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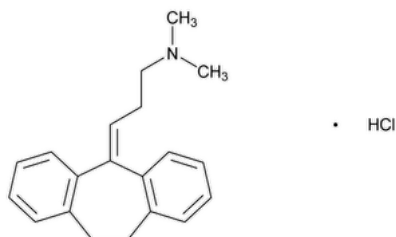
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Amitriptyline Hydrochloride

Change to read:



$C_{20}H_{23}N \cdot HCl$ $\Delta 313.87$ Δ (ERR 1-Jun-2021)

1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-dimethyl-, hydrochloride;

10,11-Dihydro-N,N-dimethyl-5H-dibenzo[a,d]cycloheptene- Δ^5 , γ -propylamine hydrochloride CAS RN[®]: 549-18-8.

DEFINITION

Amitriptyline Hydrochloride contains NLT 98.0% and NMT 102.0% of amitriptyline hydrochloride ($C_{20}H_{23}N \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS** (197), *Infrared Spectroscopy*: 197A or 197K
- **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** (191), *Chemical Identification Tests, Chloride*: Meets the requirements

ASSAY

PROCEDURE

Buffer: 1.4 g/L of [anhydrous dibasic sodium phosphate](#) in [water](#), adjusted with [1.5 M phosphoric acid TS](#) to a pH of 7.7

Mobile phase: [Methanol](#) and *Buffer* (70:30)

System suitability stock solution A: 1 mg/mL of [USP Amitriptyline Related Compound A RS](#) in [methanol](#)

System suitability stock solution B: 0.4 mg/mL of [USP Amitriptyline Hydrochloride RS](#), 0.6 mg/mL each of [USP Amitriptyline Related Compound B RS](#), [USP Cyclobenzaprine Hydrochloride RS](#), and [USP Nortriptyline Hydrochloride RS](#) in *Mobile phase*

Standard solution: 0.2 mg/mL of [USP Amitriptyline Hydrochloride RS](#) in *Mobile phase*

System suitability solution: 0.5 μ g/mL of [USP Amitriptyline Related Compound A RS](#), 1 μ g/mL of [USP Amitriptyline Hydrochloride RS](#), and 1.5 μ g/mL each of [USP Amitriptyline Related Compound B RS](#), [USP Cyclobenzaprine Hydrochloride RS](#), and [USP Nortriptyline Hydrochloride RS](#) from suitable volumes of *System suitability stock solution A* and *System suitability stock solution B* in *Mobile phase*

Sample solution: 0.2 mg/mL of Amitriptyline Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm $\times$ 25-cm; 5- μ m packing [L7](#)

Column temperature: 45°

Flow rate: 1.5 mL/min

Injection volume: 20 μ L

Run time: NLT 1.5 times the retention time of amitriptyline

System suitability

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

[NOTE—For relative retention times, see [Table 1](#).]

Suitability requirements

Resolution: NLT 1.5 between amitriptyline related compound B and nortriptyline, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of amitriptyline hydrochloride ($C_{20}H_{23}N \cdot HCl$) in the portion of Amitriptyline Hydrochloride 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 Amitriptyline Hydrochloride RS](#) in the *Standard solution* (mg/mL)

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

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

IMPURITIES

• **RESIDUE ON IGNITION (281):** NMT 0.1%

• ORGANIC IMPURITIES

Buffer, Mobile phase, and Chromatographic system: Proceed as directed in the Assay.

Sensitivity solution: 0.5 µg/mL of [USP Amitriptyline Hydrochloride RS](#) in *Mobile phase*

Standard solution: Use the *System suitability solution*, prepared as directed in the Assay.

Sample solution: 1000 µg/mL of Amitriptyline Hydrochloride in *Mobile phase*

System suitability

Samples: *Sensitivity solution* and *Standard solution*

[NOTE—For relative retention times, see [Table 1](#).]

Suitability requirements

Resolution: NLT 1.5 between amitriptyline related compound B and nortriptyline, *Standard solution*

Relative standard deviation: NMT 5.0% each for amitriptyline related compound A, amitriptyline related compound B, nortriptyline, cyclobenzaprine, and amitriptyline, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentages of amitriptyline related compound A, amitriptyline related compound B, and nortriptyline hydrochloride in the portion of Amitriptyline Hydrochloride taken:

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

r_U = peak response of amitriptyline related compound A, amitriptyline related compound B, or nortriptyline from the *Sample solution*

r_S = peak response of amitriptyline related compound A, amitriptyline related compound B, or nortriptyline from the *Standard solution*

C_S = concentration of [USP Amitriptyline Related Compound A RS](#), [USP Amitriptyline Related Compound B RS](#), or [USP Nortriptyline Hydrochloride RS](#) in the *Standard solution* (µg/mL)

C_U = concentration of Amitriptyline Hydrochloride in the *Sample solution* (µg/mL)

Calculate the percentage of cyclobenzaprine in the portion of Amitriptyline Hydrochloride taken:

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

r_U = peak response of cyclobenzaprine 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_U = concentration of Amitriptyline Hydrochloride in the *Sample solution* (µg/mL)

M_{r1} = molecular weight of cyclobenzaprine, 275.39

M_{r2} = molecular weight of cyclobenzaprine hydrochloride, 311.85

Calculate the percentage of each unspecified impurity in the portion of Amitriptyline Hydrochloride taken:

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

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

r_S = peak response of [USP Amitriptyline Hydrochloride RS](#) from the *Standard solution*

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