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Ribavirin for Inhalation Solution

DEFINITION

Ribavirin for Inhalation Solution is a sterile, freeze-dried form of ribavirin. When constituted as directed in the labeling, the inhalation solution so obtained contains NLT 95.0% and NMT 105.0% of the labeled amount of ribavirin ($C_8H_{12}N_4O_5$).

IDENTIFICATION

Change to read:

• **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)

• **B.** Thin-Layer Chromatographic Identification Test ⟨201⟩

Sample solution: 10 mg/mL

Chromatographic system

Developing solvent system: Acetonitrile and 0.1 M ammonium chloride (9:2)

Spray reagent: Anisaldehyde, alcohol, glacial acetic acid, and sulfuric acid (5:90:1:5)

Analysis: Proceed as directed in the chapter. Allow the plate to air-dry for about 15 min, spray with *Spray reagent*, heat the plate at 110° for 30 min, and locate the spots on the plate by examining the plate in daylight.

Acceptance criteria: Meets the requirements

ASSAY

• **Procedure**

Mobile phase: Adjust water with sulfuric acid to a pH of 2.5 ± 0.1. Filter through a suitable filter of 0.5-µm or finer pore size.

Standard solution: 0.025 mg/mL of USP Ribavirin RS in *Mobile phase*

Sample stock solution: Constitute Ribavirin for Inhalation Solution as directed in the labeling, using a suitable volume of diluent. Transfer an aliquot of constituted solution, equivalent to 100 mg of ribavirin, to a 200-mL volumetric flask, and dilute with *Mobile phase* to volume.

Sample solution: Nominally 0.025 mg/mL of ribavirin in *Mobile phase* from the *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 207 nm

Column: 7.8-mm × 10-cm; packing L17

Column temperature: 65 ± 0.5°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: 0.7–1.5

Relative standard deviation: NMT 0.5%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ribavirin ($C_8H_{12}N_4O_5$) in the portion of Ribavirin for Inhalation Solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

C_U = nominal concentration of ribavirin in the *Sample solution* (mg/mL)

Acceptance criteria: 95.0%–105.0%

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.25%

• **Organic Impurities**

Mobile phase, Standard solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Sample solution: Prepare as directed for the *Sample stock solution* in the *Assay*.

Analysis

Sample: *Sample stock solution*

Calculate the percentage of each peak, other than that of the solvent peak and the ribavirin peak, in the portion of Ribavirin for Inhalation Solution taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = response of the individual peak

r_T = sum of all the peak responses

Acceptance criteria

Individual impurity: NMT 0.25%

Total impurities: NMT 1.0%

SPECIFIC TESTS

• **Sterility Tests ⟨71⟩:** Meets the requirements when tested as directed in *Test for Sterility of the Product to Be Examined, Membrane Filtration*.

• **Optical Rotation,** *Specific Rotation*⟨781S⟩

Sample solution: 10 mg/mL

Acceptance criteria: −33.5° to −37.0° (*t* = 20°)

• **pH ⟨791⟩**

Sample solution: A solution constituted as directed in the labeling. To each 50 mL of reconstituted solution add 0.2 mL of a saturated potassium chloride solution.

Acceptance criteria: 4.0–6.5

• **Loss on Drying ⟨731⟩**

Analysis: Dry a sample at 105° for 5 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, in a dry place at controlled room temperature.

• **Labeling:** The labeling indicates that Ribavirin for Inhalation Solution must be constituted with a measured volume of Sterile Water for Injection or with Sterile Water for Inhalation containing no preservatives, and that the constituted solution is to be administered only by a small-particle aerosol generator.

• **USP Reference Standards ⟨11⟩**

USP Ribavirin RS

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

Topic/Question	Contact	Expert Committee
RIBAVIRIN FOR INHALATION SOLUTION	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. Information currently unavailable
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