Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-Aug-2017
Document Type: USP Monographs
DocId: GUID-08AEA603-DADB-46C9-B932-B0C7103FC807_1_en-US
DOI: https://doi.org/10.31003/USPNF_M88083_01_01
DOI Ref: 8u60p



# Venlafaxine Tablets

**DEFINITION**

Venlafaxine Tablets contain an amount of venlafaxine hydrochloride equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of venlafaxine free base ($C_{17}H_{27}NO_2$).

**IDENTIFICATION**

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

**Buffer:** 3.4 g of potassium dihydrogen phosphate in 700 mL of water. Add 5 mL of triethylamine, and adjust with phosphoric acid to a pH of 3.0.

**Diluent:** Methanol and 0.1 N hydrochloric acid (80:20)

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

**Standard solution:** 0.3 mg/mL of venlafaxine free base from a suitable quantity of USP Venlafaxine Hydrochloride RS in *Diluent*

**Sample solution:** Nominally 0.3 mg/mL of venlafaxine (from NLT 20 finely powdered Tablets) in *Diluent*. Sonicate for 30 min. Centrifuge and pass a portion of the supernatant through a suitable membrane filter of 0.45-µm pore size. [Note—A centrifuge speed of 4000 rpm for 10 min may be suitable.]

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 275 nm. For *Identification A*, use a diode array detector in the range of 200–400 nm.

**Column:** 4.6-mm × 25-cm; 5-µm packing L1

**Flow rate:** 1.0 mL/min

**Injection volume:** 10 µL

**Run time:** 5 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 the labeled amount of venlafaxine free base ($C_{17}H_{27}NO_2$) in the portion of Tablets 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 venlafaxine free base in the *Standard solution* (mg/mL)

$C_U$ = nominal concentration of venlafaxine in the *Sample solution* (mg/mL)

**Acceptance criteria:** 90.0%–110.0% of the labeled amount of venlafaxine free base ($C_{17}H_{27}NO_2$)

 

**PERFORMANCE TESTS**

• **Dissolution ⟨711⟩**

**Medium:** Water, deaerated; 900 mL

**Apparatus 2:** 50 rpm

**Time:** 30 min

**Standard stock solution:** 0.84 mg/mL of venlafaxine free base from a suitable quantity of USP Venlafaxine Hydrochloride RS in methanol

**Standard solution:** (*L*/1000) mg/mL of venlafaxine free base in *Medium*, where *L* is the label claim in mg/Tablet, from the *Standard stock solution*

**Sample solution:** Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

**Detector:** UV 275 nm

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of venlafaxine free base ($C_{17}H_{27}NO_2$) dissolved:

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times V \times 100$$

$A_U$ = absorbance of the *Sample solution*

$A_S$ = absorbance of the *Standard solution*

$C_S$ = concentration of venlafaxine free base in the *Standard solution* (mg/mL)

$L$ = label claim (mg/Tablet)

$V$ = volume of *Medium*, 900 mL

**Tolerances:** NLT 80% (*Q*) of the labeled amount of venlafaxine free base ($C_{17}H_{27}NO_2$) is dissolved.

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

**IMPURITIES**

• **Organic Impurities**

**Buffer:** Prepare as directed in the *Assay*.

**Solution A:** Acetonitrile and *Buffer* (20:80)

**Solution B:** Acetonitrile and *Buffer* (35:65)

**Diluent:** Acetonitrile and *Buffer* (30:70)

**Mobile phase:** See *Table 1*.

**Table 1**

| Time (min) | Solution A (%) | Solution B (%) |
|---|---|---|
| 0 | 100 | 0 |
| 5 | 100 | 0 |
| 25 | 0 | 100 |
| 30 | 0 | 100 |
| 32 | 100 | 0 |
| 45 | 100 | 0 |

**System suitability solution:** 0.0018 mg/mL of USP Venlafaxine Related Compound A RS and 0.6 mg/mL of USP Venlafaxine Hydrochloride RS in *Diluent*

**Standard stock solution:** 0.6 mg/mL of USP Venlafaxine Hydrochloride RS in *Diluent*

**Standard solution:** 0.0018 mg/mL of USP Venlafaxine Hydrochloride RS in *Diluent* from the *Standard stock solution*

**Sample solution:** Nominally 0.6 mg/mL of venlafaxine (from NLT 20 finely powdered Tablets) in *Diluent*. Centrifuge and pass a portion through a suitable membrane filter of 0.45-µm pore size. [Note—Sonicate, if necessary. A centrifuge speed of 4000 rpm for 10 min may be

 

suitable.]

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 225 nm

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

**Flow rate:** 1.0 mL/min

**Injection volume:** 20 µL

**System suitability**

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

**Suitability requirements**

**Resolution:** NLT 1.5 between venlafaxine related compound A and venlafaxine, *System suitability solution*

**Tailing factor:** NMT 1.8, *Standard solution*

**Relative standard deviation:** NMT 10.0%, *Standard solution*

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of each individual degradation product in the portion of Tablets taken:

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

$r_U$ = peak response of each individual degradation product 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)

$C_U$ = nominal concentration of venlafaxine in the *Sample solution* (mg/mL)

$M_{r1}$ = molecular weight of venlafaxine, 277.40

$M_{r2}$ = molecular weight of venlafaxine hydrochloride, 313.86

$F$ = relative response factor (see *Table 2*)

**Acceptance criteria:** See *Table 2*.

**Table 2**

| Name | Relative Retention Time | Relative Response Factor | Acceptance Criteria, NMT (%) |
|---|---|---|---|
| Descyclohexanol venlafaxine[a] | 0.4 | 1.3 | 0.20 |
| Venlafaxine related compound A[b] | 0.9 | — | — |
| Venlafaxine | 1.0 | — | — |
| Any unspecified degradation product | — | 1.0 | 0.20 |
| Total degradation products | — | — | 1.0 |

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

[b] Process impurity, included for system suitability and identification only. Controlled in the drug substance and is not to be reported or included in the total degradation products for the drug product.

 

**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 TABLETS | Documentary Standards Support | SM42020 Small Molecules 4 |
| REFERENCE STANDARD SUPPORT | RS Technical Services<br>RSTECH@usp.org | SM42020 Small Molecules 4 |

**Chromatographic Database Information:** Chromatographic Database

**Most Recently Appeared In:**
Pharmacopeial Forum: Volume No. PF 42(3)

**Current DocID: GUID-08AEA603-DADB-46C9-B932-B0C7103FC807_1_en-US**

**DOI: https://doi.org/10.31003/USPNF_M88083_01_01**

**DOI ref: 8u60p**