Status: Currently Official on 13-Feb-2025
Official Date: Official as of 26-May-2023
Document Type: USP Monographs
DocId: GUID-90EC7411-085B-407A-87C2-2FBE3333F84F_7_en-US
DOI: https://doi.org/10.31003/USPNF_M3550_07_01
DOI Ref: k1j4j

Amitriptyline Hydrochloride Tablets

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click www.uspnf.com/rb-amitriptyline-hcl-tabs-20230630.

DEFINITION

Amitriptyline Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of amitriptyline hydrochloride ($C_{20}H_{23}N \cdot HCl$).

IDENTIFICATION

- **A.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **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: 11.04 g of monobasic sodium phosphate in 900 mL of water. Adjust with phosphoric acid to a pH of 2.5 ± 0.5, and dilute to make 1000 mL.

Mobile phase: Acetonitrile and *Buffer* (42:58)

Standard solution: 0.2 mg/mL of USP Amitriptyline Hydrochloride RS in *Mobile phase*

Sample solution: Nominally 0.2 mg/mL of amitriptyline hydrochloride in *Mobile phase*, prepared as follows. Transfer NLT 20 Tablets to a suitable volumetric flask, add 50% of the flask volume of *Mobile phase*, and shake the mixture for 1 h or until the Tablets have disintegrated. Dilute with *Mobile phase* to volume, and filter. Dilute the clear filtrate with *Mobile phase* to obtain a solution with a nominal concentration of 0.2 mg/mL of amitriptyline hydrochloride.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm. For *Identification A*, use a diode array detector in the range of 220–400 nm.

Column: 3.9-mm × 30-cm; 10-µm packing L1

Flow rate: 2 mL/min

Injection volume: 20 µL

Run time: NLT 1.5 times the retention time of amitriptyline

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of amitriptyline hydrochloride ($C_{20}H_{23}N \cdot HCl$) in each Tablet 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 = nominal concentration of amitriptyline hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- **Dissolution ⟨711⟩**

▲Test 1▲ (RB 26-May-2023)

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 1: 100 rpm

Time: 45 min

Standard solution: (*L*/900) mg/mL of USP Amitriptyline Hydrochloride RS in *Medium*, where *L* is the Tablet label claim in milligrams. Dilute with *Medium*, if necessary.

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

Instrumental conditions

Analytical wavelength: UV 239 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of amitriptyline hydrochloride ($C_{20}H_{23}N \cdot HCl$) dissolved:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times D \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

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

D = dilution factor, if necessary

Tolerances: NLT 75% (*Q*) of the labeled amount of amitriptyline hydrochloride ($C_{20}H_{23}N \cdot HCl$) is dissolved.

▲**Test 2:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: 0.1 N hydrochloric acid; 500 mL, deaerated, if necessary

Apparatus 1: 100 rpm

Time: 30 min

Diluted phosphoric acid: Phosphoric acid and water (1:10)

Buffer: Dissolve 0.87 g of potassium phosphate dibasic in 1 L of water. Adjust with *Diluted phosphoric acid* to a pH of 7.0. Add 1.0 mL of triethylamine. Adjust with *Diluted phosphoric acid* to a pH of 7.0.

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

Standard solution: (*L*/500) mg/mL of USP Amitriptyline Hydrochloride RS in *Medium*, where *L* is the label claim in mg/Tablet. Sonicate to dissolve, if necessary.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first 3 mL of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

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

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 10 µL

Run time: NLT 1.5 times the retention time of amitriptyline

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of amitriptyline hydrochloride ($C_{20}H_{23}N \cdot HCl$) dissolved:

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

r_U = peak response of amitriptyline from the *Sample solution*

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

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

V = volume of the *Medium*, 500 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of amitriptyline hydrochloride ($C_{20}H_{23}N \cdot HCl$) is dissolved.▲ (RB 26-May-2023)

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

IMPURITIES

• **Organic Impurities**

Buffer: 1.42 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)

Diluent: Methanol and water (70:30)

Standard solution: 2 µg/mL each of USP Amitriptyline Hydrochloride RS, USP Amitriptyline Related Compound A RS, USP Amitriptyline Related Compound B RS, and USP Nortriptyline Hydrochloride RS in *Diluent*

Sample solution: Nominally 1000 µg/mL of amitriptyline hydrochloride in *Diluent*, prepared as follows. Transfer NLT 10 Tablets to a suitable volumetric flask, add 80% of the flask volume of *Diluent*, and shake the mixture for 1 h or until the Tablets have disintegrated. Dilute with *Diluent* to volume. If needed, a portion of this solution can be further diluted with *Diluent*. Centrifuge a portion of the solution with a nominal concentration of 1000 µg/mL of amitriptyline hydrochloride and use the supernatant. [Note—A centrifuge speed of 3000 rpm for about 10 min may be suitable.]

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

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

Column temperature: 45°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

Run time: NLT 1.5 times the retention time of amitriptyline

System suitability

Sample: *Standard solution*

[Note—For relative retention times, see *Table 1*.]

Suitability requirements

Resolution: NLT 3.0 between amitriptyline related compound B and nortriptyline

Relative standard deviation: NMT 5.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of amitriptyline related compound A, amitriptyline related compound B, and nortriptyline hydrochloride in the portion of Tablets 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 = nominal concentration of amitriptyline hydrochloride in the *Sample solution* (µg/mL)

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

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

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

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

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

C_U = nominal concentration of amitriptyline hydrochloride in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Amitriptyline related compound A	0.32	0.2
Amitriptyline related compound B	0.48	0.2
Nortriptyline	0.62	0.2
Amitriptyline	1.0	—
Any other individual degradation product	—	0.2
Total degradation products	—	1.0

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature.

Add the following:

▲• **Labeling:** When more than one *Dissolution Test* is given, the labeling states the test used only if *Test 1* is not used.▲ (RB 26-May-2023)

• **USP Reference Standards** ⟨11⟩

USP Amitriptyline Hydrochloride RS

USP Amitriptyline Related Compound A RS

10,11-Dihydro-5*H*-dibenzo[*a*,*d*]-cycloheptен-5-one;
Also known as Dibenzosuberone.
$C_{15}H_{12}O$ 208.26

USP Amitriptyline Related Compound B RS

5-[3-(Dimethylamino)propyl]-10,11-dihydro-5*H*-dibenzo[*a*,*d*]-cycloheptен-5-ol;
Also known as Amitriptynol.
$C_{20}H_{25}NO$ 295.43

USP Nortriptyline Hydrochloride RS

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 43(3)

Current DocID: GUID-90EC7411-085B-407A-87C2-2FBE3333F84F_7_en-US

DOI: https://doi.org/10.31003/USPNF_M3550_07_01

DOI ref: k1j4j