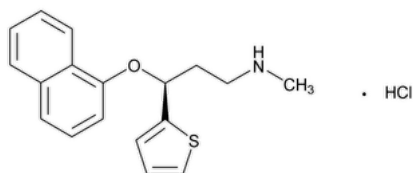


Status: Currently Official on 14-Feb-2025
 Official Date: Official as of 01-May-2020
 Document Type: USP Monographs
 DocId: GUID-A8F4DC04-4A9B-44AC-B844-897E2C0AB351_4_en-US
 DOI: https://doi.org/10.31003/USPNF_M3729_04_01
 DOI Ref: wa6hp

© 2025 USPC
 Do not distribute

Duloxetine Hydrochloride



$C_{18}H_{19}NOS \cdot HCl$ 333.88

2-Thiophenepropanamine, *N*-methyl-γ-(1-naphthalenyloxy)-, hydrochloride, (S)-;

(+)-(S)-*N*-Methyl-γ-(1-naphthoxy)-2-thiophenepropylamine hydrochloride CAS RN®: 136434-34-9; UNII: 9044SC542W.

DEFINITION

Duloxetine Hydrochloride contains NLT 97.0% and NMT 102.0% of duloxetine hydrochloride ($C_{18}H_{19}NOS \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

Change to read:

- **A.** [▲ SPECTROSCOPIC IDENTIFICATION TESTS \(197\), Infrared Spectroscopy: 197K ▲](#) (CN 1-MAY-2020)
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the duloxetine S-isomer from the *System suitability solution* in the test for *Limit of Duloxetine Related Compound A*.
- **C.** [IDENTIFICATION TESTS—GENERAL, Chloride\(191\)](#)
Sample solution: 5 mg/mL in methanol
Acceptance criteria: Meets the requirements

ASSAY

• PROCEDURE

Protect solutions of duloxetine from light.

Buffer: 2.9 g/L of phosphoric acid in water. Adjust with sodium hydroxide solution to a pH of 2.5. To each L of this solution add 10.3 g of sodium 1-hexanesulfonate monohydrate, and dissolve.

Mobile phase: Acetonitrile, *n*-propanol, and *Buffer* (13:17:70)

Diluent: Acetonitrile and water (25:75)

System suitability solution: 0.2 mg/mL of [USP Duloxetine Hydrochloride RS](#) (contains duloxetine related compound F) in *Mobile phase*. Heat the solution to at least 40° for a minimum of 1 h. [NOTE—The resulting solution contains duloxetine alcohol, duloxetine 4-naphthyl isomer, α-naphthol, duloxetine β-naphthol-1-yl isomer, and duloxetine related compound F.]

Standard solution: 0.1 mg/mL of [USP Duloxetine Hydrochloride RS](#) in *Diluent*

Sample solution: 0.1 mg/mL of Duloxetine Hydrochloride in *Diluent*

Chromatographic system

(See [Chromatography \(621\), System Suitability.](#))

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 15-cm; 3.5-μm packing L7

Column temperature: 40 ± 3°

Flow rate: 1 mL/min

Injection volume: 10 μL

Run time: 2 times the retention time of duloxetine

System suitability

Sample: *System suitability solution*

[NOTE—See [Table 1](#) for the relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between duloxetine and duloxetine related compound F

Tailing factor: NMT 1.5 for duloxetine

Relative standard deviation: NMT 1.0% for duloxetine

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of duloxetine hydrochloride ($C_{18}H_{19}NOS \cdot HCl$) in the portion of sample 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 Duloxetine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

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

Acceptance criteria: 97.0%–102.0% on the dried basis

IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#): NMT 0.2%

• **ORGANIC IMPURITIES**

Protect solutions of duloxetine from light.

Buffer, Mobile phase, Diluent, and System suitability solution: Proceed as directed in the Assay.

Sensitivity solution: 0.2 µg/mL of [USP Duloxetine Hydrochloride RS](#) in *Diluent*

Sample solution: 0.2 mg/mL of Duloxetine Hydrochloride in *Diluent*

Chromatographic system: Proceed as directed in the Assay, except for *Run time*.

Run time: 2.4 times the retention time of duloxetine

System suitability

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

[NOTE—See [Table 1](#) for the relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between duloxetine 4-naphthyl isomer and α-naphthol; NLT 1.5 between duloxetine and duloxetine related compound F, *System suitability solution*

Tailing factor: NMT 1.5 for duloxetine, *System suitability solution*

Relative standard deviation: NMT 1.0% for duloxetine, *System suitability solution*

Signal-to-noise ratio: NLT 20 for the duloxetine peak, *Sensitivity solution*

Analysis

Sample: *Sample solution*

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

$$\text{Result} = (r_U/r_T) \times (1/F) \times 100$$

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

r_T = sum of the responses of all the peaks from the *Sample solution*

F = relative response factor (see [Table 1](#))

Acceptance criteria: See [Table 1](#).

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Duloxetine alcohol ^a	0.15	0.36	0.1
Duloxetine 4-naphthyl isomer ^b	0.43	1.0	0.1
α-Naphthol ^c	0.48	1.8	0.1
Duloxetine β-naphthol-1-yl isomer ^d	0.74	1.0	0.1
Duloxetine	1.0	—	



Documents

Document Sharing Hub