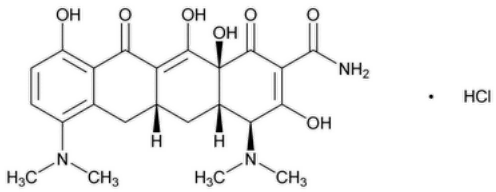
Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-F527F933-AD35-4CC7-B24C-3C754FE38BB3_5_en-US
DOI: https://doi.org/10.31003/USPNF_M54170_05_01
DOI Ref: 724ah

Minocycline Hydrochloride



$C_{23}H_{27}N_3O_7 \cdot HCl$ 493.94

2-Naphthacenecarboxamide, 4,7-bis(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,10,12,12a-tetrahydroxy-1,11dioxo-, monohydrochloride, [4*S*-(4α,4aα,5aα,12aα)]-;
4,7-Bis(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,10,12,12a-tetrahydroxy-1,11-dioxo-2-naphthacenecarboxamide monohydrochloride CAS RN®: 13614-98-7; UNII: 0020414E5U.

DEFINITION

Minocycline Hydrochloride contains the equivalent of NLT 890 µg and NMT 950 µg of minocycline ($C_{23}H_{27}N_3O_7$) per mg, calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K.▲ (CN 1-May-2020) Dry the Standard and Sample at 100° for 2 h before use.

• **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**

[Note—Protect the *Standard solution* and *Sample solution* from light, store in a refrigerator, and use within 3 h.]

Mobile phase: Dimethylformamide, tetrahydrofuran, 0.2 M ammonium oxalate, and 0.01 M edetate disodium TS (120:80:600:180). Adjust with ammonium hydroxide to a pH of 7.2.

System suitability solution: Dissolve 10 mg of USP Minocycline Hydrochloride RS in 20 mL of 0.2 M ammonium oxalate. Heat on a water bath at 60° for 3 h, allow to cool, and dilute with water to 25.0 mL.

Standard solution: Equivalent to 500 µg/mL of minocycline ($C_{23}H_{27}N_3O_7$) from USP Minocycline Hydrochloride RS in water

Sample solution: Equivalent to 500 µg/mL of minocycline ($C_{23}H_{27}N_3O_7$) from Minocycline Hydrochloride in water

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

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

[Note—The relative retention times for epiminocycline and minocycline are 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 4.6 between epiminocycline and minocycline, *System suitability solution*

Tailing factor: 0.9–2.0, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the quantity, in µg/mg, of minocycline ($C_{23}H_{27}N_3O_7$) in the portion of Minocycline Hydrochloride taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of minocycline in the *Standard solution* (µg/mL)

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

P = potency of USP Minocycline Hydrochloride RS (µg/mg)

Acceptance criteria: 890–950 µg/mg on the anhydrous basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.15%

• **Organic Impurities**

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

[Note—Protect the *Standard solution* and the *Sample solutions* from light, store in a refrigerator, and use within 3 h.]

Sample solution 1: 0.25 mg/mL of Minocycline Hydrochloride in water

Sample solution 2: 5 µg/mL of Minocycline Hydrochloride in water

Sample solution 3: 3 µg/mL of Minocycline Hydrochloride in water

Run time: 2.6 times the retention time of minocycline, *Sample solution 1*

Analysis

Samples: *Sample solution 1*, *Sample solution 2*, and *Sample solution 3*

Calculate the percentage of epiminocycline in the portion of Minocycline Hydrochloride taken:

$$\text{Result} = (r_{E1}/r_{M3}) \times D_1 \times 100$$

r_{E1} = peak response of epiminocycline from *Sample solution 1*

r_{M3} = peak response of minocycline from *Sample solution 3*

D_1 = dilution factor for *Sample solution 3*

Calculate the total percentage of impurities other than epiminocycline in the portion of Minocycline Hydrochloride taken:

$$\text{Result} = (r_T/r_{M2}) \times D_2 \times 100$$

r_T = sum of the peak responses of all impurities other than epiminocycline from *Sample solution 1*

r_{M2} = peak response of minocycline from *Sample solution 2*

D_2 = dilution factor for *Sample solution 2*

Acceptance criteria

Individual impurities: NMT 1.2% epiminocycline

Total impurities (excluding epiminocycline): NMT 2.0%

SPECIFIC TESTS

• **Crystallinity ⟨695⟩:** Meets the requirements

• **pH ⟨791⟩**

Sample: 10 mg/mL of minocycline in solution

Acceptance criteria: 3.5–4.5

• **Water Determination ⟨921⟩, *Method I*:** 4.3%–8.0%

• **Sterility Tests ⟨71⟩:** Where the label states that Minocycline Hydrochloride is sterile, it meets the requirements.

• **Bacterial Endotoxins Test ⟨85⟩:** Where the label states that Minocycline Hydrochloride is sterile or must be subjected to further processing during the preparation of injectable dosage forms, it contains NMT 1.25 USP Endotoxin Units/mg of minocycline.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, protected from light.

• **Labeling:** Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms.

• **USP Reference Standards ⟨11⟩**

USP Minocycline Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
MINOCYCLINE HYDROCHLORIDE	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 43(2)

Current DocID: GUID-F527F933-AD35-4CC7-B24C-3C754FE38BB3_5_en-US

DOI: https://doi.org/10.31003/USPNF_M54170_05_01

DOI ref: 724ah