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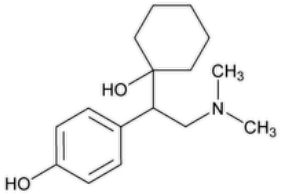
Desvenlafaxine



$C_{16}H_{25}NO_2$ 263.38

4-[2-(Dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]phenol;

1-[2-(Dimethylamino)-1-(4-hydroxyphenyl)ethyl]cyclohexanol CAS RN®: 93413-62-8; UNII: NG99554ANW.

DEFINITION

Desvenlafaxine contains NLT 98.0% and NMT 102.0% of desvenlafaxine ($C_{16}H_{25}NO_2$), calculated on the dried basis.

IDENTIFICATION

Change to read:

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

• **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**

Solution A: 4 g/L of ammonium bicarbonate in water adjusted with phosphoric acid to a pH of 7.0

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	55	45
25	35	65
30	35	65
32	55	45
40	55	45

Diluent: Acetonitrile and water (90:10)

System suitability solution: 0.701 mg/mL of USP Desvenlafaxine RS, 0.001 mg/mL of USP Desvenlafaxine Related Compound A RS, and 0.0035 mg/mL of USP Venlafaxine Hydrochloride RS in *Diluent*

Standard solution: 0.7 mg/mL of USP Desvenlafaxine RS in *Diluent*

Sample solution: 0.7 mg/mL of Desvenlafaxine in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 226 nm

Column: 4.6-mm x 25-cm; 5.0-µm packing L1

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

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

[NOTE—See *Table 2* for the relative retention times.]

Suitability requirements

Resolution: NLT 3.5 between desvenlafaxine related compound A and venlafaxine, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of desvenlafaxine ($C_{16}H_{25}NO_2$) in the portion of Desvenlafaxine 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 Desvenlafaxine RS in the *Standard solution* (mg/mL)

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

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

IMPURITIES

- **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.20%
- **ORGANIC IMPURITIES**

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

Standard solution: 0.0007 mg/mL of USP Desvenlafaxine RS, 0.001 mg/mL of USP Desvenlafaxine Related Compound A RS, and 0.0011 mg/mL of USP Venlafaxine Hydrochloride RS (equivalent to 0.001 mg/mL of venlafaxine) in *Diluent*

Sensitivity solution: 0.35 µg/mL of USP Desvenlafaxine RS from the *Standard solution* in *Diluent*

System suitability

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

[NOTE—See *Table 2* for the relative retention times.]

Suitability requirements

Resolution: NLT 3.5 between desvenlafaxine related compound A and venlafaxine, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

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

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of desvenlafaxine related compound A in the portion of Desvenlafaxine taken:

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

r_U = peak response of desvenlafaxine related compound A from the *Sample solution*

r_S = peak response of desvenlafaxine related compound A from the *Standard solution*

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

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

Calculate the percentage of venlafaxine in the portion of Desvenlafaxine taken:

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

r_U = peak response of venlafaxine 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 Desvenlafaxine in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of venlafaxine, 277.40

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

Calculate the percentage of any individual impurity in the portion of Desvenlafaxine taken:

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

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

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

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

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

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Desvenlafaxine	1.0	—
Desvenlafaxine related compound A	1.8	0.15
Venlafaxine	2.4	0.15
Any individual unspecified impurity	—	0.10
Total impurities	—	0.50

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Analysis: Dry at 105° for 3 h.

Acceptance criteria: NMT 0.50%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

• **USP Reference Standards ⟨11⟩**

USP Desvenlafaxine RS

USP Desvenlafaxine Related Compound A RS

4-[1-(Cyclohex-1-en-1-yl)-2-(dimethylamino)ethyl]phenol.

$C_{16}H_{23}NO$ 245.37

USP Venlafaxine Hydrochloride RS

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

Chromatographic Database Information: Chromatographic Database

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