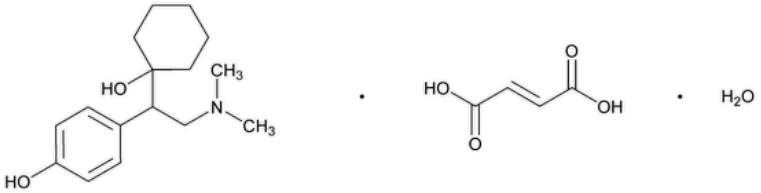
Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-Oct-2020
Document Type: USP Monographs
DocId: GUID-8F5A1E50-7626-424D-93E0-AC3334DEB615_3_en-US
DOI: https://doi.org/10.31003/USPNF_M9218_03_01
DOI Ref: rw68b

Desvenlafaxine Fumarate



$C_{16}H_{25}NO_2 \cdot C_4H_4O_4 \cdot H_2O$ 397.46
$C_{16}H_{25}NO_2 \cdot C_4H_4O_4$ 379.45

trans-Butenedioic acid, compound with 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]phenol (1:1), monohydrate;
1-[2-(Dimethylamino)-1-(4-hydroxyphenyl)ethyl]cyclohexanol hydrogen (*E*)-but-2-enedioate monohydrate CAS RN®: 313471-75-9; UNII: R5JHD7L72A.

Anhydrous CAS RN®: 93414-04-1; UNII: ATX24E9M6L.

DEFINITION

Desvenlafaxine Fumarate contains NLT 98.0% and NMT 102.0% of desvenlafaxine fumarate ($C_{16}H_{25}NO_2 \cdot C_4H_4O_4$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

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

• **B.** The retention times of the desvenlafaxine and fumaric acid peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Buffer: To each liter of water, add 1 mL of triethylamine and adjust with phosphoric acid to a pH of 3.0.

Solution A: Acetonitrile and *Buffer* (10:90)

Solution B: Acetonitrile and *Buffer* (60:40)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	80	20
4	70	30
4.1	10	90
4.5	10	90
4.6	80	20
7	80	20

Diluent: *Solution A* and *Solution B* (50:50)

Standard solution: 0.05 mg/mL of USP Desvenlafaxine Fumarate RS in *Diluent.* Sonication may be used to promote dissolution.

Sample solution: 0.05 mg/mL of Desvenlafaxine Fumarate in *Diluent.* Sonication may be used to promote dissolution.

Chromatographic system

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

Mode: LC

Detector: UV 225 nm

Column: 2.1-mm × 15-cm; 1.7-µm packing L1

Column temperature: 55°

Flow rate: 0.3 mL/min

Injection volume: 1 µL

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for fumaric acid and desvenlafaxine are 0.48 and 1.0, respectively.]

Suitability requirements

Tailing factor: NMT 2.5

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of desvenlafaxine fumarate ($C_{16}H_{25}NO_2 \cdot C_4H_4O_4$) in the portion of Desvenlafaxine Fumarate taken:

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

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

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

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

C_U = concentration of Desvenlafaxine Fumarate in the *Sample solution* (mg/mL)

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

IMPURITIES

- **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.1%
- **ORGANIC IMPURITIES**

Buffer, Solution A, Solution B, Diluent, and **Chromatographic system:** Proceed as directed in the *Assay*.

Mobile phase: See *Table 2*.

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	95	5
5	90	10
15	55	45
27	50	50
27.1	95	5
30	95	5

System suitability solution: 1 mg/mL of USP Desvenlafaxine Fumarate RS and 0.0015 mg/mL of USP Desvenlafaxine Related Compound B RS in *Diluent*

Sensitivity solution: 0.5 µg/mL of USP Desvenlafaxine Fumarate RS, equivalent to 0.3 µg/mL of desvenlafaxine, in *Diluent*

Standard solution: 0.001 mg/mL of USP Desvenlafaxine Fumarate RS, equivalent to 0.0006 mg/mL of desvenlafaxine, in *Diluent*

Sample solution: 1 mg/mL of Desvenlafaxine Fumarate in *Diluent*

System suitability

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

[NOTE—See *Table 3* for the relative retention times.]

Suitability requirements

Resolution: NLT 0.8 between desvenlafaxine related compound B and desvenlafaxine, *System suitability solution*

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

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Desvenlafaxine Fumarate taken:

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

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

r_S = peak response of desvenlafaxine fumarate from the *Standard solution*

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

C_U = concentration of Desvenlafaxine Fumarate in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 3*)

Acceptance criteria: See *Table 3*. The reporting threshold is 0.05%.

Table 3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Fumaric acid[a]	0.28	—	—
Desvenlafaxine related compound B	0.95	1.2	0.15
Desvenlafaxine	1.0	—	—
Desvenlafaxine benzyl ether[b]	4.9	1.7	0.15
Any individual unspecified impurity	—	1.0	0.10
Total impurities	—	—	1.0

[a] Included for identification only. This peak is due to the fumarate counterion; hence it is not an impurity.

[b] 1-{1-[4-(Benzyloxy)phenyl]-2-(dimethylamino)ethyl}cyclohexan-1-ol.

SPECIFIC TESTS

- **OPTICAL ROTATION** ⟨781S⟩, *Procedures, Specific Rotation*

Sample solution: 10 mg/mL of Desvenlafaxine Fumarate in methanol

Acceptance criteria: −0.5° to 0.5° on the anhydrous basis

- **pH** ⟨791⟩

Sample solution: 10 mg/mL of Desvenlafaxine Fumarate in water

Acceptance criteria: 3.0–5.0

- **WATER DETERMINATION** ⟨921⟩, *Method I*: 4.0%–6.0%

ADDITIONAL REQUIREMENTS

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

USP Desvenlafaxine Fumarate RS

USP Desvenlafaxine Related Compound B RS

4-[1-(1-Hydroxycyclohexyl)-2-(methylamino)ethyl]phenol.

$C_{15}H_{23}NO_2$ 249.35

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

Topic/Question	Contact	Expert Committee
DESVENLAFAXINE FUMARATE	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 43(5)

Current DocID: GUID-8F5A1E50-7626-424D-93E0-AC3334DEB615_3_en-US

DOI: https://doi.org/10.31003/USPNF_M9218_03_01

DOI ref: rw68b