Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-May-2019
Document Type: USP Monographs
DocId: GUID-E31580DD-183C-4B6C-8575-825504A42D38_4_en-US
DOI: https://doi.org/10.31003/USPNF_M88095_04_01
DOI Ref: a0h11

Verapamil Hydrochloride Injection

DEFINITION

Verapamil Hydrochloride Injection is a sterile solution of Verapamil Hydrochloride in Water for Injection. It contains NLT 90.0% and NMT 110.0% of the labeled amount of verapamil hydrochloride ($C_{27}H_{38}N_2O_4 \cdot HCl$).

IDENTIFICATION

Change to read:

• **A.** ▲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*.▲ (USP 1-May-2019)

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

• **C. Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Chloride*:** Meets the requirements

ASSAY

Change to read:

• **Procedure**

Solution A: 0.015 N sodium acetate solution containing 33 mL of glacial acetic acid per liter

Mobile phase: Acetonitrile, *Solution A*, and 2-aminoheptane (30:70:0.5)

System suitability solution: 1.9 mg/mL of USP Verapamil Hydrochloride RS and 1.5 mg/mL of USP Verapamil Related Compound B RS in *Mobile phase*

Standard solution: 2.5 mg/mL of USP Verapamil Hydrochloride RS in *Mobile phase*

▲**Diluted standard solution:** 0.5 mg/mL of USP Verapamil Hydrochloride RS from the *Standard solution* in *Mobile phase*▲ (USP 1-May-2019)

Sample solution: Nominally 2.5 mg/mL of verapamil hydrochloride from a volume of Injection in *Mobile phase*

▲**Diluted sample solution:** Nominally 0.5 mg/mL of verapamil hydrochloride from the *Sample solution* in *Mobile phase*▲ (USP 1-May-2019)

Chromatographic system

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

Mode: LC

Detector: UV 278 nm. ▲For *Identification A*, use a diode array detector in the range of 200–400 nm.▲ (USP 1-May-2019)

Column: 4.6-mm × ▲▲ (USP 1-May-2019) 15-cm; ▲5-µm▲ (USP 1-May-2019) packing L1

Flow rate: 0.9 mL/min

Injection volume: 10 µL

Run time: NLT 4 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 about 0.88 and 1.0, respectively.]

Suitability requirements

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

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

Analysis

Samples: *Standard solution*, ▲*Diluted standard solution*,▲ (USP 1-May-2019) *Sample solution*, ▲and *Diluted sample solution*

[Note—The *Diluted standard solution* and *Diluted sample solution* are used for *Identification A*.]▲ (USP 1-May-2019)

Calculate the percentage of the labeled amount of verapamil hydrochloride ($C_{27}H_{38}N_2O_4 \cdot HCl$) in the volume of Injection 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%

IMPURITIES

Change to read:

• **Organic Impurities**

Solution A, Mobile phase, System suitability solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 2.5 mg/mL of USP Verapamil Hydrochloride RS, and 7.5 µg/mL each of USP Verapamil Related Compound A RS, USP Verapamil Related Compound E RS, and USP Verapamil Related Compound F RS in *Mobile phase*

System suitability

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

[Note—See *Table 1* for relative retention times.]

Suitability requirements

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

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

Signal-to-noise ratio: NLT 15 for verapamil related compound F, *Standard solution*▲ (USP 1-May-2019)

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of each ▲specified degradation product▲ (USP 1-May-2019) in the portion of Injection taken:

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

r_U = peak response of ▲verapamil related compound A, E, or F▲ (USP 1-May-2019) from the *Sample solution*

r_S = peak response of ▲verapamil related compound A, E, or F▲ (USP 1-May-2019) from the *Standard solution*

C_S = concentration of ▲USP Verapamil Related Compound A RS, USP Verapamil Related Compound E RS, or USP Verapamil Related Compound F RS▲ (USP 1-May-2019) in the *Standard solution* (mg/mL) ▲▲ (USP 1-May-2019)

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

▲Calculate the percentage of any unspecified degradation product in the portion of Injection taken:

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

r_U = peak response of any unspecified degradation product 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)▲ (USP 1-May-2019)

Acceptance criteria: See *Table 1*.

▲**Table 1**

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Verapamil related compound F	0.4	0.3
Verapamil related compound A	0.5	0.3
Verapamil related compound E	0.7	0.3
Verapamil related compound B[a]	0.88	—
Verapamil	1.0	—
Any unspecified degradation product	—	0.2
Total degradation products	—	1.0▲ (USP 1-May-2019)

[a] For resolution measurement only. It is not to be reported and not to be included in the total degradation products.

SPECIFIC TESTS

- **pH ⟨791⟩:** 4.0–6.5
- **Bacterial Endotoxins Test ⟨85⟩:** NMT 16.7 USP Endotoxin Units/mg of verapamil hydrochloride
- **Particulate Matter in Injections ⟨788⟩:** Meets the requirements for small-volume injections
- **Other Requirements:** Meets the requirements in *Injections and Implanted Drug Products ⟨1⟩*

ADDITIONAL REQUIREMENTS

Change to read:

- **Packaging and Storage:** Preserve in single-dose containers, preferably of Type I glass, protected from light. ▲Store at controlled room temperature.▲ (USP 1-May-2019)

Change to read:

- **USP Reference Standards ⟨11⟩**

USP Verapamil Hydrochloride RS

USP Verapamil Related Compound A RS

▲2-(3,4-Dimethoxyphenyl)-2-isopropyl-5-(methylamino)pentanenitrile hydrochloride.▲ (USP 1-May-2019)

$C_{17}H_{26}N_2O_2 \cdot HCl$ 326.87

USP Verapamil Related Compound B RS

▲4-[(3,4-Dimethoxyphenethyl)(methyl)amino]-2-(3,4-dimethoxyphenyl)-2-isopropylbutanenitrile hydrochloride.▲ (USP 1-May-2019)

$C_{26}H_{36}N_2O_4 \cdot HCl$ ▲477.04▲ (USP 1-May-2019)

USP Verapamil Related Compound E RS

3,4-Dimethoxybenzaldehyde.

▲$C_9H_{10}O_3$ 166.17▲ (USP 1-May-2019)

USP Verapamil Related Compound F RS

(3,4-Dimethoxyphenyl)methanol.

▲$C_9H_{12}O_3$ 168.19▲ (USP 1-May-2019)

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

Topic/Question	Contact	Expert Committee
VERAPAMIL HYDROCHLORIDE INJECTION	Documentary Standards Support	SM22020 Small Molecules 2

Topic/Question	Contact	Expert Committee
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 43(3)

Current DocID: GUID-E31580DD-183C-4B6C-8575-825504A42D38_4_en-US

DOI: https://doi.org/10.31003/USPNF_M88095_04_01

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