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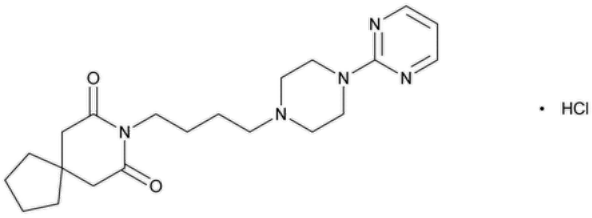
Buspirone Hydrochloride



$C_{21}H_{31}N_5O_2 \cdot HCl$ 421.96

8-Azaspiro[4,5]decane-7,9-dione, 8-[4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl]-, monohydrochloride;

N-[4-[4-(2-Pyrimidinyl)-1-piperazinyl]butyl]-1,1-cyclopentanediacetamide monohydrochloride CAS RN®: 33386-08-2; UNII: 207LT9J9OC.

DEFINITION

Buspirone Hydrochloride contains NLT 97.5% and NMT 102.5% of buspirone hydrochloride ($C_{21}H_{31}N_5O_2 \cdot HCl$), calculated on the as-is basis.

IDENTIFICATION

Change to read:

- **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay.*
- **C.** Identification Tests—General, *Chloride* ⟨191⟩

  Sample solution: 10 mg/mL in water

  Acceptance criteria: Meets the requirements

ASSAY

- **Procedure**

  Buffer A: 6.8 g/L of monobasic potassium phosphate and 0.93 g/L of sodium 1-hexanesulfonate monohydrate. Adjust with phosphoric acid to a pH of 3.4.

  Buffer B: 3.4 g/L of monobasic potassium phosphate and 3.52 g/L of sodium 1-hexanesulfonate monohydrate. Adjust with phosphoric acid to a pH of 2.2.

  Solution A: Acetonitrile and *Buffer A* (5:95)

  Solution B: Acetonitrile and *Buffer B* (75:25)

  Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
6	90	10
34	42	58
45	42	58
55	0	100
56	100	0
60	100	0
61	90	10

Diluent: *Solution A*

Impurities stock solution: 0.25 mg/mL each of USP Buspirone Related Compound A RS, USP Buspirone Related Compound G RS, USP Buspirone Related Compound K RS, USP Buspirone Related Compound L RS, and USP Buspirone Related Compound N RS in acetonitrile

System suitability solution: 1.0 mg/mL of USP Buspirone Hydrochloride RS and 0.001 mg/mL each of USP Buspirone Related Compound A RS, USP Buspirone Related Compound G RS, USP Buspirone Related Compound K RS, USP Buspirone Related Compound L RS, and USP Buspirone Related Compound N RS in *Diluent*, from *Impurities stock solution*

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

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

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between buspirone and buspirone related compound G peaks, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 0.92%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of buspirone hydrochloride ($C_{21}H_{31}N_5O_2 \cdot HCl$) in the portion of Buspirone Hydrochloride taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

Acceptance criteria: 97.5%–102.5% on the as-is basis

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.5%
- **Organic Impurities**

Buffer A, Buffer B, Solution A, Solution B, Mobile phase, Diluent, Impurities stock solution, and **System suitability solution:** Proceed as directed in the *Assay*.

Standard solution: 0.001 mg/mL each of USP Buspirone Hydrochloride RS, USP Buspirone Related Compound A RS, USP Buspirone Related Compound G RS, USP Buspirone Related Compound K RS, USP Buspirone Related Compound L RS, and USP Buspirone Related Compound N RS in *Diluent*

Sample solution: 1.0 mg/mL of Buspirone Hydrochloride in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 210 and 240 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

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

[Note—See *Table 2* and *Table 3* for relative retention times.]

Suitability requirements

Resolution at 240 nm: NLT 2.0 between buspirone and buspirone related compound G peaks, *System suitability solution*

Resolution at 210 nm: NLT 4.0 between buspirone related compound L and buspirone related compound N peaks, *System suitability solution*

Relative standard deviation: NMT 2.0% for each peak, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

For impurities detected at UV 240 nm

Calculate the percentage of buspirone related compound A or buspirone related compound G in the portion of Buspirone Hydrochloride taken:

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

r_U = peak response of buspirone related compound A or buspirone related compound G from the *Sample solution*

r_S = peak response of buspirone related compound A or buspirone related compound G from the *Standard solution*

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

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

Calculate the percentage of specified impurities and any other individual impurity in the portion of Buspirone Hydrochloride taken:

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

r_U = peak response of specified impurities and any other individual impurity from the *Sample solution*

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

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

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

F = relative response factor (see *Table 2*)

Acceptance criteria

For impurities detected at UV 240 nm: See *Table 2*. Disregard any peak below 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Buspirone related compound A[a]	0.2	—	0.10
Spiroammonium salt[b]	0.3	1.0	0.10
Bispyrimidinylpiperazinyl butane[c]	0.6	1.0	0.10
Bispyrimidinylpiperazinylbutyl ether[d]	0.7	1.0	0.10
Buspirone open ring[e]	0.8	1.0	0.3
Buspirone open ring dimer[f]	0.9	1.0	0.10
Buspirone	1.0	—	—
Buspirone related compound G[g]	1.05	—	0.10
Buspirone diester dimer[h]	1.1	1.0	0.10
Chlorobuspirone[i]	1.2	1.0	0.10

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Buspirone open ring spirodimer[j]	1.5	0.5	0.2
Any other individual impurity	—	1.0	0.10
Total impurities	—	—	0.4

[a] 2-(Piperazin-1-yl)pyrimidine.

[b] 8-(Pyrimidin-2-yl)-8-aza-5-azoniaspiro[4.5]decane.

[c] 1,4-Bis[4-(pyrimidin-2-yl)piperazin-1-yl]butane.

[d] Bis{4-[1-(pyrimidine-2-yl)piperazine-4-yl]butane-1-yl} ether.

[e] 2-{1-[2-Oxo-2-({4-[4-(pyrimidin-2-yl)piperazin-1-yl]butyl}amino)ethyl]cyclopentyl}acetic acid.

[f] 4-[4-(Pyrimidin-2-yl)piperazin-1-yl]butyl 2-{1-[2-oxo-2-({4-[4-(pyrimidin-2-yl)piperazin-1-yl]butyl}amino)ethyl]cyclopentyl}acetate.

[g] 1,4-Di(pyrimidin-2-yl)piperazine.

[h] Bis{4-[4-(pyrimidin-2-yl)piperazin-1-yl]butyl} 2,2'-(cyclopentane-1,1-diyl)diacetate.

[i] 8-{4-[4-(5-Chloropyrimidin-2-yl)piperazin-1-yl]butyl}-8-azaspiro[4.5]decane-7,9-dione.

[j] 4-(7,9-Dioxo-8-azaspiro[4.5]decan-8-yl)butyl 2-{1-[2-oxo-2-({4-[4-(pyrimidin-2-yl)piperazin-1-yl]butyl}amino)ethyl]cyclopentyl}acetate.

For impurities detected at UV 210 nm

Calculate the percentage of buspirone related compound K, buspirone related compound L, or buspirone related compound N in the portion of Buspirone Hydrochloride taken:

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

r_U = peak response of buspirone related compound K, buspirone related compound L, or buspirone related compound N from the *Sample solution*

r_S = peak response of buspirone related compound K, buspirone related compound L, or buspirone related compound N from the *Standard solution*

C_S = concentration of USP Buspirone Related Compound K RS, USP Buspirone Related Compound L RS, or USP Buspirone Related Compound N RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of buspirone bromobutyl analog and any other individual impurity in the portion of Buspirone Hydrochloride taken:

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

r_U = peak response of buspirone bromobutyl analog and any other individual impurity from the *Sample solution*

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

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

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

Acceptance criteria

For impurities detected at UV 210 nm: See *Table 3*. Disregard any peak below 0.05%.

Table 3

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Buspirone related compound K[a]	0.6	0.1
Buspirone	1.0	—

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Buspirone related compound L[b]	1.7	0.10
Buspirone bromobutyl analog[c]	1.8	0.10
Buspirone related compound N[d]	1.9	0.10
Any other individual impurity	—	0.10
Total impurities	—	0.2

[a] 8-Azaspiro[4,5]decane-7,9-dione.

[b] 8-(4-Chlorobutyl)-8-azaspiro[4.5]decane-7,9-dione.

[c] 8-(4-Bromobutyl)-8-azaspiro[4.5]decane-7,9-dione.

[d] 8,8'-(Butane-1,4-diyl)bis(8-azaspiro[4.5]decane-7,9-dione).

SPECIFIC TESTS

• **Water Determination, *Method I*⟨921⟩:** NMT 0.5%

ADDITIONAL REQUIREMENTS

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

• **USP Reference Standards ⟨11⟩**

USP Buspirone Hydrochloride RS

USP Buspirone Related Compound A RS
2-(Piperazin-1-yl)pyrimidine.
$C_8H_{12}N_4$ 164.21

USP Buspirone Related Compound G RS
1,4-Di(pyrimidin-2-yl)piperazine.
$C_{12}H_{14}N_6$ 242.28

USP Buspirone Related Compound K RS
8-Azaspiro[4.5]decane-7,9-dione.
$C_9H_{13}NO_2$ 167.21

USP Buspirone Related Compound L RS
8-(4-Chlorobutyl)-8-azaspiro[4.5]decane-7,9-dione.
$C_{13}H_{20}ClNO_2$ 257.76

USP Buspirone Related Compound N RS
8,8'-(Butane-1,4-diyl)bis(8-azaspiro[4.5]decane-7,9-dione).
$C_{22}H_{32}N_2O_4$ 388.50

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

Topic/Question	Contact	Expert Committee
BUSPIRONE HYDROCHLORIDE	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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