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Risedronate Sodium Delayed-Release Tablets

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click https://www.uspnf.com/rb-risendronate-na-drt-20240426.

DEFINITION

Risedronate Sodium Delayed-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of risedronate sodium ($C_7H_{10}NNaO_7P_2$).

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*.
- **B.** The UV spectra of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

Mobile phase: 1.8 g/L of edetate disodium in water. Adjust with 1 N sodium hydroxide solution to a pH of 9.5.

Standard solution: 0.1 mg/mL of USP Risedronate Sodium RS in *Mobile phase*. Sonicate to dissolve, if necessary.

Sample stock solution: Nominally 1 mg/mL of risedronate sodium from Tablets prepared as follows. Transfer the equivalent of 100 mg of risedronate sodium, from finely powdered Tablets (NLT 20) to a 100-mL volumetric flask and add about 70 mL of *Mobile phase*. Sonicate with intermittent shaking for about 40 min. Dilute with *Mobile phase* to volume.

Sample solution: Nominally 0.1 mg/mL of risedronate sodium from the *Sample stock solution* in *Mobile phase*. Pass the solution through a suitable filter of 0.22-µm pore size, discarding the first 5 mL.

Chromatographic system

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

Mode: LC

Detector: UV 263 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Columns

Guard: 4.0-mm × 5-cm; 10-µm packing L48

Analytical: 4.0-mm × 25-cm, 10-µm packing L48

Flow rate: 0.8 mL/min

Injection volume: 20 µL

Run time: NLT 2 times the retention time of risedronate

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of risedronate sodium ($C_7H_{10}NNaO_7P_2$) in the portion of Tablets taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

▲**Test 1**▲ (RB 1-May-2024)

Acid stage

Acid stage medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 2: 75 rpm

Time: 2 h

Standard stock solution: 0.7 mg/mL of USP Risedronate Sodium RS in water. Sonicate to dissolve, if necessary.

Acid stage standard solution: 0.007 mg/mL of USP Risedronate Sodium RS from the *Standard stock solution* in *Acid stage medium*

Acid stage sample solution: After 2 h in the *Acid stage medium*, withdraw 10 mL of the solution under test and pass through a suitable filter of 0.45-µm pore size, discarding the first 5 mL.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: UV 262 nm

Path length: 0.5 cm

Blank: *Acid stage medium*

Analysis

Samples: *Acid stage standard solution* and *Acid stage sample solution*

Calculate the percentage of the labeled amount of risedronate sodium ($C_7H_{10}NNaO_7P_2$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (1/L) \times 100$$

A_U = absorbance of the *Acid stage sample solution*

A_S = absorbance of the *Acid stage standard solution*

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

V = volume of *Acid stage medium*; 500 mL

L = label claim (mg/Tablet)

Tolerances: NMT 10% of the labeled amount of risedronate sodium ($C_7H_{10}NNaO_7P_2$) is dissolved.

Buffer stage

Buffer stage medium: pH 6.8 phosphate buffer; 500 mL

Apparatus 2: 75 rpm

Time: 45 min

Buffer stage standard solution: 0.07 mg/mL of USP Risedronate Sodium RS from the *Standard stock solution* in *Buffer stage medium*

Buffer stage sample solution: After 2 h in *Acid stage medium*, carefully discard the *Acid stage medium*, add 500 mL of *Buffer stage medium* to the same vessel, and continue with *Buffer stage* conditions for another 45 min. After 45 min, withdraw 10 mL of the solution under test and pass through a suitable filter of 0.45-µm pore size, discarding the first 5 mL.

Instrumental conditions: Proceed as directed in the *Acid stage* except for *Blank*.

Blank: *Buffer stage medium*

Analysis

Samples: *Buffer stage standard solution* and *Buffer stage sample solution*

Calculate the percentage of the labeled amount of risedronate sodium ($C_7H_{10}NNaO_7P_2$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (1/L) \times 100$$

A_U = absorbance of the *Buffer stage sample solution*

A_S = absorbance of the *Buffer stage standard solution*

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

V = volume of the *Buffer stage medium*, 500 mL

L = label claim (mg/Tablet)

Tolerances: NLT 75% (Q) of the labeled amount of risedronate sodium ($C_7H_{10}NNaO_7P_2$) is dissolved.

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

Acid stage medium: 0.1 N hydrochloric acid; 900 mL

Place 1 Tablet in each of the 12 dissolution vessels and start the dissolution test in *Acid stage medium*. At the end of the *Acid stage*, drain the *Acid stage medium* from all the vessels and retain the Tablets. 6 Tablets are to be used for *Acid stage* analysis while the remaining 6 Tablets are to be used for *Buffer stage* testing.

Buffer stage medium: pH 6.8 phosphate buffer (Dissolve 6.8 g of potassium phosphate, monobasic and 0.9 g of sodium hydroxide in 1000 mL of water. Adjust with 10% (w/v) sodium hydroxide solution or 10% (v/v) phosphoric acid to a pH of 6.8, if necessary.); 900 mL

Apparatus 2: 75 rpm, paddle coated with Teflon

Times

Acid stage: 2 h

Buffer stage: 0.5 h

Acid stage standard solution: 0.07 mg/mL of USP Risedronate Sodium RS in *Buffer stage medium*. Sonicate to dissolve, if necessary.

Buffer stage standard solution: 0.039 mg/mL of USP Risedronate Sodium RS in *Buffer stage medium*. Sonicate to dissolve, if necessary.

Acid stage sample solution: Transfer each of the 6 Tablets reserved for *Acid stage* analysis to a separate 50-mL volumetric flask and add about 80% of the flask volume of *Buffer stage medium*. Sonicate for about 45 min with intermittent shaking. Dilute with *Buffer stage medium* to volume. Allow to stand for 5 min. Dilute 5 mL with *Buffer stage medium* to 50 mL. Pass through a suitable filter of 0.45-µm pore size, discarding an appropriate volume of filtrate so that a consistent result can be obtained.

Buffer stage sample solution: At the end of the *Acid stage*, carefully discard the *Acid stage medium* without losing the Tablets. Add 900 mL of *Buffer stage medium* to each vessel containing the Tablets reserved for *Buffer stage* testing, and start the dissolution apparatus. At the time specified, pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding an appropriate volume of filtrate so that a consistent result can be obtained.

Solution A: Dissolve 0.69 g of sodium phosphate, monobasic, 0.64 g of tetrabutylammonium bromide, and 0.55 g of edetate disodium in 1000 mL of water. Adjust with 1 N sodium hydroxide solution to a pH of 7.2.

Mobile phase: Acetonitrile and *Solution A* (5:95)

Chromatographic system

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

Mode: LC

Detector: UV 262 nm

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

Column temperature: 50°

Flow rate: 1.5 mL/min

Injection volume: 50 µL

Run time: NLT 1.3 times the retention time of risedronate

System suitability

Samples: *Acid stage standard solution* and *Buffer stage standard solution*

Suitability requirements

Tailing factor: NMT 1.5, *Acid stage standard solution* and *Buffer stage standard solution*

Relative standard deviation: NMT 2.0%, *Acid stage standard solution* and *Buffer stage standard solution*

Analysis

Samples: *Acid stage standard solution*, *Acid stage sample solution*, *Buffer stage standard solution*, and *Buffer stage sample solution*

Calculate the percentage of the labeled amount of risedronate sodium ($C_7H_{10}NNaO_7P_2$) dissolved in the *Acid stage*:

$$\text{Result} = A - [(r_U/r_S) \times C_S \times V_D \times (1/L) \times 100]$$

A = percentage of risedronate sodium as determined in the *Assay*

r_U = peak response of risedronate from the *Acid stage sample solution*

r_S = peak response of risedronate from the *Acid stage standard solution*

C_S = concentration of USP Risedronate Sodium RS in the *Acid stage standard solution* (mg/mL)

V_D = dilution volume of the *Acid stage sample solution*, 500 mL

L = label claim (mg/Tablet)

Calculate the percentage of the labeled amount of risedronate sodium ($C_7H_{10}NNaO_7P_2$) dissolved in the *Buffer stage*:

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

r_U = peak response of risedronate from the *Buffer stage sample solution*

r_S = peak response of risedronate from the *Buffer stage standard solution*

C_S = concentration of USP Risedronate Sodium RS in the *Buffer stage standard solution* (mg/mL)

V = volume of *Buffer stage medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances

Acid stage: NMT 10% of the labeled amount of risedronate sodium ($C_7H_{10}NNaO_7P_2$) is dissolved.

Buffer stage: NLT 80% (*Q*) of the labeled amount of risedronate sodium ($C_7H_{10}NNaO_7P_2$) is dissolved.▲ (RB 1-May-2024)

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

IMPURITIES

• **Organic Impurities**

Mobile phase and **Standard solution:** Prepare as directed in the *Assay*.

System suitability solution: 1 mg/mL of USP Risedronate Sodium RS and 0.1 mg/mL of USP Risedronate Related Compound A RS in *Mobile phase*. Sonicate to dissolve, if necessary.

Sensitivity solution: 1 µg/mL of USP Risedronate Sodium RS from the *Standard solution* in *Mobile phase*

Sample solution: Nominally 1 mg/mL of risedronate sodium from Tablets prepared as follows. Transfer the equivalent of 100 mg of risedronate sodium, from finely powdered Tablets (NLT 20) to a 100-mL volumetric flask and add 25 mL of *Mobile phase*. Sonicate with intermittent shaking for about 40 min. Dilute with *Mobile phase* to volume. Pass the solution through a suitable filter of 0.22-µm pore size, discarding the first 5 mL.

Chromatographic system

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

Mode: LC

Detector: UV 263 nm

Columns

Guard: 4.0-mm × 5-cm; 10-µm packing L48

Analytical: 4.0-mm × 25-cm, 10-µm packing L48

Flow rate: 0.8 mL/min

Injection volume: 20 µL

Run time: NLT 3.5 times the retention time of risedronate

System suitability

[Note—The relative retention times for 2-(pyridin-3-yl)acetic acid, risedronate related compound A, and risedronate are 0.22, 0.85, and 1.00, respectively.]

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

Suitability requirements

Resolution: NLT 1.5 between risedronate related compound A and risedronate, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any degradation product in the portion of the Tablets taken:

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

r_U = peak response of any degradation product from the *Sample solution*

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

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

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

Acceptance criteria: See *Table 1*. The reporting threshold is NMT 0.1%.

Table 1

Name	Acceptance Criteria, NMT (%)
Any unspecified degradation products	0.2
Total degradation products	0.5

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Store at controlled room temperature.

Add the following:

▲• **Labeling:** The labeling states the *Dissolution* test used only if *Test 1* is not used.▲ (RB 1-May-2024)

• **USP Reference Standards** ⟨11⟩

USP Risedronate Sodium RS

USP Risedronate Related Compound A RS

[1-Hydroxy-2-(pyridin-2-yl)ethylidene]bis(phosphonic acid), monohydrate.

$C_7H_{11}NO_7P_2 \cdot H_2O$ 301.13

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

Topic/Question	Contact	Expert Committee
RISEDRONATE SODIUM DELAYED-RELEASE TABLETS	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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