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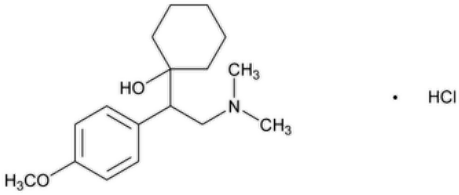
Venlafaxine Hydrochloride



$C_{17}H_{27}NO_2 \cdot HCl$ 313.86

Cyclohexanol, 1-[2-(dimethylamino)-1-(4-methoxyphenyl)ethyl]-, hydrochloride;

(±)-1-[α-[(Dimethylamino)methyl]-*p*-methoxybenzyl]cyclohexanol hydrochloride CAS RN®: 99300-78-4; UNII: 7D7RX5A8MO.

DEFINITION

Venlafaxine Hydrochloride contains NLT 98.0% and NMT 102.0% of venlafaxine hydrochloride ($C_{17}H_{27}NO_2 \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

Change to read:

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

[Note—If the spectra obtained in the solid state show differences, dissolve the substance to be examined and the Reference Standard separately in methanol or 2-propanol, evaporate to dryness, and record the new spectra of the residues.]

• **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, *Chloride*⟨191⟩:** Meets the requirements

ASSAY

• **Procedure**

Solution A: Phosphoric acid and water (1:10)

Buffer: 3.4 g of monobasic potassium phosphate in 700 mL of water. Adjust with *Solution A* to a pH of 3.0.

Diluent: Acetonitrile and water (50:50)

Mobile phase: Acetonitrile and *Buffer* (30:70)

Standard solution: 0.04 mg/mL of USP Venlafaxine Hydrochloride RS in *Diluent*

Sample solution: 0.04 mg/mL of Venlafaxine Hydrochloride in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 225 nm

Column: 4.6-mm × 25-cm; 5-µm packing L7

Column temperature: 30 ± 2°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

Run time: 2 times the retention time of the venlafaxine peak

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 venlafaxine hydrochloride ($C_{17}H_{27}NO_2 \cdot HCl$) in the portion of Venlafaxine Hydrochloride taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Organic Impurities**

Buffer and **Mobile phase:** Proceed as directed in the *Assay*.

System suitability solution: 0.5 mg/mL of USP Venlafaxine Hydrochloride RS and 1.5 µg/mL of USP Venlafaxine Related Compound A RS in *Mobile phase*

Standard solution: 0.001 mg/mL of USP Venlafaxine Hydrochloride RS in *Mobile phase*

Sample solution: 1 mg/mL of Venlafaxine Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 225 nm

Column: 4.6-mm × 25-cm; 5-µm packing L7

Column temperature: 30 ± 2°

Flow rate: 0.7 mL/min

Injection volume: 10 µL

Run time: 7 times the retention time of the venlafaxine peak

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 1.5 between venlafaxine and venlafaxine related compound A

Relative standard deviation: NMT 2.0% for the venlafaxine peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any individual impurity in the portion of Venlafaxine Hydrochloride taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each individual impurity from the *Sample solution*

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

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

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

F = relative response factor for the corresponding impurity peak (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Descyclohexanol venlafaxine[a]	0.6	1.3	0.15
Didesmethyl venlafaxine[b]	0.8	1.0	0.15
Venlafaxine related compound A	0.9	1.0	0.15
Venlafaxine	1.0	—	—
Deoxy venlafaxine[c]	3.1	0.75	0.15
Any individual unknown impurity	—	1.0	0.10
Total impurities	—	—	0.5

[a] 2-(4-Methoxyphenyl)-*N*,*N*-dimethylethylamine.

[b] 1-[2-Amino-1-(4-methoxyphenyl)ethyl]cyclohexanol.

[c] 2-Cyclohexyl-2-(4-methoxyphenyl)-*N*,*N*-dimethylethylamine.

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry under vacuum at 105° for 3 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers, and store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Venlafaxine Hydrochloride RS

USP Venlafaxine Related Compound A RS

1-(1-(4-Methoxyphenyl)-2-(methylamino)ethyl)cyclohexanol hydrochloride.

$C_{16}H_{25}NO_2 \cdot HCl$ 299.84

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

Topic/Question	Contact	Expert Committee
VENLAFAXINE HYDROCHLORIDE	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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