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Cyclobenzaprine Hydrochloride Tablets

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click https://www.uspnf.com/rb-cyclobenzaprine-hcl-tabs-20230929.

DEFINITION

Cyclobenzaprine Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of cyclobenzaprine hydrochloride ($C_{20}H_{21}N \cdot HCl$).

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197M

  Sample: Transfer an amount equivalent to 50 mg of cyclobenzaprine hydrochloride from a quantity of finely powdered Tablets to a small flask. Add 10 mL of methylene chloride, swirl to dissolve, and filter. Evaporate the clear filtrate to about 5 mL, transfer to a centrifuge tube, and add 1–2 mL of ether. Evaporate with the aid of a current of air to about 1 mL, and agitate until crystallization occurs. Wash the crystals with several portions of ether, and air-dry.

  Acceptance criteria: Meet the requirements

- **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**

  Buffer: 11.4 g/L of ammonium acetate in water. Adjust with ammonium hydroxide to a pH of 7.2.

  Mobile phase: Methanol and *Buffer* (65:35)

  Standard solution: 0.2 mg/mL of USP Cyclobenzaprine Hydrochloride RS in *Mobile phase*. Sonication may be used to aid in dissolution.

  Sample solution: Nominally 0.2 mg/mL of cyclobenzaprine hydrochloride from NLT 20 finely powdered Tablets in *Mobile phase* prepared as follows. Transfer a suitable amount of the powder to a suitable volumetric flask. Add 60% of the flask volume of *Mobile phase*, and sonicate for 30 min. Allow the solution to cool to room temperature, and then dilute with *Mobile phase* to volume. Centrifuge the solution, and use the supernatant.

  Chromatographic system

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

  Mode: LC

  Detector: UV 226 nm

  Column: 4.6-mm × 25-cm; 5-µm packing L7

  Column temperature: 30°

  Flow rate: 1 mL/min

  Injection volume: 10 µL

  System suitability

  Sample: *Standard solution*

  Suitability requirements

  Tailing factor: NMT 2.0

  Relative standard deviation: NMT 0.85%

  Analysis

  Samples: *Standard solution* and *Sample solution*

  Calculate the percentage of the labeled amount of cyclobenzaprine hydrochloride ($C_{20}H_{21}N \cdot HCl$) in the portion of Tablets taken:

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

  r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 1: 50 rpm

Time: 30 min

Sample solution: Pass a portion of the solution under test through a suitable filter, and dilute with *Medium* if necessary.

Standard solution: USP Cyclobenzaprine Hydrochloride RS in *Medium* with a concentration similar to the one expected in the *Sample solution*

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: 290 nm

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of the labeled amount of cyclobenzaprine hydrochloride ($C_{20}H_{21}N \cdot HCl$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 75% (Q) of the labeled amount of cyclobenzaprine hydrochloride ($C_{20}H_{21}N \cdot HCl$) is dissolved.

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

IMPURITIES

Change to read:

• **Organic Impurities**

Buffer and **Mobile phase:** Proceed as directed in the *Assay*.

Standard solution: 0.6 µg/mL each of USP Cyclobenzaprine Hydrochloride RS, USP Cyclobenzaprine Related Compound A RS, and USP Cyclobenzaprine Related Compound B RS in *Mobile phase*

Sample solution: Nominally 400 µg/mL of cyclobenzaprine hydrochloride from NLT 20 finely powdered Tablets in *Mobile phase* prepared as follows. Transfer a suitable amount of the powder to a suitable volumetric flask. Add 75% of the flask volume of *Mobile phase*, and sonicate for 30 min. Allow the solution to cool to room temperature, and then dilute with *Mobile phase* to volume. Centrifuge the solution, and use the supernatant.

Chromatographic system

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

Mode: LC

Detector: UV 226 nm

Column: 4.6-mm × 25-cm; 5-µm packing L7

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 3 times the retention time of cyclobenzaprine

System suitability

Sample: *Standard solution*

[NOTE—See *Table 1* for relative retention times.]

Suitability requirements

Resolution: NLT 2.0 between the cyclobenzaprine related compound A and cyclobenzaprine related compound B peaks

Relative standard deviation: NMT 2.0% for the cyclobenzaprine peak

Analysis

Sample: *Standard solution* and *Sample solution*

Calculate the percentage of any individual degradation product in the portion of Tablets taken:

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

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

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

C_S = concentration of USP Cyclobenzaprine Hydrochloride RS in the *Standard solution* (µg/mL)

C = nominal concentration of cyclobenzaprine hydrochloride in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria NMT (%)
Cyclobenzaprine related compound A[a]	0.51	—
Cyclobenzaprine related compound B[a]	0.59	—
Cyclobenzaprine *N*-oxide[b]	0.74	▲0.50▲ (RB 1-Oct-2023)
Cyclobenzaprine	1.0	—
Amitriptyline[a,c]	1.3	—
Dibenzocycloheptenone[a,d]	1.6	—
Any individual unspecified degradation product	—	0.1
Total degradation products	—	2.0

[a] Process impurity included for identification only and not included in the calculation of total degradation products.

[b] 3-(5*H*-Dibenzo[*a*,*d*]cyclohepten-5-ylidene)-*N*,*N*-dimethyl-1-propanamine *N*-oxide.

[c] 10,11-Dihydro-*N*,*N*-dimethyl-5*H*-dibenzo[*a*,*d*]cycloheptene-$\Delta^{5,\gamma}$-propylamine.

[d] Dibenzo[*a*,*d*]cyclohepten-5-one.

ADDITIONAL REQUIREMENTS

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

USP Cyclobenzaprine Hydrochloride RS

USP Cyclobenzaprine Related Compound A RS

5-[3-(Dimethylamino)propyl]-5*H*-dibenzo[*a*,*d*]-cyclohepten-5-ol.

$C_{20}H_{23}NO$ 293.40

USP Cyclobenzaprine Related Compound B RS

3-(5*H*-Dibenzo[*a*,*d*]cycloheptен-5-ylidene)-*N*-methyl-1-propanamine hydrochloride.
$C_{19}H_{19}N \cdot HCl$ 297.82

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

Topic/Question	Contact	Expert Committee
CYCLOBENZAPRINE HYDROCHLORIDE TABLETS	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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