of Suitability

Certificate No. R0-CEP 1999-184-Rev 00 was granted to Pfizer by the European Directorate for the Quality of Medicines on 13 December 2001 for five years, for the product Neomycin Sulfate. A copy of the certificate is available upon request.

### TSE Certificate of Suitability

# **Neomycin Sulfate USP**

## **Neomycin Sulfate USP Micronized**

Pfizer produces Neomycin Sulfate using no animal-derived raw materials, and states this in a “Certification of Materials from Animal Sources”. A copy of the certificate is included in this package.

The European Directorate for the Quality of Medicines does not issue TSE Certificates of Suitability for materials that contain no animal-derived raw materials.

### **Viral Safety Statement for Active Pharmaceutical Ingredients (APIs)**

Pfizer has reviewed the viral safety risks of its manufacturing practices for production of non-biological active pharmaceutical ingredients (APIs). The API Neomycin Sulfate presents no viral safety concerns. Pfizer APIs produced by bacterial or fungal fermentation and/or bioconversion processes are not considered to present viral safety risks. The raw materials used in the stages of production are sterilized prior to inoculation with a monoculture of the desired microorganisms. Only Pfizer’s bioconversion reactions that employ purified enzymes (e.g. introduction of a double bond at the 1,2-position of the steroid ring system) use animal-derived materials that are not sterilized prior to introduction to the process. To support the safety of these enzymes, suppliers are required to provide documentation to Pfizer that these materials are in compliance with the CPMP and CVMP guidances on minimization of the risk of transmitting animal spongiform encephalopathy (TSE) agents via medicinal or veterinary products. Pfizer requires suppliers to provide similar certification for all TSE-risk animal-derived materials.

Based upon the nature of our manufacturing processes and the control of animal-derived materials used in the manufacture of APIs, Pfizer is in compliance with applicable regulatory requirements for viral safety.

### **Statement Regarding Genetically Modified Materials in the Production of Active Pharmaceutical Ingredients (APIs)**

The organism(s) currently used in the fermentation/bioconversion of Neomycin Sulfate are not genetically engineered. However, Pfizer does not make any commitment that would preclude using genetically modified (recombinant) strains at some future date.

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There are a number of ingredients used in the fermentation/bioconversion process that are derived from plants that are major agricultural products in the United States. It is well known that the U.S. agriculture industry has a growing reliance upon genetically modified (recombinant) plants such as corn and soybeans. Although some grain handlers and processors have contacted farmers about needing to segregate genetically modified seeds from non-genetically modified seeds, this concept has only recently been introduced and lacks effective enforcement and monitoring components. Pfizer has not evaluated the sources of ingredients for fermentation/bioconversion-derived intermediates and APIs relative to ingredients having been derived in part from genetically engineered varieties of plants or other organisms.

### Microbiological Origin of Raw Materials

Neomycin is a product that is produced by enzymes in a microorganism (cultures of *Streptomyces fradiae*).

### Gluten

The raw materials used in the manufacture of Neomycin Sulfate are not derived from the gluten-containing grains wheat, rye, barley, or oats. Therefore, although Pfizer does not specifically assay for the presence of gluten, it is unlikely that any gluten proteins are present.

### Chirality and Stereoisomer Content

Since Neomycin is a product that is fermented by enzymes in a microorganism (cultures of *Streptomyces fradiae*), only one isomer of each of the components, Neomycin A, Neomycin B, and Neomycin C is produced. Therefore, the stereoisomer content is LT 0.1%.