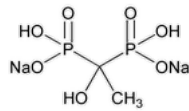


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Etidronate Disodium



$C_2H_6Na_2O_7P_2$ 249.99

Phosphonic acid, (1-hydroxyethylidene)bis-, disodium salt;

Disodium dihydrogen (1-hydroxyethylidene)diphosphonate CAS RN®: 7414-83-7; UNII: M16PXG993G.

DEFINITION

Etidronate Disodium contains NLT 97.0% and NMT 101.0% of etidronate disodium ($C_2H_6Na_2O_7P_2$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

- **A.** **SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy** (ERR 1-OCT-2020)

Standard: Recrystallize [USP Etidronate Disodium RS](#) from [water](#) and dry it at 105° for 1 h.

Sample: Recrystallize the sample from [water](#) and dry it at 105° for 1 h.

Analysis and Acceptance criteria: The spectra of [trifluorovinyl chloride polymer](#) and mineral oil dispersions of the *Sample*, separately prepared, exhibit maxima in the regions of 4000–1350 cm^{-1} and 1350–450 cm^{-1} , respectively, only at the same wavelengths as those of similar preparations of the *Standard*. The analysis and acceptance criteria described in [\(197A\)](#), may also be used.

- **B.** **IDENTIFICATION TESTS—GENERAL (191), Chemical Identification Tests, Sodium:** Meets the requirements of test A
- **C.** 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

Mobile phase: 35–40 mM [ammonium nitrate](#) solution in [water](#). Adjust with dilute [ammonium hydroxide](#) to a pH of 7.0.

Standard solution: 0.73–0.75 mg/mL of [USP Etidronic Acid Monohydrate RS](#) in [1 N sodium hydroxide VS](#) and *Mobile phase* (1:150)

Sample solution: 0.84–0.86 mg/mL of Etidronate Disodium in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: Refractive index

Column: 4.6-mm × 15-cm; 10- μ m packing [L23](#)

Temperatures

Column: 32°

Detector: 32°

Flow rate: 1.5 mL/min

Injection volume: 20 μ L

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 1.5% for replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of etidronate disodium ($C_2H_6Na_2O_7P_2$) in the portion of Etidronate Disodium taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_s = concentration of [USP Etidronic Acid Monohydrate RS](#) in the *Standard solution* (mg/mL)

C_u = concentration of Etidronate Disodium in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of etidronate disodium, 249.99

M_{r2} = molecular weight of etidronic acid monohydrate, 224.04

Acceptance criteria: 97.0%–101.0% on the anhydrous basis

IMPURITIES

• LIMIT OF PHOSPHITE

Solution A: 0.65 mg/mL of anhydrous sodium carbonate and 0.40 mg/mL of sodium bicarbonate in water

Solution B: 4.68 mg/mL of anhydrous sodium carbonate and 2.89 mg/mL of sodium bicarbonate in water

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
6.0	100	0
6.1	0	100
8.0	0	100
8.1	100	0
15	100	0

Suppressor regenerant solution: 12.5 mM sulfuric acid. [NOTE—This solution is needed only if the chemical suppression option is used.]

Standard solution: Equivalent to 0.016 mg/mL of dibasic sodium phosphite on the anhydrous basis from [USP Etidronate Disodium Related Compound A RS](#) and 0.015 mg/mL of dibasic sodium phosphate in *Solution A*. [NOTE—[USP Etidronate Disodium Related Compound A RS](#) is sodium phosphite dibasic pentahydrate.]

Sample solution: 5.0 mg/mL of Etidronate Disodium in *Solution A*

Chromatographic system

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

Mode: LC

Detector: Conductivity

Columns

Guard: 4-mm × 50-mm; packing L61. [NOTE—Use either a 4-mm anion self-regenerating suppressor or a suitable chemical suppressor.]

Analytical: 4-mm × 25-cm; packing L61

Flow rate: 1.0 mL/min. [NOTE—When a chemical suppressor is used, the flow rate is 3–5 mL/min for the *Suppressor regenerant solution*.]

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

[NOTE—The elution order is phosphite, followed by phosphate.]

Suitability requirements

Resolution: NLT 2.5 between phosphite and phosphate

Relative standard deviation: NMT 10% for each peak, for replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of phosphite, determined as monobasic sodium phosphite, in the portion of Etidronate Disodium taken:

$$\text{Result} = (r_u/r_s) \times (C_s/C_u) \times (M_{r1}/M_{r2}) \times 100$$

r_u = peak response of phosphite from the *Sample solution*

r_s = peak response of phosphite from the *Standard solution*

C_s = concentration of [USP Etidronate Disodium Related Compound A RS](#) on the anhydrous basis in the *Standard solution* (mg/mL)

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

M_{r1} = molecular weight of monobasic sodium phosphite, 103.98

M_{r2} = molecular weight of dibasic sodium phosphite, 125.96

Acceptance criteria: NMT 1.0% of phosphite, determined as monobasic sodium phosphite

SPECIFIC TESTS

• [pH \(791\)](#)

Sample solution: 10 mg/mL

Acceptance criteria: 4.2–5.2

• [WATER DETERMINATION \(921\)](#), [Method I](#), [Method Ic](#)

Sample solution: 100 mg of finely powdered Etidronate Disodium in 10 mL of a mixture of [glacial acetic acid](#) and [formamide](#) (1:1)

Acceptance criteria: NMT 5.0%

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in tight containers.

• [USP REFERENCE STANDARDS \(11\)](#)

[USP Etidronate Disodium RS](#)

[USP Etidronate Disodium Related Compound A RS](#)

Sodium phosphite dibasic pentahydrate.

$\text{Na}_2\text{HPO}_3 \cdot 5\text{H}_2\text{O}$ 216.04

[USP Etidronic Acid Monohydrate RS](#)

Phosphonic acid, (1-hydroxyethylidene)bis-, monohydrate

$\text{C}_2\text{H}_8\text{O}_7\text{P}_2 \cdot \text{H}_2\text{O}$ 224.04

Auxiliary Information - Please [check for your question in the FAQs](#) before contacting USP.

Topic/Question	Contact	Expert Committee
ETIDRONATE DISODIUM	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: [Chromatographic Database](#)

Most Recently Appeared In:

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