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Verapamil Hydrochloride Extended-Release Tablets

DEFINITION

Verapamil Hydrochloride Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of verapamil hydrochloride ($C_{27}H_{38}N_2O_4 \cdot HCl$).

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 *Diluted sample solution* corresponds to that of the *Diluted standard solution*, as obtained in the Assay.

ASSAY

PROCEDURE

Buffer: To 0.82 g of [sodium acetate](#), add 33 mL of [glacial acetic acid](#) and dilute with [water](#) to 1 L.

Mobile phase: [Acetonitrile](#), [2-aminoheptane](#), and *Buffer* (60:1:140)

System suitability solution: 2.5 mg/mL of [USP Verapamil Hydrochloride RS](#) and 2.0 mg/mL of [USP Verapamil Related Compound B RS](#) in *Mobile phase*

Standard solution: 1.2 mg/mL of [USP Verapamil Hydrochloride RS](#) in *Mobile phase*

Diluted standard solution: 0.6 mg/mL of [USP Verapamil Hydrochloride RS](#) in *Mobile phase* from the *Standard solution*

Sample solution: Nominally 1.2 mg/mL of verapamil hydrochloride from Tablets prepared as follows. Transfer an amount equivalent to 240 mg of verapamil hydrochloride, from NLT 20 powdered Tablets, to a 200-mL volumetric flask, and add about 160 mL of *Mobile phase*.

Sonicate for 15 min, stir for 15 min, dilute with *Mobile phase* to volume, and mix. Centrifuge a portion for 20 min, and use the supernatant.

Diluted sample solution: Nominally 0.6 mg/mL of verapamil hydrochloride in *Mobile phase* from the *Sample solution*

Chromatographic system

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

Mode: LC

Detector: UV 278 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 15-cm; 5-μm packing [L1](#)

Flow rate: 1 mL/min

Injection volume: 10 μL

Run time: NLT 3 times the retention time of verapamil

System suitability

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

[NOTE—The relative retention times for verapamil related compound B and verapamil are 0.85 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between verapamil and verapamil related compound B, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution*, *Diluted standard solution*, *Sample solution*, and *Diluted sample solution*

[NOTE—The *Diluted standard solution* and *Diluted sample solution* are used for *Identification B*.]

Calculate the percentage of the labeled amount of verapamil hydrochloride ($C_{27}H_{38}N_2O_4 \cdot HCl$) in the portion of Tablets taken:

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

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

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

C_s = concentration of [USP Verapamil Hydrochloride RS](#) in the *Standard solution* (mg/mL)

C_u = nominal concentration of verapamil hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• [DISSOLUTION \(711\)](#)

Test 1: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 1*. Proceed as directed in [Dissolution \(711\), Procedure, Apparatus 1 and Apparatus 2, Delayed-Release Dosage Forms, Method B Procedure](#).

Acid stage medium: Using 900 mL of simulated gastric fluid TS (without enzyme), conduct this stage of the test for 1 h.

Buffer stage medium: Using 900 mL of simulated intestinal fluid TS (without enzyme), conduct this stage of the test for 7 h.

Apparatus 2: 50 rpm

Times

Acid stage: 1 h

Buffer stage: 2, 3.5, 5, and 8 h

Standard solution: [USP Verapamil Hydrochloride RS](#) in 0.01 N [hydrochloric acid](#)

Sample solution: Pass portions of the solution under test through a suitable filter. Dilute with medium as necessary.

Blank solution: 0.01 N [hydrochloric acid](#)

Analysis: Wrap each Tablet in a wire helix to prevent the Tablets from floating. After 1 h in the *Acid stage medium*, withdraw a specimen for analysis, and carefully transfer the dosage form, including the wire helix, to a vessel containing the *Buffer stage medium*, which has been previously warmed to $37 \pm 0.5^\circ$. At each time interval, pass a portion of the solution under test through a suitable glass microfiber filter paper. Dilute, if necessary, the filtered portions of the solutions under test with water at the 1-h interval and with 0.1 N [hydrochloric acid](#) at the 2-, 3.5-, 5-, and 8-h intervals. Determine the percentage of the labeled amount of verapamil hydrochloride ($C_{27}H_{38}N_2O_4 \cdot HCl$) dissolved.

[NOTE—Use only filters that have been shown not to absorb verapamil.]

Detector: UV 278 nm

Tolerances: See [Table 1](#) and [Table 2](#).

Table 1. For Products Labeled to Contain 180 or 240 mg

Time (h)	Amount Dissolved (%)
1	7–15
2	16–30
3.5	31–50
5	51–75
8	NLT 85

Table 2. For Products Labeled to Contain 120 mg

Time (h)	Amount Dissolved (%)
1	10–21
2	18–33
3.5	35–60
5	50–82

Time (h)	Amount Dissolved (%)
8	NLT 85

The percentages of the labeled amount of verapamil hydrochloride ($C_{27}H_{38}N_2O_4 \cdot HCl$) dissolved at the times specified conform to

[Dissolution \(711\)](#), [Acceptance Table 2](#).

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*. Proceed as directed for *Test 1*, except that in the *Analysis*, the Tablet is not required to be wrapped in a wire helix.

Tolerances: See [Table 3](#), [Table 4](#), and [Table 5](#).

Table 3. For Products Labeled to Contain 240 mg

Time (h)	Amount Dissolved (%)
1	8–20
2	15–35
3.5	35–65
5	55–85
8	NLT 80

Table 4. For Products Labeled to Contain 180 mg

Time (h)	Amount Dissolved (%)
1	10–25
2	20–40
3.5	40–75
8	NLT 80

Table 5. For Products Labeled to Contain 120 mg

Time (h)	Amount Dissolved (%)
1	10–25
2	20–40
3.5	35–70
5	55–85
8	NLT 80

