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Mexiletine Hydrochloride Capsules

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click https://www.uspnf.com/rb-mexiletine-hcl-caps-20220614.

DEFINITION

Mexiletine Hydrochloride Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of mexiletine hydrochloride ($C_{11}H_{17}NO \cdot HCl$).

IDENTIFICATION

- **A.**

Sample: Transfer an amount equivalent to 250 mg of mexiletine hydrochloride, from Capsules, to a suitable test tube. Add 10 mL of methanol, and mix on a vortex mixer for 1 min. Filter the mixture, evaporate the filtrate under a stream of nitrogen to dryness, and dry in a vacuum at 60° for 1 h. Use the dried residue.

Acceptance criteria: The IR absorption spectrum of a mineral oil dispersion of the *Sample* exhibits maxima only at the same wavelengths as that of a similar preparation of USP Mexiletine Hydrochloride RS.

- **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: Dissolve 11.5 g of anhydrous sodium acetate in 500 mL of water. Add 3.2 mL of glacial acetic acid, mix, and allow to cool. Adjust with hydrochloric acid to a pH of 4.8 ± 0.1, and dilute with water to 1000 mL.

Mobile phase: Methanol and *Buffer* (60:40)

Standard solution: 2 mg/mL of USP Mexiletine Hydrochloride RS in *Mobile phase*

System suitability solution: 1 mg/mL of 2-phenylethylamine hydrochloride in *Standard solution*

Sample solution: Nominally 2 mg/mL of mexiletine hydrochloride prepared as follows. Transfer an amount nominally equivalent to 50 mg of mexiletine hydrochloride, from combined Capsule contents (NLT 20), to a suitable container with stopper. Add 25.0 mL of *Mobile phase* and shake by mechanical means for 15 min. Centrifuge and use clear supernatant. [Note—Reserve a portion of this solution for use as the *Sample solution* in the test for *Organic Impurities*.]

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Columns

Guard: Packing L1

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

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

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

[Note—The relative retention times for 2-phenylethylamine and mexiletine are about 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 3.0 between the 2-phenylethylamine and mexiletine, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of mexiletine hydrochloride ($C_{11}H_{17}NO \cdot HCl$) in the portion of Capsules taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

Change to read:

• **Dissolution ⟨711⟩**

▲Test 1▲ (RB 1-Jul-2022)

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Analysis: Determine the percentage of mexiletine hydrochloride ($C_{11}H_{17}NO \cdot HCl$) dissolved from the difference between first derivative values at the wavelengths of maximum and minimum first derivative absorbance in the wavelength range from 230–290 nm on filtered portions of the solution under test, suitably diluted with *Medium*, if necessary, in comparison with a standard solution having a known concentration of USP Mexiletine Hydrochloride RS in the same *Medium*.

Tolerances: NLT 80% (Q) of the labeled amount of mexiletine hydrochloride ($C_{11}H_{17}NO \cdot HCl$) is dissolved.

▲Test 2

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

Medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 2: 50 rpm; with sinkers, if necessary

Time: 30 min

Buffer: 11.5 g of anhydrous sodium acetate in 500 mL of water. Add 3.2 mL of glacial acetic acid and allow to cool. Adjust with hydrochloric acid to a pH of 4.8. Dilute with water to 1 L.

Mobile phase: Methanol and *Buffer* (60:40)

Standard solution: (*L*/500) mg/mL of USP Mexiletine Hydrochloride RS in *Medium*, where *L* is the label claim in mg/Capsule

Sample solution: Pass a portion of the solution under test through a suitable filter.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

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

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 2 times the retention time of mexiletine

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 3.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of mexiletine hydrochloride ($C_{11}H_{17}NO \cdot HCl$) dissolved:

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

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

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

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

V = volume of *Medium*, 500 mL

L = label claim (mg/Capsule)

Tolerances: NLT 80% (*Q*) of the labeled amount of mexiletine hydrochloride ($C_{11}H_{17}NO \cdot HCl$) is dissolved.▲ (RB 1-Jul-2022)

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

IMPURITIES

• **Organic Impurities**

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

Standard solution: 20 µg/mL of USP Mexiletine Hydrochloride RS from the *Standard solution* in the *Assay* in *Mobile phase*

System suitability

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

[Note—The relative retention times for 2-phenylethylamine and mexiletine are about 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 3.0 between the 2-phenylethylamine and mexiletine, *System suitability solution*

Relative standard deviation: NMT 3.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Capsules taken:

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

r_U = peak response for each impurity from the *Sample solution*

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

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

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

Acceptance criteria

Any individual impurity: NMT 1%

Total impurities: NMT 1.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

Add the following:

▲• **Labeling:** The labeling states the *Dissolution* test used only if *Test 1* is not used.▲ (RB 1-Jul-2022)

• **USP Reference Standards** ⟨11⟩

USP Mexiletine Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
MEXILETINE HYDROCHLORIDE CAPSULES	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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