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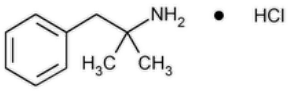
Phentermine Hydrochloride



$C_{10}H_{15}N \cdot HCl$ 185.69

Benzeneethanamine, α,α-dimethyl-, hydrochloride;

α,α-Dimethylphenethylamine hydrochloride CAS RN®: 1197-21-3; UNII: 0K2I505OTV.

Change to read:

DEFINITION

Phentermine Hydrochloride contains NLT 98.0% and NMT ▲102.0%▲ (USP 1-May-2022) of phentermine hydrochloride ($C_{10}H_{15}N \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K ▲or 197A▲ (USP 1-May-2022)

Change to read:

• **B.** ▲The retention time of the phentermine peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2022)

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

ASSAY

Change to read:

• **Procedure**

▲**Solution A:** Dissolve 2.72 g of monobasic potassium phosphate in 1000 mL of water.

Mobile phase: Methanol and *Solution A* (55:45). Adjust with 50% (v/v) phosphoric acid in water to a pH of 2.4.

Standard solution: 0.1 mg/mL of USP Phentermine Hydrochloride RS in *Mobile phase*

Sample solution: 0.1 mg/mL of Phentermine Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

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

Column temperature: 25°

Flow rate: 0.8 mL/min

Injection volume: 10 µL

Run time: NLT 8 times the retention time of phentermine

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 phentermine hydrochloride ($C_{10}H_{15}N \cdot HCl$) in the portion of Phentermine Hydrochloride taken:

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

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

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

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

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

Acceptance criteria: 98.0%–102.0% on the dried basis▲ (USP 1-May-2022)

IMPURITIES

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

Change to read:

• **Organic Impurities**

▲**Buffer:** 2 mg/mL of sodium 1-heptanesulfonate in water. Adjust with 25% (v/v) phosphoric acid in water to a pH of 2.3.

Mobile phase: Acetonitrile, methanol, and *Buffer* (20:25:55)

Diluent: Methanol and water (35:65)

Sensitivity solution: 0.5 µg/mL of USP Phentermine Hydrochloride RS in *Diluent*

Standard solution: 0.001 mg/mL each of USP Phentermine Hydrochloride RS and USP Phentermine Related Compound A RS in *Diluent*

Sample solution: 1 mg/mL of Phentermine Hydrochloride in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

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

Column temperature: 45°

Flow rate: 1.5 mL/min

Injection volume: 10 µL

Run time: NLT 10 times the retention time of phentermine

System suitability

Samples: *Sensitivity solution* and *Standard solution*

Suitability requirements

Resolution: NLT 3.0 between phentermine and phentermine related compound A, *Standard solution*

Relative standard deviation: NMT 5% for phentermine, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual impurity in the portion of Phentermine Hydrochloride taken:

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

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

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

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

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

F = relative response factor of each impurity (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Phentermine	1.0	1.0	—
Phentermine related compound A	1.4	1.5	0.15
Phentermine alcohol[a]	1.8	1.1	0.1
Phentermine related compound C[b]	—	—	0.1
Any unspecified impurity	—	1.0	0.10
Total impurities	—	—	1.0▲ (USP 1-May-2022)

[a] 2-Methyl-1-phenylpropan-2-ol.

[b] Result obtained in the test for *Limit of Phentermine Related Compound C*.

Add the following:

▲• **Limit of Phentermine Related Compound C**

Buffer: Dissolve 4.04 g of sodium 1-heptanesulfonate in 1000 mL of water. Adjust with 25% (v/v) phosphoric acid in water to a pH of 2.3.

Mobile phase: Acetonitrile, methanol, and *Buffer* (50:25:25)

Sensitivity solution: 0.2 µg/mL of USP Phentermine Related Compound C RS in methanol

Standard solution: 0.001 mg/mL of USP Phentermine Related Compound C RS in methanol

Sample solution: 1 mg/mL of Phentermine Hydrochloride in methanol

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

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

Column temperature: 45°

Flow rate: 1.2 mL/min

Injection volume: 10 µL

Run time: NLT 1.5 times the retention time of phentermine related compound C

System suitability

Samples: *Sensitivity solution* and *Standard solution*

Suitability requirements

Relative standard deviation: NMT 5%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of phentermine related compound C in the portion of Phentermine Hydrochloride taken:

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

r_U = peak response of phentermine related compound C from the *Sample solution*

r_S = peak response of phentermine related compound C from the *Standard solution*

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

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

Acceptance criteria: See *Table 1*.▲ (USP 1-May-2022)

SPECIFIC TESTS

• **Melting Range or Temperature ⟨741⟩:** 202°–205°

• **pH ⟨791⟩**

Sample solution: 20 mg/mL of Phentermine Hydrochloride in water

Acceptance criteria: 5.0–6.0

• **Loss on Drying ⟨731⟩**

Analysis: Dry at 105° for 3 h.

Acceptance criteria: NMT 2.0%

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in tight containers. ▲Store at 25°, excursions permitted between 15° and 30°.▲ (USP 1-May-2022)

Change to read:

• **USP Reference Standards ⟨11⟩**

USP Phentermine Hydrochloride RS

▲ USP Phentermine Related Compound A RS

N-(2-Methyl-1-phenylpropan-2-yl)formamide.

$C_{11}H_{15}NO$ 177.25

USP Phentermine Related Compound C RS

(2-Methylprop-1-en-1-yl)benzene.

$C_{10}H_{12}$ 132.21▲ (USP 1-May-2022)

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

Topic/Question	Contact	Expert Committee
PHENTERMINE HYDROCHLORIDE	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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