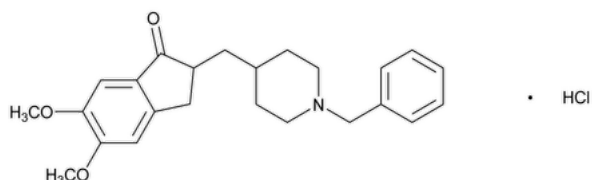


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Donepezil Hydrochloride



$C_{24}H_{29}NO_3 \cdot HCl$ 415.95

$C_{24}H_{29}NO_3 \cdot HCl \cdot H_2O$ 433.97

5,6-Dimethoxyindan-1-one, 2-[(1-benzyl-4-piperidyl)methyl]-, (±)-, hydrochloride;

(±)-2-[(1-Benzyl-4-piperidyl)methyl]-5,6-dimethoxy-1-indanone hydrochloride CAS RN[®]: 120011-70-3; UNII: 3O2T2PJ89D.

Monohydrate CAS RN[®]: 884740-09-4.

DEFINITION

Donepezil Hydrochloride contains NLT 98.0% and NMT 102.0% of donepezil hydrochloride ($C_{24}H_{29}NO_3 \cdot HCl$), calculated on the anhydrous 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 [USP Donepezil Hydrochloride RS](#) separately in dichloromethane, evaporate to dryness, and record new spectra using 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 \(191\)](#)

Sample solution: 10 mg/mL

Acceptance criteria: Meets the requirements

ASSAY

PROCEDURE

Buffer: 3.9 g/L of sodium 1-decane sulfonate in water

Mobile phase: Acetonitrile and *Buffer* (35:65). Adjust with perchloric acid to a pH of 1.8.

System suitability solution: 0.4 mg/mL of [USP Donepezil Hydrochloride RS](#) and 0.016 mg/mL of [USP Donepezil Related Compound A RS](#) prepared as follows. Dissolve suitable quantities of [USP Donepezil Hydrochloride RS](#) and [USP Donepezil Related Compound A RS](#) using 40% of the flask volume of methanol, and dilute with water to volume.

Standard solution: 0.4 mg/mL of [USP Donepezil Hydrochloride RS](#) in *Mobile phase*

Sample solution: 0.4 mg/mL of Donepezil Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 271 nm

Column: 4.6-mm × 15-cm; 5-μm packing L1

Column temperature: 35°

Flow rate: 1.4 mL/min

Injection volume: 20 μL

System suitability

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

[NOTE—Refer to [Table 1](#) under *Organic Impurities, Procedure 1* for the relative retention times.]

Suitability requirements

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

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of donepezil hydrochloride ($C_{24}H_{29}NO_3 \cdot HCl$) in the portion of Donepezil Hydrochloride taken:

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

r_U = peak response of donepezil hydrochloride from the *Sample solution*

r_S = peak response of donepezil hydrochloride from the *Standard solution*

C_S = concentration of [USP Donepezil Hydrochloride RS](#) in the *Standard solution* (mg/mL)

C_U = concentration of Donepezil Hydrochloride 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, PROCEDURE 1**

[NOTE—On the basis of the synthetic route, perform either *Procedure 1* or *Procedure 2*. *Procedure 2* is recommended if any of the impurities included in [Table 3](#) are potential related compounds.]

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

Standard solution: 0.8 µg/mL of [USP Donepezil Hydrochloride RS](#) in *Mobile phase*

System suitability

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

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

Suitability requirements

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

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

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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

r_S = peak response of donepezil hydrochloride from the *Standard solution*

C_S = concentration of [USP Donepezil Hydrochloride RS](#) in the *Standard solution* (mg/mL)

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

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

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Desbenzyl donepezil ^a	0.33	0.2
Hydroxydonepezil ^b	0.54	0.2
Donepezil related compound A ^c	0.92	0.1
Donepezil hydrochloride	1.0	—
Any individual unspecified impurity	—	0.1
Total impurities	—	1.0

^a 5,6-Dimethoxy-2-(piperidin-4-ylmethyl)indan-1-one.

^b 2-[(1-Benzylpiperidin-4-yl)(hydroxy)methyl]-5,6-dimethoxyindan-1-one.

^c (E)-2-[(1-Benzylpiperidin-4-yl)methylene]-5,6-dimethoxyindan-1-one.

• **ORGANIC IMPURITIES, PROCEDURE 2**