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Donepezil Hydrochloride Orally Disintegrating Tablets

DEFINITION

Donepezil Hydrochloride Orally Disintegrating Tablets contains NLT 93.0% and NMT 107.0% of the labeled amount of donepezil hydrochloride ($C_{24}H_{29}NO_3 \cdot HCl$).

IDENTIFICATION

Change to read:

• **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: **197U**▲ (CN 1-May-2020)

Sample solution: Crush a suitable number of Tablets, and transfer an amount of powder, equivalent to 10 mg of donepezil hydrochloride, to a 100-mL volumetric flask. Add 80 mL of 0.1 N hydrochloric acid, and sonicate for 5 min. Cool to room temperature, and dilute with 0.1 N hydrochloric acid to volume. Transfer a portion to a centrifuge tube, and centrifuge for 15 min. Transfer 5 mL of the clear supernatant to a 25-mL volumetric flask, and dilute with 0.1 N hydrochloric acid to volume.

Analysis

Wavelength range: 220–360 nm

Acceptance criteria: 230, 271, and 315 nm

• **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**

Diluent: Methanol and 0.1 N hydrochloric acid (3:1)

Mobile phase: Dissolve 2.5 g of sodium decanesulfonate in 650 mL of water, and add 1.0 mL of perchloric acid and 350 mL of acetonitrile. If necessary, adjust with an additional 0.5 mL of perchloric acid to a pH of about 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 by dissolving in 40% of the flask volume of methanol and diluting with water to volume.

Standard solution: 0.4 mg/mL of USP Donepezil Hydrochloride RS in *Diluent*

Sample solution: 0.4 mg/mL of donepezil hydrochloride in *Diluent*, prepared by transferring a suitable number of Tablets to an appropriate volumetric flask containing 10 mL of 0.1 N hydrochloric acid. Shake to disintegrate the Tablets. Add 60% of the flask volume of *Diluent*, sonicate for 10 min, allow to cool to room temperature, and dilute with *Diluent* to volume.

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 size: 20 µL

System suitability

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

[Note—The relative retention times of donepezil related compound A and donepezil are about 0.92 and 1.0, respectively.]

Suitability requirements

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

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

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{24}H_{29}NO_3 \cdot HCl$ in the portion of Tablets 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 = nominal concentration of donepezil hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 93.0%–107.0%

PERFORMANCE TESTS

• **Disintegration ⟨701⟩**

Time: NMT 60 s

• **Dissolution ⟨711⟩**

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Diluent: Methanol and 0.1 N hydrochloric acid (3:1)

Mobile phase: Acetonitrile, perchloric acid, and water (350:1:650)

Standard stock solution: 1.1 mg/mL of USP Donepezil Hydrochloride RS in *Diluent*. Dilute with *Medium* to obtain a concentration of 0.11 mg/mL.

Standard solution: Dilute the *Standard stock solution* with *Medium* to obtain a concentration of L/1000 mg/mL, where L is the Tablet label claim in mg.

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

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 mL/min

Injection size: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 5000 theoretical plates

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{24}H_{29}NO_3 \cdot HCl$ dissolved.

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of 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 $C_{24}H_{29}NO_3 \cdot HCl$ is dissolved.

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

IMPURITIES

Organic Impurities

• **Procedure**

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 *Diluent*

System suitability

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

[Note—The relative retention times of donepezil related compound A and donepezil are about 0.92 and 1.0, respectively.]

Suitability requirements

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

Relative standard deviation: NMT 8.0%, *Standard solution*

Analysis

Samples: *Sample solution* and *Standard solution*.[NOTE—Identify the impurities, using the relative retention times given in *Impurity Table 1*.]

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

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

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 = nominal concentration of donepezil hydrochloride in the *Sample solution* (mg/mL)

F = relative response factor of each related compound, as listed in *Impurity Table 1*

Acceptance criteria

Individual impurities: See *Impurity Table 1*.

Impurity Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Desbenzyl donepezil[a]	0.35	1.0	0.5
Donepezil open ring[b]	0.70	0.6	0.5
Donepezil hydrochloride	1.0	—	—
Donepezil *N*-oxide[c]	1.2	1.0	0.5
Individual unspecified degradation impurity	—	—	0.2
Total impurities	—	—	1.0

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

[b] 2-(3-(1-Benzylpiperidin-4-yl)-2-oxopropyl)-4,5-dimethoxybenzoic acid.

[c] 2-[(1-Benzylpiperidin-4-yl)methyl]-5,6-dimethoxyindan-1-one *N*-oxide.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers, and store at controlled room temperature.
- **USP REFERENCE STANDARDS ⟨11⟩**

USP Donepezil Hydrochloride RS

USP Donepezil Related Compound A RS

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

$C_{24}H_{27}NO_3$ 377.48

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

Topic/Question	Contact	Expert Committee
DONEPEZIL HYDROCHLORIDE ORALLY DISINTEGRATING TABLETS	Documentary Standards Support	SM42020 Small Molecules 4
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