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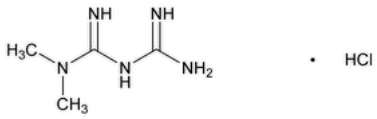
Metformin Hydrochloride



$C_4H_{11}N_5 \cdot HCl$ 165.62

Imidodicarbonimidic diamide, *N*,*N*-dimethyl-, monohydrochloride;

1,1-Dimethylbiguanide monohydrochloride CAS RN®: 1115-70-4; UNII: 786Z46389E.

DEFINITION

Change to read:

Metformin Hydrochloride contains ▲NLT 98.0% and NMT 102.0%▲ (USP 1-May-2020) of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

Change to read:

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

• **B. Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Chloride*:** Meets the requirements

Add the following:

▲• C. The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2020)

ASSAY

Change to read:

• **Procedure**

▲Buffer: 9.8 g/L of monobasic ammonium phosphate in water

Mobile phase: *Buffer* and acetonitrile (95:5). Adjust with phosphoric acid to a pH of 3.0.

Standard solution: 0.05 mg/mL of USP Metformin Hydrochloride RS in *Mobile phase*. Sonication may be used to promote dissolution. Allow the solution to equilibrate to ambient temperature.

Sample solution: 0.05 mg/mL of Metformin Hydrochloride in *Mobile phase*. Sonication may be used to promote dissolution. Allow the solution to equilibrate to ambient temperature.

[Note—Silanized HPLC vials may be used.]

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 25-cm; 10-µm packing L9

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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

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

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

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

Acceptance criteria: 98.0%–102.0% on the dried basis▲ (USP 1-May-2020)

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

Change to read:

• **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 ▲USP Metformin Hydrochloride RS▲ (USP 1-May-2020) and 0.1 mg/mL of ▲USP Melamine RS▲ (USP 1-May-2020) in water

System suitability solution: ▲5 µg/mL of USP Metformin Hydrochloride RS and 2 µg/mL of USP Melamine RS from *System suitability stock solution* in *Mobile phase*▲ (USP 1-May-2020)

Standard stock solution: 0.2 mg/mL of USP Metformin Related Compound A RS in water

Standard solution: 0.001 mg/mL of USP Metformin Related Compound A RS from *Standard stock solution* in *Mobile phase*

Sample solution: 5 mg/mL of Metformin Hydrochloride in *Mobile phase*

Diluted sample solution: 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

Injection volume: 20 µL

Run time: NLT 2 times the retention time of metformin

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 10 between melamine and metformin

Analysis

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

Calculate the percentage of metformin related compound A in the portion of Metformin Hydrochloride taken:

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

r_U = peak response of metformin related compound A from the *Sample solution*

r_S = peak response of metformin related compound A from the *Standard solution*

C_S = concentration of USP Metformin Related Compound A RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of any other impurity in the portion of Metformin Hydrochloride 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

Individual impurities: NMT 0.02% for metformin related compound A; NMT 0.1% for any other impurity

Total impurities: NMT 0.5%

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Analysis: Dry at 105° for 5 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

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

Change to read:

• **USP Reference Standards** (11)

▲ USP Melamine RS

2,4,6-Triamino-1,3,5-triazine.

$C_3H_6N_6$ 126.12▲ (USP 1-May-2020)

USP Metformin Hydrochloride RS

USP Metformin Related Compound A RS

1-Cyanoguanidine.

$C_2H_4N_4$ 84.08

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

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

Chromatographic Database Information: Chromatographic Database

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