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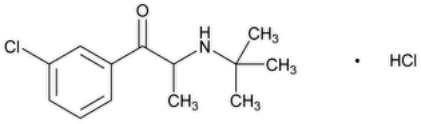
Bupropion Hydrochloride

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click https://www.uspnf.com/rb-bupropion-hcl-notice-20210430.



$C_{13}H_{18}ClNO \cdot HCl$ 276.20

1-Propanone, 1-(3-chlorophenyl)-2-[(1,1-dimethylethyl) amino]-, hydrochloride, (±)-;

(±)-2-(*tert*-Butylamino)-3'-chloropropiophenone hydrochloride CAS RN®: 31677-93-7; UNII: ZG7E5POY8O.

DEFINITION

Bupropion Hydrochloride contains NLT 98.0% and NMT 102.0% of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$), calculated on the anhydrous basis.

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

Change to read:

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

Sample solution: 1 mg/mL of Bupropion Hydrochloride ▲in water▲ (USP 1-Aug-2021)

Acceptance criteria: Meets the requirements of test *A*

ASSAY

Change to read:

• **Procedure**

Diluent: Methanol and water (50:50)

Buffer: 3.4 g/L of monobasic potassium phosphate in water. Adjust with 1 N sodium hydroxide ▲VS▲ (USP 1-Aug-2021) to a pH of 7.0.

Mobile phase: Methanol, tetrahydrofuran, and *Buffer* (39:11:50)

▲**System suitability solution:** 1 mg/mL of ▲USP Bupropion Hydrochloride RS▲ (RB 1-Aug-2021) and 2 µg/mL each of USP Bupropion Related Compound A RS and USP Bupropion Related Compound B RS in *Diluent*▲ (USP 1-Aug-2021)

Standard solution: 1 mg/mL of USP Bupropion Hydrochloride RS▲▲ (USP 1-Aug-2021) in *Diluent*

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

Chromatographic system

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

Mode: LC

Detector: UV 250 nm

Column: 3.9-mm × 15-cm; 5-µm packing L7

Flow rate: 1.1 mL/min

Injection volume: 20 µL

▲**Run time:** NLT 2 times the retention time of bupropion▲ (USP 1-Aug-2021)

System suitability

Samples: ▲*System suitability solution* and▲ (USP 1-Aug-2021) *Standard solution*

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

Suitability requirements

Resolution: NLT 1.3 between bupropion ▲▲ (USP 1-Aug-2021) related compound A and bupropion; NLT ▲1.5▲ (USP 1-Aug-2021) between bupropion and bupropion ▲▲ (USP 1-Aug-2021) related compound B, ▲*System suitability solution*▲ (USP 1-Aug-2021)

Relative standard deviation: NMT 2.0% for bupropion, ▲*Standard solution*▲ (USP 1-Aug-2021)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) in the portion of Bupropion 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 Bupropion Hydrochloride RS in the *Standard solution* (mg/mL)

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

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

IMPURITIES

Change to read:

• **Limit of 3-Chlorobenzoic Acid**

Protect all analytical solutions from light and use within one day.

Diluent: Methanol and 0.001 N hydrochloric acid ▲TS▲ (USP 1-Aug-2021) (20:80)

Solution A: Acetonitrile and water (10:90). Add 0.4 mL of trifluoroacetic acid per L of the mixture.

Solution B: Acetonitrile and water (95:5). Add 0.3 mL of trifluoroacetic acid per L of the mixture.

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
3.4	87	13
10.0	15	85
10.1	0	100
13.0	0	100
13.2	90	10
19.0	90	10

System suitability stock solution: 0.02 mg/mL of ▲USP Bupropion Related Compound C RS▲ (USP 1-Aug-2021) and 0.012 mg/mL of USP 3-Chlorobenzoic Acid RS in methanol

System suitability solution: 0.002 mg/mL of ▲USP Bupropion Related Compound C RS▲ (USP 1-Aug-2021) and 0.0012 mg/mL of ▲USP 3-Chlorobenzoic Acid RS▲ (USP 1-Aug-2021) from *System suitability stock solution* in *Diluent*

Standard stock solution: 0.06 mg/mL of USP 3-Chlorobenzoic Acid RS in methanol

Standard solution: 1.2 µg/mL of USP 3-Chlorobenzoic Acid RS from *Standard stock solution* in *Diluent*

Sample solution: 600 µg/mL of Bupropion Hydrochloride in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 226 nm

Column: 4.6-mm × 10-cm; 3.5-µm packing L1

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 5 µL

System suitability

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

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

Suitability requirements

Resolution: ▲▲ (USP 1-Aug-2021) NLT 1.5 between bupropion ▲▲ (USP 1-Aug-2021) related compound C and 3-chlorobenzoic acid, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of 3-chlorobenzoic acid in the portion of Bupropion Hydrochloride taken:

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

r_U = peak response of 3-chlorobenzoic acid from the *Sample solution*

r_S = peak response of 3-chlorobenzoic acid from the *Standard solution*

C_S = concentration of USP 3-Chlorobenzoic Acid RS in the *Standard solution* (µg/mL)

C_U = concentration of Bupropion Hydrochloride in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Bupropion	1.0	—
▲▲ (USP 1-Aug-2021)	▲▲ (USP 1-Aug-2021)	▲▲ (USP 1-Aug-2021)
Bupropion ▲▲ (USP 1-Aug-2021) related compound C[a]	1.75	—
3-Chlorobenzoic acid	1.80	0.2

[a] Included for system suitability purposes only. ▲This impurity is quantified using the test for *Organic Impurities*.▲ (USP 1-Aug-2021)

Change to read:

• **Organic Impurities**

Diluent, Buffer, Mobile phase, ▲System suitability solution,▲ (USP 1-Aug-2021) Standard solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

▲Sensitivity solution: 0.0005 mg/mL of USP Bupropion Hydrochloride RS in *Diluent*

Mode: LC

Detector: UV 250 nm

Column: 3.9-mm × 15-cm; 5-µm packing L7

Flow rate: 1.1 mL/min

Injection volume: 20 µL

Run time: NLT 3 times the retention time of bupropion▲ (USP 1-Aug-2021)

System suitability

Samples: ▲*System suitability solution* and *Sensitivity solution*▲ (USP 1-Aug-2021)

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

Suitability requirements

Resolution: NLT 1.3 between bupropion ▲▲ (USP 1-Aug-2021) related compound A and bupropion; NLT ▲1.5▲ (USP 1-Aug-2021) between bupropion and bupropion ▲▲ (USP 1-Aug-2021) related compound B, ▲*System suitability solution*▲ (USP 1-Aug-2021)

Relative standard deviation: NMT 2.0% for bupropion; NMT 5.0% for bupropion ▲▲ (USP 1-Aug-2021) related compound B, ▲*System suitability solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*▲ (USP 1-Aug-2021)

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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

r_S = peak response for bupropion from the *Standard solution*

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

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

F = relative response factor for each impurity relative to bupropion (see *Table 3*)

Acceptance criteria: See *Table 3*. ▲The reporting threshold is 0.05%.▲ (USP 1-Aug-2021)

Table 3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Deschloro bupropion[a]	0.38	1.5	0.5
Bupropion dione derivative[b]	0.58	1.0	0.2
o-Bupropion[c]	0.71	0.45	0.1
Chloropropiophenone[d]	0.78	1.2	0.1
Bupropion ▲▲ (USP 1-Aug-2021) related compound A	0.92	1.4	0.2
Bupropion	1.0	—	—
Bupropion ▲▲ (USP 1-Aug-2021) related compound B	1.14	0.81	0.2
▲▲ (USP 1-Aug-2021)	▲▲ (USP 1-Aug-2021)	▲▲ (USP 1-Aug-2021)	▲▲ (USP 1-Aug-2021)
4-Chlorobupropion[e]	2.30	1.1	0.2
5-Chlorobupropion[f]	2.74	0.69	0.2
Any ▲unspecified▲ (USP 1-Aug-2021) impurity	—	1.0	0.1
Total impurities[g]	—	—	1.0

[a] 2-(*tert*-Butylamino)-1-phenylpropan-1-one; also known as 2-(*tert*-butylamino)propiophenone.

[b] 1-(3-Chlorophenyl)propane-1,2-dione; also known as 1-(3-chlorophenyl)-1,2-propanedione.

[c] 2-(*tert*-Butylamino)-1-(2-chlorophenyl)propan-1-one; also known as 2-(*tert*-butylamino)-2'-chloropropiophenone.

[d] 1-(3-Chlorophenyl)propan-1-one; also known as 3'-chloropropiophenone.

[e] 2-(*tert*-Butylamino)-1-(3,4-dichlorophenyl)propan-1-one; also known as 2-(*tert*-butylamino)-3',4'-dichloropropiophenone.

[f] 2-(*tert*-Butylamino)-1-(3,5-dichlorophenyl)propan-1-one; also known as 2-(*tert*-butylamino)-3',5'-dichloropropiophenone.

[g] Sum of all impurities found in the tests for *Limit of 3-Chlorobenzoic Acid* and *Organic Impurities*.

SPECIFIC TESTS

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

ADDITIONAL REQUIREMENTS

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

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Bupropion Hydrochloride RS

▲ USP Bupropion Related Compound A RS

[Note—May also be labeled as USP Bupropion Hydrochloride Related Compound A RS.]

2-(*tert*-Butylamino)-1-(4-chlorophenyl)propan-1-one hydrochloride;

Also known as▲ (USP 1-Aug-2021) 2-(*tert*-Butylamino)-4'-chloropropiophenone hydrochloride.

$C_{13}H_{18}ClNO \cdot HCl$ ▲276.21

USP Bupropion Related Compound B RS

[Note—May also be labeled as USP Bupropion Hydrochloride Related Compound B RS.]

2-(*tert*-Butylamino)-1-(3-bromophenyl)propan-1-one hydrochloride;

Also known as▲ (USP 1-Aug-2021) 2-(*tert*-Butylamino)-3'-bromopropiophenone hydrochloride.

$C_{13}H_{18}BrNO \cdot HCl$ 320.66

▲ USP Bupropion Related Compound C RS

[Note—May also be labeled as USP Bupropion Hydrochloride Related Compound C RS]▲ (USP 1-Aug-2021)

1-(3-Chlorophenyl)-2-hydroxypropan-1-one.

▲$C_9H_9ClO_2$▲ (USP 1-Aug-2021) 184.62

▲▲ (USP 1-Aug-2021)

USP 3-Chlorobenzoic Acid RS

3-Chlorobenzoic acid.

$C_7H_5ClO_2$ 156.57

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

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

Chromatographic Database Information: Chromatographic Database

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