Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-May-2017
Document Type: USP Monographs
DocId: GUID-87CFF116-873F-445A-BA83-971652D3D3F8_1_en-US
DOI: https://doi.org/10.31003/USPNF_M73405_01_01
DOI Ref: 3f725

Ribavirin Capsules

DEFINITION
Ribavirin Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of ribavirin ($C_8H_{12}N_4O_5$).

IDENTIFICATION
• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY
• **Procedure**

Mobile phase: Water. Adjust with sulfuric acid to a pH of 2.5.

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

Sample stock solution: Transfer an equivalent to 50 mg of ribavirin, from contents of Capsules (NLT 20), to a 100-mL volumetric flask. Add about 50 mL of *Mobile phase*, and sonicate with occasional shaking for about 20 min. Cool to room temperature, and dilute with *Mobile phase* to volume.

Sample solution: Nominally 0.025 mg/mL of ribavirin in *Mobile phase* from *Sample stock solution*. Pass the solution through a suitable filter of 0.45-µm pore size.

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

Mode: LC

Detector: UV 207 nm

Column: 7.8-mm × 15-cm; 7-µm packing L17

Column temperature: 65°

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 2.0%

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 Capsules 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: 90.0%–110.0%

PERFORMANCE TESTS
• **Dissolution ⟨711⟩**

Test 1

Medium: Water; 900 mL

Apparatus 1: 100 rpm

Time: 30 min

Determine the percentage of the labeled amount of ribavirin ($C_8H_{12}N_4O_5$) dissolved by using one of the following procedures.

Procedure 1

Mobile phase: Proceed as directed in the *Assay*.

Standard solution: 22.5 µg/mL of USP Ribavirin RS in *Medium*

Sample solution: Pass the solution through a suitable filter of 0.45-µm pore size. Transfer 5.0 mL of the filtrate to a 50.0-mL volumetric flask, and dilute with *Medium* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 207 nm

Column: 7.8-mm × 30-cm; 9-µm packing L17

Column temperature: 65°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ribavirin ($C_8H_{12}N_4O_5$) dissolved:

$$\text{Result} = (r_U/r_S) \times (C_S/L) \times V \times D \times 100$$

r_U = peak area from the *Sample solution*

r_S = peak area from the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

L = label claim (mg/Capsule)

V = volume of *Medium*, 900 mL

D = dilution factor of the solution under test

Procedure 2

Sulfuric acid solution: 3% sulfuric acid

Mobile phase: Water. Adjust with *Sulfuric acid solution* to a pH of 2.5.

Standard solution: 0.02 mg/mL of USP Ribavirin RS in *Medium*

Sample solution: Pass the solution through a suitable filter of 0.8-µm pore size. Transfer 5.0 mL of the filtrate to a 50.0-mL volumetric flask, and dilute with water to volume.

Chromatographic system

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

Mode: LC

Detector: UV 207 nm

Column: 7.8-mm × 10-cm; 9-µm packing L17

Column temperature: 40 ± 2°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ribavirin ($C_8H_{12}N_4O_5$) dissolved:

$$\text{Result} = (r_U/r_S) \times (C_S/L) \times V \times D \times 100$$

r_U = peak area from the *Sample solution*

r_S = peak area from the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

L = label claim (mg/Capsule)

V = volume of *Medium*, 900 mL

D = dilution factor of the solution under test

Tolerances: NLT 80% (Q) of the labeled amount of ribavirin ($C_8H_{12}N_4O_5$) is dissolved.

Test 2: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 2*.

Medium: Water; 900 mL, deaerated

Apparatus 1: 100 rpm

Time: 15 min

Buffer: 4 g/L of sodium dihydrogen orthophosphate dihydrate in water. Adjust with 5% (v/v) sodium hydroxide solution to a pH of 5.0. Pass through a suitable filter of 0.45-µm or finer pore size.

Mobile phase: Acetonitrile and *Buffer* (2:98)

Standard solution: 0.22 mg/mL of USP Ribavirin RS in *Medium*. Sonicate, if necessary, to dissolve.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 225 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 1.9 times the retention time of ribavirin

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ribavirin ($C_8H_{12}N_4O_5$) dissolved:

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

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)

L = label claim (mg/Capsule)

V = volume of *Medium*, 900 mL

Tolerances: NLT 80% (Q) of the labeled amount of ribavirin ($C_8H_{12}N_4O_5$) is dissolved.

Test 3: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 3*.

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 1: 100 rpm

Time: 30 min

Standard solution: 0.22 mg/mL of USP Ribavirin RS in *Medium*. Sonicate, if necessary, to dissolve.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm or finer pore size.

Capsule blank solution: Dissolve 6 empty Capsule shells in 900 mL of *Medium*. Pass through a suitable filter of 0.45-µm or finer pore size.

Instrumental conditions

Mode: UV

Analytical wavelength: UV 225 nm

Cell: 0.1 cm

Blank: *Medium*

Analysis

Samples: *Standard solution*, *Sample solution*, and *Capsule blank solution*

Calculate the percentage of the labeled amount of ribavirin ($C_8H_{12}N_4O_5$) dissolved:

$$\text{Result} = \{[A_U - (A_B/6)]/A_S\} \times C_S \times (1/L) \times V \times 100$$

A_U = absorbance of the *Sample solution*

A_B = absorbance of the *Capsule blank solution*

A_S = absorbance of the *Standard solution*

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

L = label claim (mg/Capsule)

V = volume of *Medium*, 900 mL

Tolerances: NLT 80% (Q) of the labeled amount of ribavirin ($C_8H_{12}N_4O_5$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

• **Organic Impurities**

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

Sample solution: Nominally 0.5 mg/mL of ribavirin in *Mobile phase* prepared as follows. Transfer an amount equivalent to 50 mg of ribavirin, from contents of Capsules (NLT 20), to a 100-mL volumetric flask. Add about 50 mL of *Mobile phase*, and sonicate with occasional shaking for about 20 min. Cool to room temperature, dilute with *Mobile phase* to volume, and mix. Pass the solution through a suitable filter of 0.45-µm pore size.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ribose triazolole carboxylic acid and any other unknown impurity in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of ribose triazolole carboxylic acid or any other unknown impurity from the *Sample solution*

r_S = peak response of ribavirin 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)

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Ribose triazolole carboxylic acid[a]	0.7	0.7	0.25
Ribavirin	1.0	—	—
Any individual unknown impurity	—	1.0	0.10
Total impurities	—	—	1.0

[a] 1-β-D-Ribofuranosyl-1*H*-1,2,4-triazole-3-carboxylic acid.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers, and store between 15° and 30°.
- **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **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 CAPSULES	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

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 38(3)

Current DocID: GUID-87CFF116-873F-445A-BA83-971652D3D3F8_1_en-US

DOI: https://doi.org/10.31003/USPNF_M73405_01_01

DOI ref: 3f725