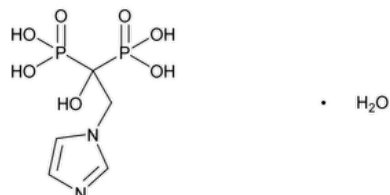


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Zoledronic Acid



$C_5H_{10}N_2O_7P_2 \cdot H_2O$ 290.10

Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis-, monohydrate;

(1-Hydroxy-2-imidazol-1-ylethylidene)diphosphonic acid, monohydrate CAS RN®: 165800-06-6.

Anhydrous CAS RN®: 118072-93-8. 272.09

DEFINITION

Zoledronic Acid contains NLT 98.0% and NMT 102.0% of zoledronic acid ($C_5H_{10}N_2O_7P_2$), calculated on the anhydrous basis.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197K or 197A
- **B.** 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

Perchloric acid solution: Carefully add 10 mL of [perchloric acid](#) to 1 L of [water](#), then add 2 mL of [phosphoric acid](#), and mix.

Buffer: 0.037 g/L of [edetate disodium](#) and 10.8 g/L of [octanesulfonic acid sodium salt](#) in *Perchloric acid solution*

Mobile phase: [Acetonitrile](#) and *Buffer* (4:96)

System suitability solution: 2 µg/mL each of [USP Imidazole RS](#), [USP Zoledronic Acid Related Compound A RS](#), and sodium nitrate; 5 µg/mL of [USP Zoledronic Acid Related Compound B RS](#); and 1.2 mg/mL of [USP Zoledronic Acid RS](#) in *Mobile phase*

Standard solution: 1 mg/mL of [USP Zoledronic Acid RS](#) in *Mobile phase*. Sonicate with occasional shaking for about 15 min to achieve complete dissolution.

Sample solution: 1 mg/mL of Zoledronic Acid in *Mobile phase*. Sonicate with occasional shaking for about 15 min to achieve complete dissolution.

Chromatographic system

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

[NOTE—Plastic HPLC vials are recommended.]

Preconditioning of the instrument: Rinse the instrument without a column with a mixture of [acetic acid](#) and [water](#) (25:75) at 5 mL/min for 20 min. Then, rinse with [water](#) at 5 mL/min for about 2 h.

Preconditioning of the column: Rinse with *Mobile phase* at 0.6 mL/min for about 1 h. During the rinsing, inject the *Sample solution* 10–15 times, applying a run time of about 3 min for each injection.

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 25-cm; 5-µm packing [L11](#)

Flow rate: 0.6 mL/min

Injection volume: 5 µL

Run time: NLT 3 times the retention time of zoledronic acid

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 1.0 between the nitrate and zoledronic acid related compound B peaks, *System suitability solution*

Tailing factor: NMT 1.4 for the zoledronic acid peak, *System suitability solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of zoledronic acid ($C_5H_{10}N_2O_7P_2$) in the portion of Zoledronic Acid taken:

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

r_U = peak response of zoledronic acid from the *Sample solution*

r_S = peak response of zoledronic acid from the *Standard solution*

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

C_U = concentration of Zoledronic Acid in the *Sample solution* (mg/mL)

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

IMPURITIES

Change to read:

• ORGANIC IMPURITIES

Perchloric acid solution, Buffer, Mobile phase, and System suitability solution: Prepare as directed in the Assay.

Standard stock solution: 0.4 mg/mL of [USP Zoledronic Acid RS](#) in *Mobile phase*. Sonicate with occasional shaking for about 15 min to achieve complete dissolution.

Sensitivity solution: 1 µg/mL of [USP Zoledronic Acid RS](#) in *Mobile phase* from *Standard stock solution*

Standard solution: 0.002 mg/mL of [USP Zoledronic Acid RS](#) in *Mobile phase* from *Standard stock solution*

Sample solution: 2 mg/mL of Zoledronic Acid in *Mobile phase*. Sonicate with occasional shaking for about 30 min to achieve complete dissolution.

Chromatographic system: Proceed as directed in the Assay, except for *Injection volume* and *Run time*.

Injection volume: 10 µL

Run time: NLT 5 times the retention time of zoledronic acid

System suitability

Samples: *System suitability solution*, *Sensitivity solution*, and *Standard solution*

Suitability requirements

Resolution: NLT 1.0 between the nitrate and zoledronic acid related compound B peaks, *System suitability solution*

Tailing factor: NMT 1.4 for the zoledronic acid peak, *Standard solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any individual impurity in the portion of Zoledronic Acid taken:

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

r_U = peak response of ▲any individual impurity▲ (ERR 1-Mar-2022) from the *Sample solution*

r_S = peak response of zoledronic acid from the *Standard solution*

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

C_U = concentration of Zoledronic Acid in the *Sample solution* (mg/mL)

F = relative response factor (see [Table 1](#))

Acceptance criteria: See [Table 1](#). The reporting threshold is 0.05%.

Table 1