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Alendronate Sodium Tablets

DEFINITION

Alendronate Sodium Tablets contain an amount of Alendronate Sodium equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of alendronic acid ($C_4H_{13}NO_7P_2$).

IDENTIFICATION

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**

Solution A: 14.7 g/L of sodium citrate dihydrate and 7.05 g/L of anhydrous dibasic sodium phosphate in water. [Note—Adjust with phosphoric acid to a pH of 8.0 before bringing the solution to volume.]

Solution B: 38.1 g/L of sodium borate in water

Solution C: 1 mg/mL of 9-fluorenylmethyl chloroformate in acetonitrile. [Note—Prepare this solution fresh just before use.]

Mobile phase: Acetonitrile, methanol, and *Solution A* (20:5:75)

Diluent: 29.4 g/L of sodium citrate dihydrate in water

Standard stock solution: 0.03 mg/mL of anhydrous alendronate sodium in *Diluent*, from USP Alendronate Sodium RS

Standard solution: Transfer 5.0 mL of the *Standard stock solution* to a 50-mL polypropylene screw-cap centrifuge tube containing 5 mL of *Solution B*, and mix for 3 min. Add 4 mL of *Solution C*, and agitate for 30 s. Allow the solution to stand at room temperature for 25 min. Add 25 mL of methylene chloride, and agitate for 40 s. Centrifuge the mixture for 10 min. Use the clear upper aqueous layer.

Sample stock solution: Transfer NLT 10 Tablets to a 1000-mL volumetric flask. Add 500 mL of *Diluent*, shake by mechanical means for 30 min, and sonicate for 5 min. Dilute with *Diluent* to volume, and centrifuge a portion of this solution. Quantitatively dilute a portion of the clear supernatant to a concentration of 0.02–0.03 mg/mL of alendronic acid.

Sample solution: Transfer 5.0 mL of the *Sample stock solution* to a 50-mL polypropylene screw-cap centrifuge tube containing 5 mL of *Solution B*, and mix for 3 min. Add 4 mL of *Solution C*, and agitate for 30 s. Allow the solution to stand at room temperature for 25 min. Add 25 mL of methylene chloride, and agitate for 40 s. Centrifuge the mixture for 10 min. Use the clear upper aqueous layer.

Blank: Transfer 5 mL of *Diluent* to a 50-mL polypropylene screw-cap centrifuge tube containing 5 mL of *Solution B*, and mix for 3 min. Add 4 mL of *Solution C*, and agitate for 30 s. Allow the solution to stand at room temperature for 25 min. Add 25 mL of methylene chloride, and agitate for 40 s. Centrifuge the mixture for 10 min. Use 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 mL/min

Injection size: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Capacity factor: NLT 2.0

Relative standard deviation: NMT 2.0% for replicate injections

Analysis

Samples: *Standard solution*, *Sample solution*, and *Blank*

Calculate the percentage of the label claim in the portion of $C_4H_{13}NO_7P_2$ taken:

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

r_U = peak area from the *Sample solution*

r_S = peak area from the *Standard solution*

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

C_U = nominal concentration of alendronic acid in the *Sample stock solution* (mg/mL)

M_{r1} = molecular weight of alendronic acid, 249.10

M_{r2} = molecular weight of anhydrous alendronate sodium, 271.09

Acceptance criteria: $C_4H_{12}NNaO_7P_2$ equivalent to 90.0%–110.0% of the labeled amount of $C_4H_{13}NO_7P_2$

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Test 1

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Time: 15 min

Determine the amount of $C_4H_{13}NO_7P_2$ dissolved by using the following method.

Solution A and **Mobile phase:** Proceed as directed in the *Assay*.

Diluent: 176.4 g/L of sodium citrate in *Medium*

Solution B: Dissolve 6.2 g of boric acid in approximately 950 mL of water. Adjust with 1 N sodium hydroxide to a pH of 9.0, and dilute with water to 1 L.

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

Standard stock solution: USP Alendronate Sodium RS in *Medium* to make a concentration equivalent to dissolving 1 Tablet in 900 mL of the same *Medium*. Calculate the concentration, C (mg/mL), of anhydrous alendronate sodium in this solution.

Standard solution: Transfer 5.0 mL of the *Standard stock solution* to a 50-mL polypropylene screw-cap centrifuge tube containing 1.0 mL of *Diluent* and 5.0 mL of *Solution B*, and mix for 3 min. Add 4.0 mL of *Solution C*, and agitate for 30 s. Allow the solution to stand at room temperature for 25 min. Add 25 mL of methylene chloride, and agitate for 40 s. Centrifuge the mixture for 5 min. Use a portion of the clear, upper aqueous layer.

Blank: Transfer 5 mL of water to a 50-mL polypropylene screw-cap centrifuge tube containing 1.0 mL of *Diluent* and 5.0 mL of *Solution B*, and mix for 3 min. Add 4.0 mL of *Solution C*, and agitate for 30 s. Allow the solution to stand at room temperature for 25 min. Add 25 mL of methylene chloride, and agitate for 40 s. Centrifuge the mixture for 5 min. Use a portion of the clear, upper aqueous layer.

Sample solution: Withdraw a portion of the solution under test, and centrifuge immediately. Transfer 5.0 mL of the supernatant to a 50-mL polypropylene screw-cap centrifuge tube containing 1.0 mL of *Diluent* and 5.0 mL of *Solution B*, and mix for 3 min. Add 4.0 mL of *Solution C*, and agitate for 30 s. Allow the solution to stand at room temperature for 25 min. Add 25 mL of methylene chloride, and agitate for 40 s. Centrifuge the mixture for 5 min. Use a portion of the clear, upper aqueous layer.

Chromatographic system and **System suitabilitity:** Proceed as directed in the *Assay*.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_4H_{13}NO_7P_2$ dissolved:

$$\text{Result} = (r_U/r_S) \times C \times (M_{r1}/M_{r2}) \times V \times (100/L)$$

r_U = peak area from the *Sample solution*

r_S = peak area from the *Standard solution*

C = defined under the *Standard stock solution*

M_{r1} = molecular weight of alendronic acid, 249.10

M_{r2} = molecular weight of alendronate sodium, 271.09

V = volume of the *Medium*, 900 mL

L = Tablet label claim (mg)

Tolerances: NLT 80% (Q) of the labeled amount of $C_4H_{13}NO_7P_2$ is dissolved; for tablets labeled for weekly dosing, NLT 75% (Q) of the labeled amount of $C_4H_{13}NO_7P_2$ 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

Apparatus 2: 50 rpm

Time: 30 min

Determine the amount of $C_4H_{12}NNaO_7P_2 \cdot 3H_2O$ dissolved using the following method.

Solution B and **Solution C:** Proceed as directed in the *Assay*.

0.6 M citrate buffer: 176.4 g/L of sodium citrate dihydrate in water

0.05 M buffer: Transfer 14.7 g of sodium citrate dihydrate and 7.05 g of anhydrous dibasic sodium phosphate to a 1000-mL volumetric flask, dissolve in about 900 mL of water, adjust with phosphoric acid to a pH of 8.0, and dilute with water to volume.

Mobile phase: *0.05 M buffer*, acetonitrile, and methanol (76:19:5)

Standard stock solution: Prepare a solution of USP Alendronate Sodium RS in *Medium* with a final concentration corresponding to the concentration obtained by dissolving 1 tablet in 900 mL of *Medium*. Calculate the concentration, C (mg/mL), of anhydrous alendronate sodium in this solution.

Standard solution: Transfer 5.0 mL of the *Standard stock solution* to a 50-mL screw-cap polypropylene centrifuge tube containing 1.0 mL of *0.6 M citrate buffer* and 5.0 mL of *Solution B*, and mix for about 3 min. Add 4.0 mL of *Solution C*, and agitate for about 30 s. Allow the solution to stand at room temperature for about 30 min. Add 25 mL of methylene chloride, and agitate vigorously for about 40 s. Centrifuge the mixture for 10 min. Use a portion of the clear upper aqueous layer.

Blank: Using 5 mL of water, proceed as directed for the *Standard solution*, beginning with “to a 50-mL screw-cap polypropylene centrifuge tube”.

Sample solution

For Tablets labeled to contain 5 mg, 10 mg, 35 mg, or 40 mg: After 30 min, withdraw 30 mL of the solution under test, and pass through a suitable 0.45-µm filter, discarding the first 10 mL. Using 5.0 mL of the filtrate, proceed as directed for the *Standard solution*, beginning with “to a 50-mL screw-cap polypropylene centrifuge tube”.

For Tablets labeled to contain 70 mg: After 30 min, withdraw 30 mL of the solution under test, and pass through a suitable 0.45-µm filter, discarding the first 10 mL. Transfer 6.0 mL of the filtrate to a 10-mL volumetric flask, and dilute with water to volume. Using 5.0 mL of this dilution, proceed as directed for the *Standard solution*, beginning with “to a 50-mL screw-cap polypropylene centrifuge tube”.

Chromatographic system and **System suitability:** Proceed as directed in the *Assay*.

Analysis: Proceed as directed in *Test 1*.

Tolerances: NLT 80% (Q) of the labeled amount of alendronate sodium ($C_4H_{12}NNaO_7P_2 \cdot 3H_2O$) is dissolved.

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

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers. Store between 15° and 30°.

• **Labeling:** The labeling indicates weekly dosing where appropriate. When more than one *Dissolution* test is given, the labeling states the test used only if *Test 1* is not used.

• **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 TABLETS	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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