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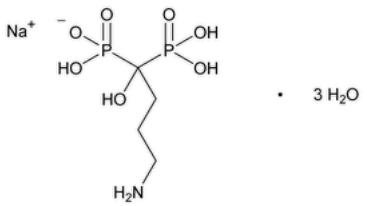
Alendronate Sodium



$C_4H_{12}NNaO_7P_2 \cdot 3H_2O$ 325.12

Phosphonic acid, (4-amino-1-hydroxybutylidene) bis-, monosodium salt, trihydrate;

Sodium trihydrogen (4-amino-1-hydroxybutylidene)diphosphonate, trihydrate CAS RN®: 121268-17-5; UNII: 2UY4M2U3RA.

DEFINITION

Alendronate Sodium contains NLT 98.0% and NMT 102.0% of alendronate sodium ($C_4H_{12}NNaO_7P_2$), calculated on the dried basis.

IDENTIFICATION

Change to read:

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

• **B.** **Identification Tests—General ⟨191⟩, *Sodium*:** Meets the requirements of test *A*

ASSAY

• **Procedure**

Buffer solution: 14.7 g/L of sodium citrate dihydrate and 7.05 g/L of anhydrous dibasic sodium phosphate. Adjust with phosphoric acid to a pH of 8.

Mobile phase: Acetonitrile, methanol, and *Buffer solution* (25:5:70)

Diluent: 29.4 g/L of sodium citrate dihydrate

Borate solution: 19.1 g/L of sodium borate

Solution A: 0.5 mg/mL of 9-fluorenylmethyl chloroformate in acetonitrile. [Note—Prepare this solution fresh just before use.]

Standard stock solution: 0.1 mg/mL of USP Alendronate Sodium RS in *Diluent*

Standard solution: Transfer 5.0 mL of the *Standard stock solution* to a 50-mL polypropylene, screw-cap centrifuge tube containing 5 mL of *Borate solution*. Add 5 mL of *Solution A*, and shake for 30 s. Allow to stand at room temperature for 25 min. Add 25 mL of methylene chloride, and shake vigorously for 1 min. Centrifuge for 5–10 min. Use a portion of the clear upper aqueous layer.

Reagent blank: Transfer 5.0 mL of *Diluent* to a 50-mL polypropylene, screw-cap centrifuge tube containing 5 mL of *Borate solution*. Add 5 mL of *Solution A*, and shake for 30 s. Allow to stand at room temperature for 25 min. Add 25 mL of methylene chloride, and shake vigorously for 1 min. Centrifuge for 5–10 min. Use a portion of the clear upper aqueous layer.

Sample stock solution: 0.1 mg/mL of Alendronate Sodium in *Diluent*

Sample solution: Transfer 5.0 mL of the *Sample stock solution* to a 50-mL polypropylene, screw-cap centrifuge tube containing 5 mL of *Borate solution*. Add 5 mL of *Solution A*, and shake for 30 s. Allow to stand at room temperature for 25 min. Add 25 mL of methylene chloride, and shake vigorously for 1 min. Centrifuge for 5–10 min. Use a portion of the clear upper aqueous layer.

Chromatographic system

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

Mode: LC

Detector: UV 266 nm

Column: 4.1-mm × 25-cm; packing L21

Column temperature: 35°

Flow rate: 1.2 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0% for replicate injections

Analysis

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

Calculate the percentage of alendronate sodium ($C_4H_{12}NNaO_7P_2$) in the portion of Alendronate Sodium taken:

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

r_U = peak area from the *Sample solution*

r_S = peak area from the *Standard solution*

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

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

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

• **Organic Impurities**

Buffer solution: 2.94 g/L of sodium citrate dihydrate and 1.42 g/L of anhydrous dibasic sodium phosphate. Adjust with phosphoric acid to a pH of 8 and pass through a filter of 0.5-µm or finer pore size.

Solution A: Acetonitrile and *Buffer solution* (3:17)

Solution B: Acetonitrile and *Buffer solution* (7:3)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
15	50	50
25	0	100
27	100	0
32	100	0

Diluent and **Borate solution:** Proceed as directed in the *Assay*.

Solution C: 4 mg/mL of 9-fluorenylmethyl chloroformate in acetonitrile. [Note—Prepare this solution fresh just before use.]

Standard stock solution: 0.6 mg/mL of USP Alendronate Sodium RS in *Diluent*

Standard solution A: Transfer 5.0 mL of the *Standard stock solution* to a 50-mL polypropylene, screw-cap centrifuge tube containing 5 mL of *Borate solution*. Add 5 mL of acetonitrile and 5 mL of *Solution C*, and shake for 45 s. Allow to stand at room temperature for 30 min. Add 20 mL of methylene chloride, and shake vigorously for 1 min. Centrifuge for 5–10 min, and use a portion of the clear upper aqueous layer.

Standard solution B: 0.6 µg/mL of USP Alendronate Sodium RS in *Diluent* from *Standard stock solution*. Transfer 5 mL of this diluted solution (0.6 µg/mL) to a 50-mL polypropylene, screw-cap centrifuge tube containing 5 mL of *Borate solution*. Add 5 mL of acetonitrile and 5 mL of *Solution C*, and shake for 45 s. Allow to stand at room temperature for 30 min. Add 20 mL of methylene chloride, and shake vigorously for 1 min. Centrifuge for 5–10 min, and use a portion of the clear upper aqueous layer.

Reagent blank: Transfer 5.0 mL of *Diluent* to a 50-mL polypropylene, screw-cap centrifuge tube containing 5 mL of *Borate solution*. Add 5 mL of acetonitrile and 5 mL of *Solution C*, and shake for 45 s. Allow to stand at room temperature for 30 min. Add 20 mL of methylene chloride, and shake vigorously for 1 min. Centrifuge for 5–10 min, and use a portion of the clear upper aqueous layer.

Sample stock solution: 0.6 mg/mL of Alendronate Sodium in *Diluent*

Sample solution: Transfer 5.0 mL of *Sample stock solution* to a 50-mL polypropylene, screw-cap centrifuge tube containing 5 mL of *Borate solution*. Add 5 mL of acetonitrile and 5 mL of *Solution C*, and shake for 45 s. Allow to stand at room temperature for 30 min. Add 20 mL of methylene chloride, and shake vigorously for 1 min. Centrifuge for 5–10 min, and use a portion of the clear upper aqueous layer.

Chromatographic system

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

Mode: LC

Detector: UV 266 nm

Column: 4.1-mm × 25-cm; packing L21

Column temperature: 45°

Flow rate: 1.8 mL/min

Injection volume: 20 µL

System suitability

Samples: *Standard solution A* and *Standard solution B*

Suitability requirements

Tailing factor: NMT 2.0 for the main peak, *Standard solution A*

Signal-to-noise ratio: NLT 3 for the main peak, *Standard solution B*

Analysis

Samples: *Reagent blank* and *Sample solution*

[NOTE—Disregard any peak corresponding to those obtained from the *Reagent blank*.]

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

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

r_U = peak area of each impurity

r_T = sum of all impurity peaks and the main peak

Acceptance criteria

Individual impurities: NMT 0.1%

Total impurities: NMT 0.5%

SPECIFIC TESTS

• **LOSS ON DRYING** ⟨731⟩

Sample: Dry at a pressure of NMT 5 mm of mercury at 140° to constant weight.

Acceptance criteria: 16.1%–17.1%

ADDITIONAL REQUIREMENTS

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

• **USP REFERENCE STANDARDS** ⟨11⟩

USP Alendronate Sodium RS

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

Topic/Question	Contact	Expert Committee
ALENDRONATE 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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