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Pamidronate Disodium for Injection

Change to read:

DEFINITION

Pamidronate Disodium for Injection ▲▲ (USP 1-May-2023) contains ▲an amount of Pamidronate Disodium equivalent to▲ (USP 1-May-2023) NLT 93.0% and NMT 108.0% of the labeled amount of pamidronate disodium ($C_3H_9NNa_2O_7P_2$).

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*.

ASSAY

Change to read:

• **Procedure**

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

Standard solution: 2.5 mg/mL of USP Pamidronate Disodium RS in water. [Note—Calculate the concentration, C_S, of anhydrous pamidronate disodium, the molecular weights of anhydrous and pentahydrate pamidronate disodium being 279.06 and 369.11, respectively.]

Sample solution: Nominally 2 mg/mL of anhydrous pamidronate disodium prepared by reconstituting and combining a suitable number of vials of Pamidronate Disodium for Injection in water

Chromatographic system

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

Mode: LC

Detector: Refractive index

Column: 4.6-mm × 10-cm; ▲12-µm▲ (USP 1-May-2023) packing L23. ▲[Note—It is required to saturate new columns for at least 12 h before starting analysis.]▲ (USP 1-May-2023)

Column temperature: 35°

Flow rate: 1▲▲ (USP 1-May-2023) mL/min

Injection volume: 100 µL

▲**Run time:** NLT 2.5 times the retention time of pamidronate▲ (USP 1-May-2023)

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 for Injection 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 anhydrous USP Pamidronate Disodium RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of anhydrous pamidronate disodium in the *Sample solution* (mg/mL)

Acceptance criteria: 93.0%–108.0%

PERFORMANCE TESTS

• **Uniformity of Dosage Units ⟨905⟩, *Weight Variation*:** Meets the requirements

IMPURITIES

Change to read:

• **Limit of Beta Alanine**

▲**Buffer 1:** 13.6 g/L of monobasic potassium phosphate and 5.6 g/L of sodium 1-hexanesulfonate in water. Adjust with phosphoric acid to a pH of 2.5.

Buffer 2: 27.2 g/L of monobasic potassium phosphate and 2% phosphoric acid solution in water

Mobile phase: Acetonitrile and *Buffer 1* (5:95)

Diluent: Acetonitrile and *Buffer 2* (5:95)

Standard solution: 0.01 mg/mL of USP Beta Alanine RS in *Diluent*

Sample stock solution: Nominally 9 mg/mL of pamidronate disodium from Pamidronate Disodium for Injection prepared as follows. Reconstitute NLT 1 vial with a suitable amount of water and shake to mix.

Sample solution: Nominally 5 mg/mL of pamidronate disodium from the *Sample stock solution* in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

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

Temperature: 40°

Flow rate: 1 mL/min

Injection volume: 100 µL

Run time: NLT 2 times the retention time of beta alanine

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 5.0%

Signal-to-noise ratio: NLT 10

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of beta alanine in the portion of Pamidronate Disodium for Injection taken:

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

r_U = peak response of beta alanine from the *Sample solution*

r_S = peak response of beta alanine from the *Standard solution*

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

C_U = nominal concentration of pamidronate disodium in the *Sample solution* (mg/mL)▲ (USP 1-May-2023)

Acceptance criteria: NMT 0.25%

SPECIFIC TESTS

• **pH ⟨791⟩**

Sample solution: Use the solution constituted as directed in the labeling.

Acceptance criteria: 6.0–7.0

• **Water Determination ⟨921⟩, *Method I, Method Ia*:** NMT 5%

• **Constituted Solution:** At the time of use, it meets the requirements for *Injections and Implanted Drug Products ⟨1⟩, Product Quality Tests Common to Parenteral Dosage Forms, Specific Tests, Completeness and Clarity of Solutions*.

Change to read:

• **Particulate Matter in Injections ⟨788⟩:**

▲**Sample solution:** Use solution constituted as directed in the labeling.▲ (USP 1-May-2023)

Acceptance criteria: Meets the requirements for small-volume injections

Change to read:

• **Bacterial Endotoxins Test ⟨85⟩:** ▲Meets the requirements▲ (USP 1-May-2023)

• **Sterility Tests ⟨71⟩:** Meets the requirements

• **Other Requirements:** It meets the requirements under *Labeling ⟨7⟩, Labels and Labeling for Injectable Products*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve as described under *Packaging and Storage Requirements ⟨659⟩, Injection Packaging, Packaging for Constitution*. Store at controlled room temperature.

Change to read:

• **USP Reference standards ⟨11⟩**

USP Beta Alanine RS

▲3-Aminopropanoic▲ (USP 1-May-2023) acid.

▲$C_3H_7NO_2$ 89.09▲ (USP 1-May-2023)

USP Pamidronate Disodium RS

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

Topic/Question	Contact	Expert Committee
PAMIDRONATE DISODIUM FOR INJECTION	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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