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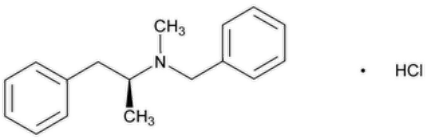
Add the following:

▲Benzphetamine Hydrochloride



$C_{17}H_{21}N \cdot HCl$ 275.82

(+)-*N*-Benzyl-*N*, α-dimethylphenethylamine hydrochloride;

(*S*)-*N*-Benzyl-*N*-methyl-1-phenylpropan-2-amine hydrochloride CAS RN®: 5411-22-3; UNII: 43DWT87QT7.

DEFINITION

Benzphetamine Hydrochloride contains NLT 98.0% and NMT 102.0% of benzphetamine hydrochloride ($C_{17}H_{21}N \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

Change to read:

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

• **B.** The retention time of the benzphetamine peak of the *Sample solution* corresponds to that of the *System suitability solution*, as obtained in the *Enantiomeric Purity* test.

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

ASSAY

• **Procedure**

Buffer: 0.01 M monobasic sodium phosphate in water

Solution A: Acetonitrile and *Buffer* (10:90)

Solution B: Acetonitrile and water (70:30)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
5	100	0
30	70	30
35	60	40
40	10	90
45	0	100
47	100	0
55	100	0

Diluent: Methanol and water (50:50)

Standard solution: 0.1 mg/mL of USP Benzphetamine Hydrochloride RS in *Diluent*

Sample solution: 0.1 mg/mL of Benzphetamine Hydrochloride in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 207 nm

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

Column temperature: 30°

Flow rate: 1.0 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.5

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of benzphetamine hydrochloride ($C_{17}H_{21}N \cdot HCl$) in the portion of Benzphetamine Hydrochloride taken:

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

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

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

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

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

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.2%
- **Organic Impurities**

Buffer, Solution A, Solution B, and **Diluent:** Prepare as directed in the *Assay*.

Mobile phase: See *Table 2*.

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	100	0
5	100	0
30	70	30
35	60	40
45	55	45
60	15	85
62	100	0
70	100	0

System suitability solution: 1 mg/mL of USP Benzphetamine Hydrochloride RS and 0.001 mg/mL each of USP Benzphetamine Related Compound E RS and USP Benzphetamine Related Compound F RS in *Diluent*

Sensitivity solution: 0.0001 mg/mL of USP Benzphetamine Hydrochloride RS in *Diluent*

Standard solution: 0.001 mg/mL of USP Benzphetamine Hydrochloride RS in *Diluent*

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

Chromatographic system: Proceed as directed in the *Assay*, except for *Injection volume*.

Injection volume: 20 µL

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between benzphetamine related compound E and benzphetamine; NLT 2.0 between benzphetamine related compound F and benzphetamine, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Benzphetamine Hydrochloride taken:

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

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

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

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

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

F = relative response factor of each individual impurity (see *Table 3*)

Acceptance criteria: See *Table 3*.

Table 3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Pseudoephedrine hydrochloride	0.22	0.62	0.10
Methamphetamine hydrochloride	0.37	0.65	0.10
Benzyl alcohol	0.57	1.18	0.10
Benzphetamine related compound E	0.87	0.93	0.10
Benzphetamine hydrochloride	1.00	1.00	—
Benzphetamine related compound F	1.11	0.50	0.10
Any other individual impurity	—	1.00	0.10
Total impurities[a]	—	—	0.5

[a] Benzphetamine related compound A monitored in the *Enantiomeric Purity* test is not included in the total impurities.

• **Limit of Benzyl Chloride**

Buffer: 0.01 M monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 3.0.

Mobile phase: Acetonitrile and *Buffer* (50:50)

Diluent: Acetonitrile and water (50:50)

Standard solution: 0.001 mg/mL of USP Benzyl Chloride RS in *Diluent*

Sample solution: 10 mg/mL of Benzphetamine Hydrochloride in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 207 nm

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

Column temperature: 30°

Flow rate: 1.0 mL/min

Injection volume: 20 µL

Run time: NLT 1.4 times the retention time of benzyl chloride

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 5.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of benzyl chloride in the portion of Benzphetamine Hydrochloride taken:

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

r_U = peak response of benzyl chloride from the *Sample solution*

r_S = peak response of benzyl chloride from the *Standard solution*

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

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

Acceptance criteria: NMT 0.010%

- **Enantiomeric Purity**

Mobile phase: Methanol and diethylamine (100: 0.1)

System suitability solution: 0.1 mg/mL each of USP Benzphetamine Hydrochloride RS and USP Benzphetamine Related Compound A RS in *Mobile phase*

Standard solution: 0.0015 mg/mL of USP Benzphetamine Related Compound A RS in *Mobile phase*

Sample solution: 1 mg/mL of Benzphetamine Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 207 nm

Column: 4.6-mm × 25-cm; 5-µm packing L80

Flow rate: 0.8 mL/min

Injection volume: 35 µL

Run time: NLT 1.9 times the retention time of benzphetamine

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between benzphetamine and benzphetamine related compound A, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of benzphetamine related compound A in the portion of Benzphetamine Hydrochloride taken:

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

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

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

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

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

Acceptance criteria: See *Table 4*.

Table 4

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Benzphetamine	1.00	—

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Benzphetamine related compound A	1.16	0.15

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Analysis: Dry at 105° for 3h.

Acceptance criteria: NMT 1.0%

• **pH ⟨791⟩**

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

Acceptance criteria: 4.0–6.0

ADDITIONAL REQUIREMENTS

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

• **USP Reference Standards ⟨11⟩**

USP Benzphetamine Hydrochloride RS

USP Benzphetamine Related Compound A RS

(*R*)-*N*-Benzyl-*N*-methyl-1-phenylpropan-2-amine hydrochloride.

$C_{17}H_{21}N \cdot HCl$ 275.82

USP Benzphetamine Related Compound E RS

(1*S*,2*S*)-2-[Benzyl(methyl)amino]-1-phenylpropan-1-ol hydrochloride.

$C_{17}H_{21}NO \cdot HCl$ 291.82

USP Benzphetamine Related Compound F RS

(1*S*,2*S*)-2-[Benzyl(methyl)amino]-1-cyclohexylpropan-1-ol hydrochloride.

$C_{17}H_{27}NO \cdot HCl$ 297.87

USP Benzyl Chloride RS

(Chloromethyl)benzene.

C_7H_7Cl 126.58▲ (USP 1-Aug-2019)

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

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

Chromatographic Database Information: Chromatographic Database

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