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Etidronate Disodium Tablets

DEFINITION
Etidronate Disodium Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of etidronate disodium ($C_2H_6Na_2O_7P_2$).

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 197M▲ (CN 1-May-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** ▲**for ⟨197M⟩:**▲ (CN 1-May-2020) 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*. ▲▲ (CN 1-May-2020)

• **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**

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: Transfer a quantity of finely powdered Tablets (NLT 20), nominally equivalent to 160–170 mg of etidronate disodium, to a 200-mL volumetric flask, and dilute with *Mobile phase* to volume. Agitate the solution for at least 5 min, and pass through a nylon filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: Refractive index

Column: 4.6-mm × 15-cm; 10-µm packing L23

Temperatures

Detector: 32°

Column: 32°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 1.5%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of etidronate disodium ($C_2H_6Na_2O_7P_2$) in the portion of Tablets 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 = nominal 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: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: Water; 900 mL

Apparatus 1: 100 rpm

Time: 30 min

Mobile phase: Prepare as directed in the *Assay*.

Standard solution

For products labeled to contain 200 mg of etidronate disodium: Transfer 20 mg of USP Etidronic Acid Monohydrate RS to a 100-mL volumetric flask, dissolve in 50 mL of water, add 2.0 mL of 0.1 N sodium hydroxide VS, and dilute with water to volume.

For products labeled to contain 400 mg of etidronate disodium: Transfer 20 mg of USP Etidronic Acid Monohydrate RS to a 50-mL volumetric flask, dissolve in 25 mL of water, add 2.0 mL of 0.1 N sodium hydroxide VS, and dilute with water to volume.

Sample solution: Transfer a portion of the solution under test to an HPLC vial.

Chromatographic system

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

Mode: LC

Detector: Refractive index

Column: 4.6-mm × 15-cm; 10-µm packing L23

Temperatures

Detector: 32°

Column: 32°

Flow rate: 1.5 mL/min

Injection volume: See *Table 1*.

Table 1

Tablet Strength (mg)	Injection Volume (µL)
200	100
400	50

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 1.5%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of etidronate disodium ($C_2H_6Na_2O_7P_2$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (M_{r1}/M_{r2}) \times (1/L) \times 100$$

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)

V = volume of *Medium*, 900 mL

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

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

L = label claim (mg/Tablet)

Tolerances: NLT 70% (*Q*) of the labeled amount of etidronate disodium ($C_2H_6Na_2O_7P_2$) is dissolved.

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

IMPURITIES

• **Limit of Phosphite and Phosphate**

Mobile phase: 20 mM ammonium nitrate solution in water. Adjust with dilute ammonium hydroxide to a pH of 7.0.

Standard solution: A mixture of 0.04 mg/mL of dibasic sodium phosphite, on the anhydrous basis from USP Etidronate Disodium Related Compound A RS, and anhydrous dibasic sodium phosphate in *Mobile phase*

Sample solution: Nominally equivalent to 4.0 mg/mL of etidronate disodium in *Mobile phase* prepared as follows. Transfer a quantity of finely powdered Tablets (NLT 20), equivalent to 200 mg of etidronate disodium, to a 50-mL volumetric flask. Add about 40 mL of *Mobile phase*, dissolved by sonication, and dilute with *Mobile phase* to volume. Centrifuge a portion and use the clear supernatant.

Chromatographic system

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

Mode: LC

Detector: Refractive index

Column: 4.6-mm × 15-cm; 10-µm packing L23

Column temperature: 35°

Flow rate: 1.5 mL/min

Injection volume: 100 µL

System suitability

Sample: *Standard solution*

[NOTE—The typical relative retention times are about 0.7 for the phosphate, relative to the phosphite, and 1.0 for the phosphite.]

Suitability requirements

Resolution: NLT 1.5 between the phosphite and phosphate peaks

Relative standard deviation: NMT 5% for both the phosphite and phosphate peaks

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of phosphite, determined as monobasic sodium phosphite, in the portion of Tablets 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 = nominal concentration of etidronate disodium in 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

Calculate the percentage of phosphate, determined as dibasic sodium phosphate, in the portion of Tablets taken:

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

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

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

C_S = concentration of dibasic sodium phosphate in the *Standard solution* (mg/mL)

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

Acceptance criteria

Phosphite: NMT 1.0%, determined as monobasic sodium phosphite

Phosphate: NMT 1.0%, determined as dibasic sodium phosphate

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.

$Na_2HPO_3 \cdot 5H_2O$ 216.04

USP Etidronic Acid Monohydrate RS

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

$C_2H_8O_7P_2 \cdot H_2O$ 224.04

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

Chromatographic Database Information: Chromatographic Database

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