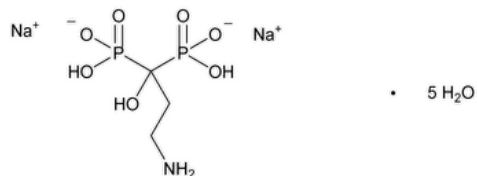


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Pamidronate Disodium



$C_3H_9NNa_2O_7P_2 \cdot 5H_2O$ 369.11

Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, disodium salt, pentahydrate;

Disodium dihydrogen (3-amino-1-hydroxypropylidene)diphosphonate, pentahydrate CAS RN®: 109552-15-0; UNII: 8742T8ZQZA.

Anhydrous

$C_3H_9NNa_2O_7P_2$ 279.03 CAS RN®: 57248-88-1; UNII: C7S8VWP5DH.

DEFINITION

Pamidronate Disodium contains NLT 98.0% and NMT 102.0% of Pamidronate Disodium ($C_3H_9NNa_2O_7P_2$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197K ▲ or 197A ▲ (USP 1-Aug-2022)
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.
- **C. IDENTIFICATION TESTS—GENERAL (191), Chemical Identification Tests, Sodium:** Meets the requirements

ASSAY

Change to read:

PROCEDURE

Mobile phase: 0.47 mL of [formic acid, anhydrous](#) in 2500 mL of [water](#). Adjust with [2 N sodium hydroxide](#) to a pH of 3.5. [NOTE—The small amounts of formic acid have a strong influence on the retention times.]

Standard solution: 2.0 mg/mL of [USP Pamidronate Disodium RS](#) in [water](#)

Sample solution: 2.0 mg/mL of Pamidronate Disodium in [water](#)

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: Refractive index

Column: 4.6-mm × 10-cm; packing [L23](#). ▲ [NOTE—It is required to saturate the column for at least 12 h before starting analysis.] ▲ (USP 1-Aug-2022)

Column temperature: 35°

Flow rate: 1 mL/min

Injection volume: 100 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: 0.3–1.2

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of pamidronate disodium ($C_3H_9NNa_2O_7P_2$) in the portion of Pamidronate Disodium taken:

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

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

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

C_S = concentration of [USP Pamidronate Disodium RS](#) in the *Standard solution* (mg/mL)

C_U = concentration of Pamidronate Disodium in the *Sample solution* (mg/mL)

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

IMPURITIES

Change to read:

• ORGANIC IMPURITIES, PROCEDURE 1

▲**Buffer:** 2.94 g/L of [sodium citrate dihydrate](#) and 1.42 g/L of [anhydrous dibasic sodium phosphate](#) in [water](#). Adjust with [phosphoric acid](#) to a pH of 8.0.

Solution A: [Acetonitrile](#) and *Buffer* (15:85)

Solution B: [Acetonitrile](#) and *Buffer* (70:30)

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
42	100	0

Diluent: 29.4 g/L of [sodium citrate dihydrate](#) in [water](#)

Derivatizing reagent solution: 4.0 mg/mL of [9-fluorenylmethyl chloroformate](#) in [acetonitrile](#). [NOTE—Prepare fresh prior to use.]

Borate solution: 19.1 mg/mL of [sodium borate](#) in [water](#)

Standard stock solution: 0.6 µg/mL of [USP Pamidronate Disodium RS](#) in *Diluent*

Standard solution: 0.15 µg/mL of [USP Pamidronate Disodium RS](#) from the *Standard stock solution* as follows. Transfer 5.0 mL of *Standard stock solution* into a 50-mL polypropylene screw-cap centrifuge tube containing about 5.0 mL of *Borate solution* and 5.0 mL of [acetonitrile](#). Add 5.0 mL of *Derivatizing reagent solution* and shake for 45 s. Allow the solution to stand at room temperature for 30 min. Add 20 mL of [methylene chloride](#) and shake for 1 min. Centrifuge for 5–10 min and use a portion of the clear supernatant layer.

Sensitivity stock solution: 0.3 µg/mL of [USP Pamidronate Disodium RS](#) in *Diluent*, from the *Standard stock solution*

Sensitivity solution: 0.075 µg/mL of [USP Pamidronate Disodium RS](#) from the *Sensitivity stock solution* as follows. Transfer 5.0 mL of *Sensitivity stock solution* into a 50-mL polypropylene screw-cap centrifuge tube containing about 5.0 mL of *Borate solution* and 5.0 mL of [acetonitrile](#). Add 5.0 mL of *Derivatizing reagent solution* and shake for 45 s. Allow the solution to stand at room temperature for 30 min. Add 20 mL of [methylene chloride](#) and shake for 1 min. Centrifuge for 5–10 min and use a portion of the clear supernatant layer.

Sample stock solution: 0.6 mg/mL of Pamidronate Disodium in *Diluent*

Sample solution: 0.15 mg/mL of Pamidronate Disodium from the *Sample stock solution* as follows. Transfer 5.0 mL of the *Sample stock solution* into a 50-mL polypropylene screw-cap centrifuge tube containing about 5.0 mL of *Borate solution* and 5.0 mL of [acetonitrile](#). Add 5.0 mL of *Derivatizing reagent solution* and shake for 45 s. Allow the solution to stand at room temperature for 30 min. Add 20 mL of [methylene chloride](#) and shake for 1 min. Centrifuge for 5–10 min and use a portion of the clear supernatant layer.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)