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Divalproex Sodium Delayed-Release Tablets

DEFINITION

Divalproex Sodium Delayed-Release Tablets contain an amount of Divalproex Sodium equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of valproic acid ($C_8H_{16}O_2$).

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*.
- **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

Solution A: 0.50 g/L of citric acid and 0.40 g/L of dibasic sodium phosphate in water

Mobile phase: Acetonitrile and *Solution A* (30:70). Adjust with phosphoric acid to a pH of 3.0 ± 0.1.

Standard solution: 0.5 mg/mL of USP Valproic Acid RS in *Mobile phase*

Sample stock solution: Nominally 10 mg/mL of valproic acid, prepared as follows. Transfer a number of whole Tablets to an appropriate volumetric flask. Add 60% of the flask volume of *Mobile phase*, and sonicate with frequent swirling for 30 min or until the Tablets completely disintegrate. Allow the solution to cool down to room temperature, and then dilute with *Mobile phase* to volume.

Sample solution: Nominally 0.5 mg/mL of valproic acid from *Sample stock solution* in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 210 nm. For *Identification B*, use a diode array detector in the range of 190–400 nm.

Column: 3.9-mm × 15-cm; 4-µm packing L11

Flow rate: 0.9 mL/min

Injection volume: 15 µL

Run time: NLT 1.8 times the retention time of valproic acid

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of valproic acid ($C_8H_{16}O_2$) in the portion of Tablets taken:

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

r_U = peak area of valproic acid from the *Sample solution*

r_S = peak area of valproic acid from the *Standard solution*

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

C_U = nominal concentration of valproic acid in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Acid stage

Acid stage medium: 0.08 N hydrochloric acid (prepared by adding 40 mL of hydrochloric acid to 5000 mL of water, adjusting with 2 N hydrochloric acid to a pH of 1.2, and diluting with water to 6000 mL); 900 mL

Apparatus 2: 50 rpm

Time: 1 h

At the end of 1 h, carefully transfer the Tablet to a dissolution vessel containing the *Buffer stage medium*. [Note—Do not perform an analysis of the *Acid stage medium*.]

Buffer stage

Buffer stage medium: pH 7.5 phosphate buffer (6.8 g/L of monobasic potassium phosphate and 1.6 g/L of sodium hydroxide in water, prepared as follows. Transfer suitable quantities of monobasic potassium phosphate and sodium hydroxide to an appropriate container. Dilute with water to 80% of the final volume, adjust with 0.08 N hydrochloric acid to a pH of 7.5, and dilute with water to the final volume); 900 mL

Apparatus 2: 50 rpm

Time: 1 h

Solution A: 0.5 g/L of citric acid and 0.4 g/L of dibasic sodium phosphate in water

Solution B: 6.8 g/L of monobasic potassium phosphate and 1.7 g/L of sodium hydroxide in water. Adjust with phosphoric acid to a pH of 7.4 ± 0.1.

Mobile phase: Acetonitrile, *Solution A*, and *Solution B* (30:35:35). Adjust with phosphoric acid to a pH of 3.0 ± 0.1.

Standard solution: 0.12 mg/mL of USP Valproic Acid RS in *Buffer stage medium*. [Note—NMT 10.0% of the flask volume of acetonitrile may be used to dissolve the USP Valproic Acid RS.]

Sample solution: Nominally 0.12 mg/mL of valproic acid, prepared as follows. Pass a portion of the solution under test through a suitable filter. Dilute with *Buffer stage medium*, if necessary.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 3.9-mm × 15-cm; 4-µm packing L11

Flow rate: 1.2 mL/min

Injection volume: 50 µL

Run time: NLT 1.5 times the retention time of valproic acid

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of valproic acid ($C_8H_{16}O_2$) dissolved:

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

r_U = peak area of valproic acid from the *Sample solution*

r_S = peak area of valproic acid from the *Standard solution*

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

V = volume of *Buffer stage medium*, 900 mL

D = dilution factor of the *Sample solution*

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of valproic acid ($C_8H_{16}O_2$) is dissolved.

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

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers, and store at controlled room temperature.
- **USP Reference Standards** ⟨11⟩

  USP Valproic Acid RS

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

Topic/Question	Contact	Expert Committee
DIVALPROEX SODIUM DELAYED-RELEASE TABLETS	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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