Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-BE09CDF5-9F23-41EC-9856-7C88487236E2_2_en-US
DOI: https://doi.org/10.31003/USPNF_M49800_02_01
DOI Ref: g2hwl

Metformin Hydrochloride Tablets

DEFINITION

Metformin Hydrochloride Tablets contain NLT 95.0% and NMT 105.0% of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$).

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

Sample: Transfer an amount of powdered Tablets, equivalent to 20 mg of metformin hydrochloride, to a suitable flask. Add 20 mL of dehydrated alcohol, and shake. Filter, evaporate the filtrate on a water bath to dryness, and dry the residue at 105° for 2 h.

Acceptance criteria: Meet the requirements

• **B.**

Solution A: Dissolve 1 g of 1-naphthol in a solution containing 6 g of sodium hydroxide and 16 g of anhydrous sodium carbonate in 100 mL of water.

Sample solution: Triturate an amount of powdered Tablets, equivalent of 50 mg of metformin hydrochloride, with 10 mL of water, filter, and use the filtrate.

Analysis: To 5 mL of the *Sample solution* add 1.5 mL of 5 N sodium hydroxide solution and 1 mL of *Solution A*. Add 0.5 mL of sodium hypochlorite TS, dropwise, and with shaking.

Acceptance criteria: An orange-red color is produced that darkens on standing.

• **C. Identification Tests—General, *Chloride*⟨191⟩**

Sample solution: Prepare as directed for the *Sample solution* in *Identification* test *B*.

Acceptance criteria: Meet the requirements

ASSAY

• **Procedure**

Standard solution: 10 µg/mL of USP Metformin Hydrochloride RS in water

Sample solution: Weigh and finely powder NLT 20 Tablets. Transfer the amount of powder, equivalent to 100 mg of metformin hydrochloride, to a 100-mL volumetric flask. Add 70 mL of water, shake by mechanical means for 15 min, dilute with water to volume, and filter, discarding the first 20 mL of the filtrate. Dilute 10.0 mL of the filtrate with water to 100.0 mL, and dilute 10.0 mL of the resulting solution with water to 100.0 mL. The nominal concentration of this solution is 10 µg/mL.

Instrumental conditions

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

Mode: UV

Analytical wavelength: Wavelength of maximum absorbance at about 232 nm

Cell: 1 cm

Blank: Water

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) in the portion of the Tablets taken:

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

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

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

Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Test 1

Medium: pH 6.8 phosphate buffer; 1000 mL

Apparatus 1: 100 rpm

Time: 45 min

Standard solution: USP Metformin Hydrochloride RS in *Medium*

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

Instrumental conditions

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

Mode: UV

Analytical wavelength: Wavelength of maximum absorbance at about 233 nm

Analysis: Determine the amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) dissolved by using UV absorption of filtered portions of the *Sample solution*, suitably diluted with *Medium*, if necessary, in comparison with the *Standard solution*.

Tolerances: NLT 70% (*Q*) of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) is dissolved.

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

For products labeled to contain 500 mg of metformin hydrochloride

Medium: pH 6.8 phosphate buffer; 1000 mL

Apparatus 2: 50 rpm

Time: 30 min

Standard solution, Sample solution, Instrumental conditions, and **Analysis:** Proceed as directed in *Test 1*.

Tolerances: NLT 80% (*Q*) of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) is dissolved.

For products labeled to contain 850 or 1000 mg of metformin hydrochloride

Medium: pH 6.8 phosphate buffer; 1000 mL

Apparatus 2: 75 rpm

Time: 30 min

Standard solution, Sample solution, Instrumental conditions, and **Analysis:** Proceed as directed in *Test 1*.

Tolerances: NLT 75% (*Q*) of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) is dissolved.

Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

Medium: pH 6.8 phosphate buffer; 1000 mL

Apparatus 1: 100 rpm

Time: 60 min

Buffer: Dissolve 1.38 g of monobasic sodium phosphate in about 1800 mL of water. Add 3.484 g of 1-pentanesulfonic acid sodium salt. Adjust with diluted phosphoric acid to a pH of 3.00 ± 0.05. Dilute with water to 2000 mL.

Mobile phase: Acetonitrile and *Buffer* (1:19)

Standard stock solution: 0.25 mg/mL of USP Metformin Hydrochloride RS in *Medium*. Use sonication to dissolve.

Standard solution: 0.05 mg/mL of USP Metformin Hydrochloride RS in *Medium* from the *Standard stock solution*

Sample solution: Pass a portion of the solution under test through a nylon filter of 0.45-µm pore size. Dilute with *Medium*, if necessary, to obtain a solution with a concentration similar to that of the *Standard solution*.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

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

Flow rate: 1.0 mL/min

Injection volume: 40 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Column efficiency: NLT 1500 theoretical plates

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) dissolved:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

L = label claim (mg/Tablet)

V = volume of *Medium*, 1000 mL

D = dilution factor of the *Sample solution*

Tolerances: NLT 70% (*Q*) of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) is dissolved.

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

IMPURITIES

• **Organic Impurities**

Mobile phase: 17 g/L of monobasic ammonium phosphate in water, adjusted with phosphoric acid to a pH of 3.0

System suitability stock solution: 0.25 mg/mL of metformin hydrochloride and 0.1 mg/mL of melamine in water

System suitability solution: Transfer 1.0 mL of the *System suitability stock solution* to a 50-mL volumetric flask, and dilute with *Mobile phase* to volume.

Sample solution: Weigh and finely powder NLT 20 Tablets. Transfer the amount of powder, equivalent to 500 mg of metformin hydrochloride, to a 100-mL volumetric flask. Dissolve in *Mobile phase* with shaking, dilute with *Mobile phase* to volume, and filter.

Diluted sample solution: Nominally 0.005 mg/mL of metformin hydrochloride in *Mobile phase* from the *Sample solution*

Chromatographic system

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

Mode: LC

Detector: UV 218 nm

Column: 4.6-mm × 25-cm; packing L9

Flow rate: 1.0–1.7 mL/min

Run time: NLT twice the retention time of metformin

Injection volume: 20 µL

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 10 between melamine and metformin

Analysis

Samples: *Sample solution* and *Diluted sample solution*

Calculate the percentage of any individual impurity in the portion of the Tablets taken:

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

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

r_S = peak response of metformin from the *Diluted sample solution*

D = dilution factor for the preparation of the *Diluted sample solution*, 0.001

Acceptance criteria

Any individual impurity: NMT 0.1%

Total impurities: NMT 0.6%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers. Store at controlled room temperature.

• **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.

• **USP Reference Standards ⟨11⟩**

USP Metformin Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
METFORMIN HYDROCHLORIDE TABLETS	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 40(4)

Current DocID: GUID-BE09CDF5-9F23-41EC-9856-7C88487236E2_2_en-US

DOI: https://doi.org/10.31003/USPNF_M49800_02_01

DOI ref: g2hwl