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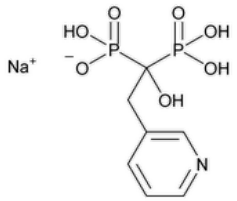
Risedronate Sodium



$C_7H_{10}NNaO_7P_2$ 305.09
$C_7H_{10}NNaO_7P_2 \cdot H_2O$ 323.12
$C_7H_{10}NNaO_7P_2 \cdot 2.5\ H_2O$ 350.13
Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis-, monosodium salt;
Sodium trihydrogen [1-hydroxy-2-(3-pyridyl) ethylidene]diphosphonate;
Hemi-pentahydrate CAS RN®: 329003-65-8; UNII: HU2YAQ274O.
Monohydrate CAS RN®: 353228-19-0; UNII: F67L43UT5C.

DEFINITION

Risedronate Sodium contains one or two-and-one-half molecules of hydration. The monohydrate form contains NLT 98.0% and NMT 102.0% of risedronate sodium ($C_7H_{10}NNaO_7P_2$), calculated on the dried basis. The hemi-pentahydrate form contains NLT 98.0% and NMT 102.0% of risedronate sodium ($C_7H_{10}NNaO_7P_2$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

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

• **B.** **Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Sodium*:** Meets the requirements of test *A*. [Note—Complete dissolution of the sample is achieved only after the addition of the 15% potassium carbonate.]

Add the following:

▲• **C.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2020)

ASSAY

Change to read:

• **Procedure**

Mobile phase: 1.8 g/L of edetate disodium in water. Adjust with 1 N sodium hydroxide to a pH of 9.5 ± 0.1.

Standard solution: ▲1.0 mg/mL of USP Risedronate Sodium RS and 0.1 mg/mL of USP Risedronate Related Compound A RS in *Mobile phase*▲ (USP 1-May-2020)

Sample solution: 1.1 mg/mL of Risedronate Sodium in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 263 nm

Column: 4.0-mm × 25-cm; 10-µm packing L48

Flow rate: 0.8 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 2.3 between risedronate related compound A and risedronate

Tailing factor: NMT 1.6 for the risedronate peak

Relative standard deviation: NMT 1.0% for the risedronate peak ▲▲ (USP 1-May-2020)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of risedronate sodium ($C_7H_{10}NNaO_7P_2$) in the portion of Risedronate Sodium taken:

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

r_U = peak response ▲of risedronate▲ (USP 1-May-2020) from the *Sample solution*

r_S = peak response ▲of risedronate▲ (USP 1-May-2020) from the *Standard solution*

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

C_U = concentration of Risedronate Sodium in the *Sample solution* (mg/mL)

Acceptance criteria

Monohydrate: 98.0%–102.0% on the dried basis

Hemi-pentahydrate: 98.0%–102.0% on the anhydrous basis

IMPURITIES

Change to read:

• **Organic Impurities, Procedure 1**

[Note—Perform both *Procedure 1* and *Procedure 2*.]

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

Diluted standard solution: ▲0.005 mg/mL of USP Risedronate Sodium RS and 0.5 µg/mL of USP Risedronate Related Compound A RS in *Mobile phase* from the *Standard solution*▲ (USP 1-May-2020)

System suitability

Samples: *Standard solution* and *Diluted standard solution*

Suitability requirements

Resolution: NLT 2.3 between risedronate related compound A and risedronate, *Standard solution*

Tailing factor: NMT 1.6 for the risedronate peak, *Standard solution*

Relative standard deviation: NMT 1.0% for the risedronate peak, ▲▲ (USP 1-May-2020) *Standard solution*; NMT 15% for the risedronate related compound A peak, ▲▲ (USP 1-May-2020) *Diluted standard solution*

Analysis

Samples: *Sample solution* and *Diluted standard solution*

Calculate the percentage of each impurity in the portion of Risedronate Sodium taken:

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

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of risedronate from the *Diluted standard solution*

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

C_U = concentration of Risedronate Sodium in the *Sample solution* (mg/mL)

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

Table 1

Acceptance criteria: ▲The reporting threshold is 0.05%.▲ (USP 1-May-2020)

Any individual impurity: NMT 0.10%

Name	Relative Retention Time	Relative Response Factor
3-Pyridyl acetic acid	0.22	1.65
▲Risedronate related compound A▲ (USP 1-May-2020) (2-Pyridinyl isomer)	0.84	1.0
Risedronate sodium	1.0	—

[NOTE—Disregard the peak due to the sodium ion, eluting at about 1.6 min, and any peak observed in the blank.▲▲ (USP 1-May-2020)]

Change to read:

• **ORGANIC IMPURITIES, PROCEDURE 2**

Mobile phase: Transfer 16.15 g of dibasic potassium phosphate and 0.46 g of edetate disodium to a 1-L beaker, and dissolve in about 400 mL of water. Add 1 vial of commercially available tetrabutylammonium dihydrogen phosphate buffered solution in methanol[1] and 1 mL of hydrochloric acid. Adjust with 1 N sodium hydroxide or 1 N hydrochloric acid, as necessary, to a pH of 7.5 ± 0.1, and dilute with water to 480 mL. Add 20 mL of methanol, mix well, pass the solution through a nylon filter of 0.45-µm pore size, and degas.

Diluent: Transfer 0.46 g of edetate disodium to a 1-L beaker, and dissolve in 500 mL of water. Adjust with 1 N sodium hydroxide to a pH of 7.5 ± 0.1.

Standard solution: ▲0.005 mg/mL▲ (USP 1-May-2020) of USP Risedronate Related Compound B RS in *Diluent*

Diluted standard solution: 0.5 µg/mL of USP Risedronate Related Compound B RS in *Diluent* from the *Standard solution*

Sample solution: 2 mg/mL of Risedronate Sodium in *Diluent*, using sonication if necessary

Chromatographic system

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

Mode: LC

Detector: UV 263 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 1.0 mL/min

Injection volume: 10 µL

System suitability

Samples: *Standard solution* and *Diluted standard solution*

Suitability requirements

▲▲ (USP 1-May-2020)

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: ▲▲ (USP 1-May-2020) NMT 10%, ▲▲ (USP 1-May-2020) *Diluted standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

[NOTE—Disregard any peak eluting before risedronate related compound B. The risedronate peak elutes unretained at the void volume.]

Calculate the percentage of each impurity in the portion of Risedronate Sodium taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of risedronate related compound B from the *Standard solution*

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

C_U = concentration of Risedronate Sodium in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of risedronate related compound B as a free acid, 530.20

M_{r2} = molecular weight of risedronate related compound B as a tetrahydrate disodium salt, 646.22

Acceptance criteria: ▲The reporting threshold is 0.05%.▲ (USP 1-May-2020)

Risedronate related compound B: NMT 0.10%

Individual impurities: NMT 0.10%

Total impurities: NMT 0.50%, *Procedure 1* and *Procedure 2* being combined. [NOTE—Disregard any peak observed in the blank. ▲▲ (USP 1-May-2020)]

SPECIFIC TESTS

Change to read:

• **WATER DETERMINATION ⟨921⟩▲▲ (USP 1-MAY-2020):** Perform the test by direct introduction of solid sample into the titrator. ▲▲ (USP 1-May-2020)

Acceptance criteria: 11.9%–13.9%; where it is labeled as a hemi-pentahydrate

Change to read:

• **LOSS ON DRYING**

(See *Thermal Analysis* ⟨891⟩.)

▲▲ (USP 1-May-2020)

Sample: 7–15 mg of Risedronate Sodium

Heating rate: 10°/min in a stream of nitrogen at a flow rate of about 40 mL/min

Temperature range: Ambient temperature to 250°

Acceptance criteria: 5.5%–7.5%; where it is labeled as a monohydrate

ADDITIONAL REQUIREMENTS

• **LABELING:** Label to indicate whether it is the monohydrate or the hemi-pentahydrate form.

• **PACKAGING AND STORAGE:** Preserve in well-closed containers. Store at room temperature.

Change to read:

• **USP REFERENCE STANDARDS ⟨11⟩**

USP Risedronate Sodium RS

USP Risedronate Related Compound A RS

▲▲ (USP 1-May-2020) [1-hydroxy-2-(2-pyridinyl)ethylidene]bis(phosphonic acid) monohydrate.

$C_7H_{11}NO_7P_2 \cdot {}^{▲}H_2O$ 301.13▲ (USP 1-May-2020)

USP Risedronate Related Compound B RS

Cyclic dimer;
Disodium tetrahydrate salt;
[3,6-Bis[(3-pyridinyl)methyl]-2,5-dihydroxy-2,5-dioxido-1,4,2,5-dioxadiphosphorinane-3,6-diyl]bis[phosphonic acid] disodium tetrahydrate salt.

$C_{14}H_{16}N_2O_{12}P_4Na_2 \cdot 4H_2O$ 646.22

[1] Available from Waters Corp. as Part #85101 (PIC A).

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

Topic/Question	Contact	Expert Committee
RISEDRONATE SODIUM	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

Most Recently Appeared In:
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