Bupropion Hydrochloride Extended-Release Tablets

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In accordance with the Rules and Procedures of the Council of Experts, the Small Molecules 4 Expert Committee has revised the Bupropion Hydrochloride Extended-Release Tablets monograph. The purpose for the revision is to add *Dissolution Test 26* to accommodate FDA-approved drug products with different dissolution conditions and/or tolerances than the existing dissolution test(s). The revision also necessitates a change in the table numbering in the test for *Organic Impurities.*

The Bupropion Hydrochloride Extended-Release Tablets Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Nicholas Garito Jr., Sr. Scientific Liaison (301-816-8321 or njg@usp.org).

Revision Bulletin
Official: January 1, 2021

Bupropion Hydrochloride Extended-Release Tablets

DEFINITION

Bupropion Hydrochloride Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$).

IDENTIFICATION

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

  Sample: Crush 1 Tablet using a mortar and pestle. Prepare an approximate 1% (w/w) dispersion of the sample in potassium bromide.

  Acceptance criteria: The *Sample* shows strong bands at about 1690, 1560, and 1240 cm^{-1} and a weaker band at about 740 cm^{-1}, similar to the reference preparation.

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

ASSAY

Change to read:

- **Procedure**

  Diluent 1: Methanol and 0.001 N hydrochloric acid (20:80)

  Solution A: Acetonitrile, trifluoroacetic acid, and water (10: 0.04: 90)

  Solution B: Acetonitrile, trifluoroacetic acid, and water (95: 0.03: 5)

  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 Hydrochloride Related Compound C RS and 0.2 mg/mL of USP Bupropion Hydrochloride Related Compound F RS in methanol

System suitability solution: 0.002 mg/mL of bupropion hydrochloride related compound C and 0.02 mg/mL of bupropion hydrochloride related compound F from the *System suitability stock solution* in *Diluent 1*

Standard solution: 0.6 mg/mL of USP Bupropion Hydrochloride RS in *Diluent 1*

Sample stock solution A: Transfer a number of Tablets, intact or crushed, to a suitable homogenizer vessel containing sufficient methanol to obtain a concentration of 3.0 mg/mL of bupropion hydrochloride.

Immediately homogenize the sample for 30 s at 20,000 rpm. Allow extraction for 3 min, and follow by two additional 10-s pulses, each at 20,000 rpm, pausing 3 min between these pulses to ensure complete extraction. Pass a portion of the solution through a nylon filter of 0.45-µm pore size, discarding the first 2–4 mL of the filtrate.

Sample solution A: Nominally 0.6 mg/mL of bupropion hydrochloride from *Sample stock solution A* in 0.001 N hydrochloric acid

Alternatively, the *Sample solution* can be prepared as follows.

Buffer: Dissolve 100 g of anhydrous dibasic sodium phosphate in 1 L of water. Add 50 mL of phosphoric acid, stir or sonicate until dissolved, and mix. Adjust with phosphoric acid to a pH of 3.0.

Diluent 2: Methanol and *Buffer* (20:80)

Sample stock solution B: Weigh and grind NLT 20 Tablets to prepare a solution having a nominal concentration of 3 mg/mL. Initially add *Diluent 2* (75% of the volume of the flask), stir for 30 min, and sonicate for 15 min. Dilute with *Diluent 2* to volume. Centrifuge a portion of the resulting solution, and use the supernatant.

Sample solution B: Nominally 0.6 mg/mL of bupropion hydrochloride from *Sample stock solution B* in *Diluent 2*

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 ▲26▲ (RB 1-Jan-2021) for the relative retention times.]

Suitability requirements

Resolution: NLT 1.3 between bupropion hydrochloride related compound F and bupropion hydrochloride related compound C, *System suitability solution*

Tailing factor: NMT 1.9, *Standard solution*

Relative standard deviation: NMT 1.5%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution A* or *Sample solution B*

Calculate the percentage of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) in the portion of Tablets taken:

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

r_U = peak response of bupropion hydrochloride from *Sample solution A* or *Sample solution B*

r_S = peak response of bupropion hydrochloride from the *Standard solution*

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

C_U = nominal concentration of bupropion hydrochloride in *Sample solution A* or *Sample solution B* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- **Dissolution** ⟨711⟩

For products labeled for dosing every 12 h

Test 1

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Times: 1, 4, and 8 h

Standard solution: (*L*/900) mg/mL of USP Bupropion Hydrochloride RS in *Medium*, where *L* is the label claim, in mg/Tablet. Dilute with *Medium*, if necessary.

Sample solution: Pass a portion of the solution under test through a suitable filter, and dilute with *Medium*, if necessary.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV-Vis

Analytical wavelength: 298 nm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Determine the percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved.

Tolerances: See *Table 2*.

Table 2

Time (h)	Amount Dissolved (%)
1	25–45
4	60–85
8	NLT 80

The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: 0.1 N hydrochloric acid, pH 1.5 (prepared by transferring 50 mL of hydrochloric acid to 6000 mL of water, adding 18 g of sodium hydroxide, mixing, and adjusting with either diluted sodium hydroxide or hydrochloric acid to a pH of 1.5); 900 mL, deaerated

Apparatus 1: 50 rpm

Times: 1, 2, 4, and 6 h

Buffer: 3.45 g of monobasic sodium phosphate in 996 mL of water. Add 4.0 mL of triethylamine, and adjust with phosphoric acid to a pH of 2.80.

Mobile phase: Methanol and *Buffer* (35:65)

Standard solution: (*L*/900) mg/mL of USP Bupropion Hydrochloride RS in *Medium*, where *L* is the label claim, in mg/Tablet

Sample solution: Use portions of the solution under test, and pass through a nylon filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 298 nm

Column: 4.6-mm × 15-cm; packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 2000 theoretical plates

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Determine the percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved.

Tolerances: See *Table 3*.

Table 3

Time (h)	Amount Dissolved (%)
1	25–50
2	40–65
4	65–90
6	NLT 80

The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Dissolution ⟨711⟩*, *Acceptance Table 2*.

Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

Medium: Water; 900 mL

Apparatus 2: 50 rpm. Use wire coil sinkers, if necessary.

Times: 1, 2, 4, and 6 h

Standard solution: (*L*/900) mg/mL of USP Bupropion Hydrochloride RS in *Medium*, where *L* is the label claim, in mg/Tablet. Dilute with *Medium*, if necessary.

Sample solution: Pass a portion of the solution under test through a suitable filter, and dilute with *Medium*, if necessary.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: UV-Vis

Analytical wavelength: 250 nm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Determine the percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved.

Tolerances: See *Table 4*.

Table 4

Time (h)	Amount Dissolved (for Tablets that contain 200 mg of bupropion hydrochloride) (%)	Amount Dissolved (for Tablets that contain all other strengths of bupropion hydrochloride) (%)
1	30–50	30–55
2	45–65	50–75
4	65–85	70–90
6	NLT 78	NLT 80

The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Dissolution ⟨711⟩*, *Acceptance Table 2*.

Test 5: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 5*.

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Times: 1, 3, and 6 h

Standard solution: (*L*/900) mg/mL of USP Bupropion Hydrochloride RS in *Medium*, where *L* is the label claim, in mg/Tablet. Dilute with *Medium*, if necessary.

Sample solution: Pass a portion of the solution under test through a suitable filter, and dilute with *Medium*, if necessary.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: UV-Vis

Analytical wavelength: 298 nm

Cell: 0.5 cm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Determine the percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved.

Tolerances: See *Table 5*.

Table 5

Time (h)	Amount Dissolved (%)
1	35–55
3	65–85
6	NLT 80

The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Dissolution ⟨711⟩*, *Acceptance Table 2*.

Test 7: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 7*.

Medium: 0.1 N hydrochloric acid, pH 1.5 (prepared by transferring 50 mL of hydrochloric acid to 6000 mL of water, adding 18 g of sodium hydroxide, mixing, and adjusting with either diluted sodium hydroxide or hydrochloric acid to a pH of 1.5); 900 mL, deaerated

Apparatus 1: 50 rpm

Times: 1, 2, 4, and 6 h

Buffer: 3.45 g of monobasic sodium phosphate in 996 mL of water. Add 4.0 mL of triethylamine, and adjust with phosphoric acid to a pH of 2.80.

Mobile phase: Methanol and *Buffer* (45:55)

Standard solution: (*L*/900) mg/mL of USP Bupropion Hydrochloride RS in *Medium*, where *L* is the label claim, in mg/Tablet

Sample solution: Use portions of the solution under test, and pass through a nylon filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 298 nm

Column: 4.6-mm × 15-cm; packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 2000 theoretical plates

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Determine the percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved.

Tolerances: See *Table 6*.

Table 6

Time (h)	Amount Dissolved (%)
1	25–50
2	45–70
4	NLT 70
6	NLT 80

The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Dissolution ⟨711⟩*, *Acceptance Table 2*.

Test 9: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 9*.

Medium: 0.1 N hydrochloric acid, pH 1.5 (prepared by transferring 50 mL of hydrochloric acid to 6000 mL of water, adding 18 g of sodium hydroxide, mixing, and adjusting with either diluted sodium

hydroxide or hydrochloric acid to a pH of 1.5); 900 mL

Apparatus 1: 50 rpm

Times: 1, 2, 4, and 8 h

Standard solution: (*L*/1000) mg/mL of USP Bupropion Hydrochloride RS in *Medium*, where *L* is the label claim, in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV-Vis

Analytical wavelength: 298 nm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Determine the percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved.

Tolerances: See *Table 7*.

Table 7

Time (h)	Amount Dissolved (%)
1	20–45
2	35–55
4	55–85
8	NLT 80

The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 10: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 10*.

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Times: 1, 2, 4, and 8 h

Standard solution: (*L*/900) mg/mL of USP Bupropion Hydrochloride RS in *Medium*, where *L* is the label claim, in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV-Vis

Analytical wavelength: 298 nm

Cell: 0.5 cm

Blank: *Medium*

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at each time point (i):

$$Result_i = (A_i/A_S) \times C_S \times V \times (1/L) \times 100$$

A_i = absorbance of bupropion hydrochloride from the *Sample solution* at time point i

A_S = absorbance of bupropion hydrochloride from the *Standard solution*

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: See *Table 8*.

Table 8

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	1	20–40
2	2	35–60
3	4	55–85
4	8	NLT 80

The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Dissolution ⟨711⟩*, *Acceptance Table 2*.

Test 17: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 17*.

Medium: 0.1 N hydrochloric acid, pH 1.5 (prepared by transferring 50 mL of hydrochloric acid to 6 L of water containing 18 g of sodium hydroxide, mixing, and adjusting with either diluted sodium hydroxide or diluted hydrochloric acid to a pH of 1.5); 900 mL, deaerated

Apparatus 1: 50 rpm

Times: 1, 2, 4, and 8 h

Buffer: To each liter of water add 6.8 g of monobasic potassium phosphate. Adjust with phosphoric acid to a pH of 3.0.

Mobile phase: Methanol and *Buffer* (60:40)

Standard solution: (L/900) mg/mL of USP Bupropion Hydrochloride RS in *Medium,* where L is the label claim, in mg/Tablet. Sonication may be used to promote dissolution.

Sample solution: Pass a portion of the solution under test through a suitable filter. [NOTE—A 0.45-µm nylon membrane filter may be suitable.]

Chromatographic system

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

Mode: LC

Detector: UV 298 nm

Column: 4.6-mm × 15-cm; 5-µm packing L7

Flow rate: 1 mL/min

Injection volume: 25 µL

Run time: NLT 1.5 times the retention time of bupropion

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) in the sample withdrawn from the vessel at time point *i*:

$$\text{Result}_i = (r_i/r_S) \times C_S$$

r_i = peak response of bupropion from the *Sample solution* at time point *i*

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

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

Calculate the percentage of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at each time point (*i*):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

$$\text{Result}_3 = (\{C_3 \times [V - (2 \times V_S)]\} + [(C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

$$\text{Result}_4 = (\{C_4 \times [V - (3 \times V_S)]\} + [(C_3 + C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

C_i = concentration of bupropion hydrochloride in the portion of the sample withdrawn at time point *i* (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

V_S = volume of *Sample solution* withdrawn at each time point (mL)

Tolerances: See *Table 9*.

Table 9

Time Point (*i*)	Time (h)	Amount Dissolved (for Tablets that contain 100 mg of bupropion hydrochloride) (%)	Amount Dissolved (for Tablets that contain 150 mg or 200 mg of bupropion hydrochloride) (%)
1	1	20–40	15–35
2	2	40–60	35–55
3	4	60–85	55–80

Time Point (*i*)	Time (h)	Amount Dissolved (for Tablets that contain 100 mg of bupropion hydrochloride) (%)	Amount Dissolved (for Tablets that contain 150 mg or 200 mg of bupropion hydrochloride) (%)
4	8	NLT 85	NLT 80

The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 19: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 19*.

Medium: Water, degassed; 900 mL

Apparatus 1: 50 rpm

Times: 1, 2, 4, and 8 h

Standard stock solution: 0.56 mg/mL of USP Bupropion Hydrochloride RS in *Medium*

Standard solution: (*L*/900) mg/mL of USP Bupropion Hydrochloride RS in *Medium*, where *L* is the label claim, in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter of 10-µm pore size.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV-Vis

Analytical wavelength: 298 nm

Cell: 1 cm

Blank: *Medium*

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at each time point (*i*):

$$\text{Result}_i = (A_i/A_S) \times C_S \times V \times (1/L) \times 100$$

A_i = absorbance of bupropion from the *Sample solution* at time point *i*

A_S = absorbance of bupropion from the *Standard solution*

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: See *Table 10*.

Table 10

Time Point (*i*)	Time (h)	Amount Dissolved (for Tablets that contain 100 mg of bupropion hydrochloride) (%)	Amount Dissolved (for Tablets that contain 150 or 200 mg of bupropion hydrochloride) (%)
1	1	32–52	25–45
2	2	50–70	45–65
3	4	NLT 75	65–85
4	8	NLT 85	NLT 85

The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

For products labeled for dosing every 24 h

Test 4: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 4*.

Medium: 0.1 N hydrochloric acid; 900 mL, deaerated

Apparatus 1: 75 rpm

Times: 2, 4, 8, and 16 h

Standard solution: (*L*/900) mg/mL of USP Bupropion Hydrochloride RS in *Medium*, where *L* is the label claim, in mg/Tablet. Dilute with *Medium*, if necessary.

Sample solution: Pass a portion of the solution under test through a suitable filter, and dilute with *Medium*, if necessary.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV-Vis

Analytical wavelength: 252 nm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Determine the percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved.

Tolerances: See *Table 11*.

Table 11

Time (h)	Amount Dissolved (%)
2	NMT 20
4	20–45
8	65–90
16	NLT 80

The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 6: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 6*.

Medium: 0.1 N hydrochloric acid; 900 mL, deaerated

Apparatus 1: 75 rpm

Times: 1, 2, 4, 8, and 12 h

Standard solution: (*L*/900) mg/mL of USP Bupropion Hydrochloride RS in *Medium*, where *L* is the label claim, in mg/Tablet. Dilute with *Medium*, if necessary.

Sample solution: Pass a portion of the solution under test through a suitable filter, and dilute with *Medium*, if necessary.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV-Vis

Analytical wavelength: 298 nm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Determine the percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved.

Tolerances: See *Table 12*.

Table 12

Time (h)	Amount Dissolved (%)
1	15–35
2	25–50
4	40–65
8	65–90
12	NLT 80

The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 8: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 8*.

Acid stage medium: 0.1 N hydrochloric acid; 900 mL

Buffer stage medium: pH 6.8 phosphate buffer; 900 mL

Apparatus 1: 75 rpm

Times: 2 h in *Acid stage medium*; 3, 8, and 16 h in *Buffer stage medium*. The time in the *Buffer stage medium* includes the time in the *Acid stage medium*.

Standard solution: (*L*/900) mg/mL of USP Bupropion Hydrochloride RS in *Acid stage medium*, where *L* is the label claim, in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV-Vis

Analytical wavelength: 298 nm

Cell: 0.5 cm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Determine the percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved.

Tolerances: See *Table 13*.

Table 13

Time (h)	Amount Dissolved (%)
2	NMT 10
3	10–30
8	60–90
16	NLT 80

The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Dissolution ⟨711⟩*, *Acceptance Table 2*.

Test 11: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 11*.

Acid stage medium: 0.1 N hydrochloric acid; 750 mL

Buffer stage medium: pH 6.8 phosphate buffer (add 250 mL of 76 g/L tribasic sodium phosphate to the *Acid stage medium*, adjust with 2 N hydrochloric acid or 2 N sodium hydroxide to a pH of 6.8, if necessary); 1000 mL

Apparatus 2: 50 rpm

Times: 2 h in *Acid stage medium*; 3, 8, and 16 h in *Buffer stage medium*. The time in the *Buffer stage medium* includes the time in the *Acid stage medium*.

Acid stage standard solution: 0.06 mg/mL of USP Bupropion Hydrochloride RS in *Acid stage medium*. Sonication may be used to aid in dissolution.

Buffer stage standard solution: 0.15 mg/mL of USP Bupropion Hydrochloride RS in *Buffer stage medium*. Sonication may be used to aid in dissolution.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: UV-Vis

Analytical wavelength: 298 nm

Cell: 0.5 cm

Blank: *Acid stage medium* or *Buffer stage medium*

Analysis

Samples: *Acid stage standard solution*, *Buffer stage standard solution*, and *Sample solution*

Calculate the concentration (C_i) of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) in the sample withdrawn from the vessel at time point *i*:

$$\text{Result}_i = (A_i/A_S) \times C_S$$

A_i = absorbance of bupropion hydrochloride from the *Sample solution* at time point *i*

A_S = absorbance of bupropion hydrochloride from the *Acid stage standard solution* or

Buffer stage standard solution

C_S = concentration of USP Bupropion Hydrochloride RS in the *Acid stage standard solution* or *Buffer stage standard solution* (mg/mL)

Calculate the percentage of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at each time point (*i*):

$$Result_1 = C_1 \times V_A \times (1/L) \times 100$$

$$Result_2 = \{[C_2 \times (V_B - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

$$Result_3 = (\{C_3 \times [V_B - (2 \times V_S)]\} + [(C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

$$Result_4 = (\{C_4 \times [V_B - (3 \times V_S)]\} + [(C_3 + C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

C_i = concentration of bupropion hydrochloride in the portion of the sample withdrawn at time point *i* (mg/mL)

V_A = volume of *Acid stage medium*, 750 mL

L = label claim (mg/Tablet)

V_B = volume of *Buffer stage medium*, 1000 mL

V_S = volume of *Sample solution* withdrawn from the *Acid stage medium* or *Buffer stage medium* (mL)

Tolerances: See *Table 14*.

Table 14

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	2	NMT 10
2	3	10–30
3	8	55–85
4	16	NLT 75

The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 12: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 12*.

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 1: 75 rpm

Times: 2, 4, 8, and 12 h

Standard solution: (*L*/900) mg/mL of USP Bupropion Hydrochloride RS in *Medium*, where *L* is the label claim, in mg/Tablet

Sample solution: Withdraw at least 10 mL of the solution under test and pass through a suitable filter.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV-Vis

Analytical wavelength: 252 nm

Cell

For Tablets labeled to contain 150 mg: 0.1 cm

For Tablets labeled to contain 300 mg: 0.05 cm

Blank: *Medium*

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 3.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) in the sample withdrawn from the vessel at time point *i*:

$$\text{Result}_i = (A_i/A_S) \times C_S$$

A_i = absorbance of bupropion hydrochloride from the *Sample solution* at time point *i*

A_S = absorbance of bupropion hydrochloride from the *Standard solution*

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

Calculate the percentage of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at each time point (*i*):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

$$\text{Result}_3 = (\{C_3 \times [V - (2 \times V_S)]\} + [(C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

$$\text{Result}_4 = (\{C_4 \times [V - (3 \times V_S)]\} + [(C_3 + C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

C_i = concentration of bupropion hydrochloride in the portion of the sample withdrawn at time point *i* (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

V_S = volume of *Sample solution* withdrawn from the *Medium* (mL)

Tolerances: See *Table 15*.

Table 15

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	2	NMT 25
2	4	25–50
3	8	60–85
4	12	NLT 80

The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 13: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 13*.

Medium: 0.1 N hydrochloric acid; 900 mL, deaerated

Apparatus 1: 75 rpm

Times: 2, 4, 8, and 12 h

Standard solution: (*L*/900) mg/mL of USP Bupropion Hydrochloride RS in *Medium*, where *L* is the label claim, in mg/Tablet

Sample solution: Withdraw at least 10 mL of the solution under test and centrifuge. Use the supernatant.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV-Vis

Analytical wavelength: 252 nm

Cell: 0.1 cm

Blank: *Medium*

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) in the sample withdrawn from the vessel at time point *i*:

$$\text{Result}_i = (A_i/A_S) \times C_S$$

A_i = absorbance of bupropion hydrochloride from the *Sample solution* at time point *i*

A_S = absorbance of bupropion hydrochloride from the *Standard solution*

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

Calculate the percentage of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at each time point (*i*):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

$$\text{Result}_3 = (\{C_3 \times [V - (2 \times V_S)]\} + [(C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

$$\text{Result}_4 = (\{C_4 \times [V - (3 \times V_S)]\} + [(C_3 + C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

C_i = concentration of bupropion hydrochloride in the portion of the sample withdrawn at time point *i* (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

V_S = volume of *Sample solution* withdrawn from the *Medium* (mL)

Tolerances: See *Table 16*.

Table 16

Time Point (*i*)	Time (h)	Amount Dissolved (150 mg/Tablet) (%)	Amount Dissolved (300 mg/Tablet) (%)
1	2	NMT 25	NMT 25
2	4	30–55	25–45
3	8	65–90	60–80
4	12	NLT 80	NLT 80

The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Dissolution ⟨711⟩*, *Acceptance Table 2*.

Test 14: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 14*.

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 1: 75 rpm

Times: 2, 4, 8, and 16 h

Standard solution: (*L*/900) mg/mL of USP Bupropion Hydrochloride RS in *Medium*, where *L* is the label claim, in mg/Tablet. If necessary, dilute the solution with *Medium.*

Sample solution: Pass a portion of the solution under test through a suitable filter. Replace the portion removed with the same volume of *Medium.* If necessary, dilute the filtrate with *Medium*.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: UV-Vis

Analytical wavelength: 252 nm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) in the sample withdrawn from the vessel at time point *i*:

$$\text{Result}_i = (A_i/A_S) \times C_S \times D$$

A_i = absorbance from the *Sample solution* at time point *i*

A_S = absorbance from the *Standard solution*

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

D = dilution factor for the *Sample solution,* if needed

Calculate the percentage of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at each time point (*i*):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = [(C_2 \times V) + (C_1 \times V_S)] \times (1/L) \times 100$$

$$\text{Result}_3 = \{(C_3 \times V) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

$$\text{Result}_4 = \{(C_4 \times V) + [(C_3 + C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

C_i = concentration of bupropion hydrochloride in the portion of the sample withdrawn at time point *i* (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

V_S = volume of *Sample solution* withdrawn at each time point and replaced with *Medium* (mL)

Tolerances: See *Table 17*.

Table 17

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	2	NMT 20
2	4	20–45
3	8	55–85
4	16	NLT 80

The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Dissolution ⟨711⟩*, *Acceptance Table 2*.

Test 15: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 15*.

Acid stage

Acid stage medium: 0.1 N hydrochloric acid, degassed; 900 mL

Apparatus 1: 100 rpm

Time: 2 h in *Acid stage medium*

Buffer: 3.5 g/L of monobasic sodium phosphate prepared as follows. Dissolve 3.45 g of monobasic sodium phosphate in 996 mL of water, add 4.0 mL of triethylamine, and adjust with phosphoric acid to a pH of 2.8.

Mobile phase: Methanol and *Buffer* (45:55)

Acid stage standard solution: 0.033 mg/mL of USP Bupropion Hydrochloride RS in *Acid stage medium*. Sonication may be used to promote dissolution.

Acid stage sample solution: Pass a portion of the solution under test through a suitable filter, discard the first 5 mL, and use the filtrate. Then discard the Tablets and remaining solution. [NOTE—A 0.45-µm nylon membrane filter may be suitable.]

Chromatographic system

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

Mode: LC

Detector: UV 298 nm

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

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 1.5 times the retention time of bupropion

System suitability

Sample: *Acid stage standard solution*

Suitability requirements **Tailing factor:** NMT 2.0 **Relative standard deviation:** NMT 2.0%

Analysis

Samples: *Acid stage standard solution* and *Acid stage sample solution*

Calculate the percentage of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved:

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

r_U = peak response of bupropion from the *Acid stage sample solution*

r_S = peak response of bupropion from the *Acid stage standard solution*

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

V = volume of *Acid stage medium*, 900 mL

L = label claim (mg/Tablet)

Buffer stage: Use fresh Tablets.

Buffer stage medium: pH 6.8 tribasic sodium phosphate buffer and 0.5% sodium lauryl sulfate (Dissolve 19 g of tribasic sodium phosphate in 1 L of water, add 7 mL of hydrochloric acid, and adjust with 0.2 N sodium hydroxide or dilute hydrochloric acid to a pH of 6.8. Add 5 g of sodium dodecyl sulfate. To promote dissolution, the resulting solution can be continuously stirred and heated to 41°. Allow the solution to cool to 37° before use. Do not allow the temperature to fall below 36.5° before beginning the test.); 900 mL

Apparatus 1: 100 rpm

Times: 1, 2, 4, and 8 h

Buffer: 1.4 g/L of dibasic ammonium phosphate and 0.5 g/L of sodium 1-hexanesulfonate prepared as follows. Dissolve 1.4 g of dibasic ammonium phosphate and 0.5 g of sodium 1-hexanesulfonate in 1 L of water. To each 1 L of this solution, add 2.0 mL of triethylamine, and adjust with phosphoric acid to a pH of 7.0.

Mobile phase: Acetonitrile and *Buffer* (60:40)

Buffer stage standard solution: 0.33 mg/mL of USP Bupropion Hydrochloride RS in *Buffer stage medium*

Buffer stage sample solution: Pass a portion of the solution under test through a suitable filter, discard the first 5 mL, and use the filtrate.

Chromatographic system: Proceed as directed under the *Acid stage*.

System suitability

Sample: *Buffer stage standard solution*

Suitability requirements **Tailing factor:** NMT 2.0 **Relative standard deviation:** NMT 2.0%

Analysis

Samples: *Buffer stage standard solution* and *Buffer stage sample solution*

Calculate the concentration (C_i) of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) in the sample withdrawn from the vessel at time point i:

$$\text{Result}_i = (r_i/r_S) \times C_S$$

r_i = peak response of bupropion from the *Buffer stage sample solution* at time point *i*

r_S = peak response of bupropion from the *Buffer stage standard solution*

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

Calculate the percentage of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at each time point (*i*):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

$$\text{Result}_3 = (\{C_3 \times [V - (2 \times V_S)]\} + [(C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

$$\text{Result}_4 = (\{C_4 \times [V - (3 \times V_S)]\} + [(C_3 + C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

C_i = concentration of bupropion hydrochloride in the portion of the sample withdrawn at time point *i* (mg/mL)

V = volume of *Buffer stage medium*, 900 mL

L = label claim (mg/Tablet)

V_S = volume of *Buffer stage sample solution* withdrawn at each time point (mL)

Tolerances

Acid stage: NMT 10%; the percentage of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the time specified conforms to *Dissolution* ⟨711⟩, *Acceptance Table 3*.

Buffer stage: See *Table 18*.

Table 18

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	1	5–25
2	2	25–45
3	4	60–85
4	8	NLT 85

The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 16: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 16*.

Medium: 0.1 N hydrochloric acid; 900 mL, deaerated

Apparatus 1: 75 rpm

Times: 2, 5, 8, and 16 h

Buffer: 3.5 g/L of monobasic sodium phosphate prepared as follows. Dissolve 3.45 g of monobasic sodium phosphate in 996 mL of water, add 4.0 mL of triethylamine, and adjust with phosphoric acid to a pH of 2.8.

Mobile phase: Methanol and *Buffer* (35:65)

Standard solution: 0.17 mg/mL of USP Bupropion Hydrochloride RS in *Medium*. Sonication may be used to promote dissolution

Sample solution: Pass a portion of the solution under test through a suitable filter, and discard NLT 1 mL. Dilute the filtrate with *Medium* if necessary. Replace the portion removed with the same volume of *Medium*. [NOTE—A 0.45-µm nylon membrane filter may be suitable.]

Chromatographic system

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

Mode: LC

Detector: UV 298 nm

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

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 1.5 times the retention time of bupropion

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) in the sample withdrawn from the vessel at time point *i*:

$$\text{Result}_i = (r_i/r_S) \times C_S \times D$$

r_i = peak response of bupropion from the *Sample solution* at time point *i*

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

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

D = dilution factor for the *Sample solution,* if needed

Calculate the percentage of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at each time point (*i*):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = [(C_2 \times V) + (C_1 \times V_S)] \times (1/L) \times 100$$

$$\text{Result}_3 = \{(C_3 \times V) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

$$\text{Result}_4 = \{(C_4 \times V) + [(C_3 + C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

C_i = concentration of bupropion hydrochloride in the portion of the sample withdrawn at time point *i* (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

V_S = volume of *Sample solution* withdrawn at each time point and replaced with *Medium* (mL)

Tolerances: See *Table 19*.

Table 19

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	2	NMT 10
2	5	30–60
3	8	65–88
4	16	NLT 85

The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Dissolution ⟨711⟩*, *Acceptance Table 2*.

Test 18: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 18*.

Medium: 0.1 N hydrochloric acid; 900 mL, deaerated

Apparatus 1: 75 rpm

Times: 2, 4, 8, and 16 h

Buffer: 6.8 g/L of monobasic potassium phosphate in water adjusted with phosphoric acid to a pH of 3.0

Mobile phase: Methanol and *Buffer* (60:40)

Standard solution: (L/900) mg/mL of USP Bupropion Hydrochloride RS in *Medium*, where L is the label claim, in mg/Tablet. Sonication may be used to promote dissolution.

Sample solution: Centrifuge a portion of the solution under test for 15 min.

Chromatographic system

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

Mode: LC

Detector: UV 298 nm

Column: 4.6-mm × 15-cm; 5-µm packing L7

Flow rate: 1 mL/min

Injection volume: 25 µL

Run time: NLT 1.5 times the retention time of bupropion

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) in the sample withdrawn from the vessel at time point *i*:

$$\text{Result}_i = (r_i/r_S) \times C_S$$

r_i = peak response of bupropion from the *Sample solution* at time point *i*

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

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

Calculate the percentage of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at each time point (*i*):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

$$\text{Result}_3 = (\{C_3 \times [V - (2 \times V_S)]\} + [(C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

$$\text{Result}_4 = (\{C_4 \times [V - (3 \times V_S)]\} + [(C_3 + C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

C_i = concentration of bupropion hydrochloride in the portion of the sample withdrawn at time point *i* (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

V_S = volume of *Sample solution* withdrawn at each time point (mL)

Tolerances: See *Table 20*.

Table 20

Time Point (*i*)	Time (h)	Amount Dissolved (for Tablets that contain 150 mg of bupropion hydrochloride) (%)	Amount Dissolved (for Tablets that contain 300 mg of bupropion hydrochloride) (%)
1	2	NMT 20	NMT 20
2	4	25–50	25–50
3	8	65–95	60–85
4	16	NLT 80	NLT 80

The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Dissolution ⟨711⟩*, *Acceptance Table 2*.

Test 20: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 20*.

Medium: 0.1 N hydrochloric acid VS; 900 mL, deareated

Apparatus 1: 75 rpm

Times: 2, 4, 8, and 16 h

Standard solution: 0.1 mg/mL of USP Bupropion Hydrochloride RS in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter, and dilute with *Medium*, if necessary. Replace the portion removed with the same volume of *Medium*.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: UV-Vis

Analytical wavelength: 298 nm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) in the sample withdrawn from the vessel at time point *i*:

$$\text{Result}_i = (A_i/A_S) \times C_S \times D$$

A_i = absorbance from the *Sample solution* at time point *i*

A_S = absorbance from the *Standard solution*

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

D = dilution factor for the *Sample solution*, if needed

Calculate the percentage of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at each time point (*i*):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = [(C_2 \times V) + (C_1 \times V_S)] \times (1/L) \times 100$$

$$\text{Result}_3 = \{(C_3 \times V) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

$$\text{Result}_4 = \{(C_4 \times V) + [(C_3 + C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

C_i = concentration of bupropion hydrochloride in the portion of the sample withdrawn at time point *i* (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

V_S = volume of *Sample solution* withdrawn at each time point and replaced with *Medium* (mL)

Tolerances: See *Table 21*.

Table 21

Time Point (*i*)	Time (h)	Amount Dissolved (for Tablets that contain 150 mg of bupropion hydrochloride) (%)	Amount Dissolved (for Tablets that contain 300 mg of bupropion hydrochloride) (%)
1	2	NMT 15	NMT 15
2	4	10–35	10–35
3	8	55–80	50–75
4	16	NLT 80	NLT 80

The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 21: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 21*.

Medium: 0.1 N hydrochloric acid VS; 900 mL, deareated

Apparatus 1: 75 rpm

Times: 4, 8, and 16 h

Standard stock solution 1: 0.84 mg/mL of USP Bupropion Hydrochloride RS prepared as follows. Transfer a suitable amount of USP Bupropion Hydrochloride RS to an appropriate volumetric flask. Add 50% of the flask volume of acetonitrile. Dilute with water to volume.

Standard stock solution 2: 0.17 mg/mL of USP Bupropion Hydrochloride RS from *Standard stock solution 1* in *Medium*

Standard solution: 0.017 mg/mL of USP Bupropion Hydrochloride RS from *Standard stock solution 2* in *Medium* passed through a suitable filter of 0.45-µm pore size

Sample solution: Dilute a portion of the solution under test with *Medium*. Pass a portion of the resulting solution through a suitable filter of 0.45-µm pore size. Replace the portion removed with the same volume of *Medium*.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV-Vis

Analytical wavelength: 252 nm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) in the sample withdrawn from the vessel at time point *i*:

$$\text{Result}_i = (A_i/A_S) \times C_S \times D$$

A_i = absorbance from the *Sample solution* at time point *i*

A_S = absorbance from the *Standard solution*

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

D = dilution factor for the *Sample solution*, if needed

Calculate the percentage of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at each time point (*i*):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = [(C_2 \times V) + (C_1 \times V_S)] \times (1/L) \times 100$$

$$\text{Result}_3 = \{(C_3 \times V) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

C_i = concentration of bupropion hydrochloride in the portion of the sample withdrawn at time point *i* (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

V_S = volume of *Sample solution* withdrawn at each time point and replaced with *Medium* (mL)

Tolerances: See *Table 22*.

Table 22

Time Point (*i*)	Time (h)	Amount Dissolved (for Tablets that contain 150 mg of bupropion hydrochloride) (%)	Amount Dissolved (for Tablets that contain 300 mg of bupropion hydrochloride) (%)
1	4	NMT 20	NMT 30
2	8	35–60	50–70
3	16	NLT 80	NLT 80

The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 22: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 22*.

Acid stage medium: 0.1 N hydrochloric acid VS; 750 mL

Buffer stage medium: Sodium phosphate buffer, pH 6.8 (after 2 h, add 250 mL of 76 g/L of tribasic sodium phosphate, previously heated to 37 ± 0.5°, to the *Acid stage medium* and adjust with 2 N hydrochloric acid TS or 2 N sodium hydroxide TS, if necessary, to a pH of 6.8); 1000 mL

Apparatus 2: 50 rpm

Times: 2 h in *Acid stage medium*; 4 and 12 h in *Buffer stage medium*. The time in the *Buffer stage medium* includes the time in the *Acid stage medium*.

Acid stage standard solution: 0.08 mg/mL of USP Bupropion Hydrochloride RS in *Acid stage medium*

Buffer stage standard solution: 0.3 mg/mL of USP Bupropion Hydrochloride RS in *Buffer stage medium*

Acid stage sample solution and **Buffer stage sample solution:** Use a portion of the solution under test.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV-Vis

Analytical wavelength: 298 nm

Blank: *Acid stage medium* or *Buffer stage medium*

System suitability

Samples: *Acid stage standard solution* and *Buffer stage standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%, *Acid stage standard solution* and *Buffer stage standard solution*

Analysis

Samples: *Acid stage standard solution*, *Buffer stage standard solution*, *Acid stage sample solution*, and *Buffer stage sample solution*

Calculate the concentration (C_i) of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) in the sample withdrawn from the vessel at time point *i*:

$$\text{Result}_i = (A_i/A_S) \times C_S \times D$$

A_i = absorbance from the *Acid stage sample solution* or *Buffer stage sample solution* at time point *i*

A_S = absorbance from the *Acid stage standard solution* or *Buffer stage standard solution* at time point *i*

C_S = concentration of USP Bupropion Hydrochloride RS in the *Acid stage standard solution* or *Buffer stage standard solution* (mg/mL)

D = dilution factor, if needed

Calculate the percentage of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved in *Acid stage medium*:

$$\text{Result}_1 = C_1 \times V_A \times (1/L) \times 100$$

C_1 = concentration of bupropion hydrochloride in the portion of the sample withdrawn at time point *1*

V_A = volume of *Acid stage medium*, 750 mL

L = label claim (mg/Tablet)

Calculate the percentage of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at each time point (*i*):

$$\text{Result}_2 = \{[C_2 \times (V_B - V_{SA})] + (C_1 \times V_{SA})\} \times (1/L) \times 100$$

$$\text{Result}_3 = \{[C_3 \times (V_B - V_{SB} - V_{SA})] + (C_2 \times V_{SB}) + (C_1 \times V_{SA})\} \times (1/L) \times 100$$

C_i = concentration of bupropion hydrochloride in the portion of the sample withdrawn at time point *i* (mg/mL)

V_B = volume of *Buffer stage medium*, 1000 mL

V_{SA} = volume of *Acid stage sample solution* withdrawn at time point 1 (mL)

L = label claim (mg/Tablet)

V_{SB} = volume of *Buffer stage sample solution* withdrawn at each time point (mL)

Tolerances: See *Table 23*.

Table 23

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	2	NMT 15
2	4	40–60
3	12	NLT 80

The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Dissolution ⟨711⟩*, *Acceptance Table 2*.

Test 23: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 23*.

Acid stage medium: 0.1 N hydrochloric acid VS; 900 mL, deaerated

Buffer stage medium: pH 6.8 phosphate buffer; 900 mL, deaerated

Apparatus 1: 75 rpm

Times: 2 h in *Acid stage medium*; 6 and 16 h in *Buffer stage medium*. The time in the *Buffer stage medium* includes the time in the *Acid stage medium*.

Acid stage standard solution: (*L*/900) mg/mL of USP Bupropion Hydrochloride RS in *Acid stage medium*, where *L* is the label claim, in mg/Tablet

Buffer stage standard solution: (*L*/900) mg/mL of USP Bupropion Hydrochloride RS in *Buffer stage medium*, where *L* is the label claim, in mg/Tablet

Acid stage sample solution and **Buffer stage sample solution:** Pass a portion of the solution under test through a suitable filter.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV-Vis

Analytical wavelength: 298 nm

Cell: 0.5 cm, flow cell

Blank: *Acid stage medium* or *Buffer stage medium*

System suitability

Samples: *Acid stage standard solution* and *Buffer stage standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%, *Acid stage standard solution* and *Buffer stage standard solution*

Analysis

Samples: *Acid stage standard solution*, *Buffer stage standard solution*, *Acid stage sample solution*, and *Buffer stage sample solution*

Calculate the concentration (C_i) of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) in the sample withdrawn from the vessel at time point *i*:

$$\text{Result}_i = (A_i/A_S) \times C_S$$

A_i = absorbance from the *Acid stage sample solution* or *Buffer stage sample solution* at time point *i*

A_S = absorbance from the *Acid stage standard solution* or *Buffer stage standard solution* at time point *i*

C_S = concentration of USP Bupropion Hydrochloride RS in the *Acid stage standard solution* or *Buffer stage standard solution* (mg/mL)

Calculate the percentage of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved in *Acid stage medium* (Q_A):

$$\text{Result}_1 = C_1 \times V_A \times (1/L) \times 100$$

C_1 = concentration of bupropion hydrochloride in the portion of the sample withdrawn at time point *1*

V_A = volume of *Acid stage medium*, 900 mL

L = label claim (mg/Tablet)

Calculate the percentage of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at each time point (i):

$$Result_2 = [C_2 \times V_B \times (1/L) \times 100] + Q_A$$

$$Result_3 = [C_3 \times V_B \times (1/L) \times 100] + Q_A$$

C_i = concentration of bupropion hydrochloride in the portion of the sample withdrawn at time point i (mg/mL)

V_B = volume of *Buffer stage medium*, 900 mL

L = label claim (mg/Tablet)

Q_A = percentage of the labeled amount of bupropion hydrochloride dissolved in the *Acid stage medium*

Tolerances: See *Table 24*.

Table 24

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	2	NMT 15
2	6	50–75
3	16	NLT 80

The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Dissolution ⟨711⟩*, *Acceptance Table 2*.

▲**Test 26:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 26*.

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 1: 75 rpm

Times: 2, 6, and 14 h

Standard stock solution: 0.17 mg/mL of USP Bupropion Hydrochloride RS in *Medium*. Sonication may be used to promote dissolution.

Standard solution: 0.017 mg/mL of USP Bupropion Hydrochloride RS from *Standard stock solution* in *Medium*

Sample solution: Dilute a portion of the solution under test with *Medium*. Pass a portion of the resulting solution through a suitable filter of 0.45-µm pore size, discarding the first few milliliters of filtrate. Replace the portion removed with the same volume of *Medium*.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: UV-Vis

Analytical wavelength: 252 nm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) in the sample withdrawn from the vessel at time point i:

$$\text{Result}_i = (A_U/A_S) \times C_S \times D$$

A_U = absorbance from the *Sample solution* at time point *i*

A_S = absorbance from the *Standard solution*

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

D = dilution factor for the *Sample solution*

Calculate the percentage of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at each time point (*i*):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = [(C_2 \times V) + (C_1 \times V_S)] \times (1/L) \times 100$$

$$\text{Result}_3 = \{(C_3 \times V) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

C_i = concentration of bupropion hydrochloride in the portion of the sample withdrawn at time point *i* (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

V_S = volume of *Sample solution* withdrawn at each time point and replaced with *Medium* (mL)

Tolerances: See *Table 25*.

Table 25

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	2	NMT 20
2	6	40–65
3	14	NLT 80

The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*. ▲ (RB 1-Jan-2021)

- **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements

IMPURITIES

Change to read:

- **Organic Impurities**

Diluent 1, Solution A, Solution B, Mobile phase, and **Sample solution A** or **Sample solution B:** Proceed as directed in the *Assay*.

System suitability stock solution A: 0.02 mg/mL of USP Bupropion Hydrochloride Related Compound C RS, 0.02 mg/mL of USP Bupropion Hydrochloride Related Compound F RS, and 0.012 mg/mL of USP 3-Chlorobenzoic Acid RS in methanol

System suitability solution A: 0.002 mg/mL of bupropion hydrochloride related compound C, 0.002 mg/mL of bupropion hydrochloride related compound F, and 0.0012 mg/mL of 3-chlorobenzoic acid from *System suitability stock solution A* in *Diluent 1*

System suitability stock solution B: 0.012 mg/mL of USP 3-Chlorobenzoic Acid RS in methanol

System suitability solution B: 0.0012 mg/mL of 3-chlorobenzoic acid from *System suitability stock solution B* in *Diluent 1*

Standard solution: 0.0012 mg/mL of USP Bupropion Hydrochloride RS in *Diluent 1*

Chromatographic system: Proceed as directed in the *Assay* except use a *Detector* as follows.

Detector: UV 226 nm, adjusted ±2 nm so that the relative response factor requirement is met. [NOTE—The peak responses of the compounds of interest are very sensitive to changes in the detection wavelength.]

System suitability

Samples: *System suitability solution A*, *System suitability solution B*, and *Standard solution*

[NOTE—See Table ▲26▲ (RB 1-Jan-2021) for the relative retention times.]

Suitability requirements

Resolution: NLT 1.3 between bupropion hydrochloride related compound F and bupropion hydrochloride related compound C, *System suitability solution A*; NLT 1.3 between bupropion hydrochloride C and 3-chlorobenzoic acid, *System suitability solution A*

Relative standard deviation: NMT 10%, *Standard solution*

Relative response factor: 3.8–4.5 for the peak response of 3-chlorobenzoic acid in *System suitability solution B* divided by the peak response from bupropion in the *Standard solution*

Analysis

Samples: *System suitability solution B*, *Standard solution*, and *Sample solution A* or *Sample solution B*

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

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

r_U = peak response of 3-chlorobenzoic acid from *Sample solution A* or *Sample solution B*

r_S = peak response of 3-chlorobenzoic acid from *System suitability solution B*

C_S = concentration of USP 3-Chlorobenzoic Acid RS in *System suitability solution B* (mg/mL)

C_U = nominal concentration of bupropion hydrochloride in *Sample solution A* or *Sample solution B* (mg/mL)

Calculate the percentage of each other degradation product in the portion of Tablets taken:

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

r_U = peak response of each other degradation product from *Sample solution A* or *Sample solution B*

r_S = peak response of bupropion hydrochloride from the *Standard solution*

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

C_U = nominal concentration of bupropion hydrochloride in *Sample solution A* or *Sample solution B* (mg/mL)

F = relative response factor for each other degradation product (see Table ▲26▲ (RB 1-Jan-2021))

Acceptance criteria: See Table ▲26.▲ (RB 1-Jan-2021)

Table ▲26▲ (RB 1-Jan-2021)

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)	
			100 mg or less	150 mg or greater
Bupropion amine[a]	0.38	1.2	0.3	0.3
S,*S*,*S*-Thiomorpholine derivative[b]	0.56	1.1	1.0	1.5
S,*R*,*R*-Thiomorpholine derivative[c]	0.78	1.1	0.5	0.4
Bupropion	1.0	—	—	—
Bupropion related compound F	1.71	1.8	1.2	2.3
Bupropion related compound C	1.75	1.7	0.3	0.3
3-Chlorobenzoic acid	1.80	—	0.3	0.3
Bupropion dione derivative[d]	2.25	1.00	0.4	0.4
Any unspecified degradation product	—	1.00	0.2	0.2
Total impurities	—	—	3.2	3.3

[a] 2-Amino-1-(3-chlorophenyl)-1-propanone.

[b] (3*S*,5*S*,6*S*)-6-(3-Chlorophenyl)-6-hydroxy-5-methyl-3-thiomorpholine carboxylic acid.

[c] (3*S*,5*R*,6*R*)-6-(3-Chlorophenyl)-6-hydroxy-5-methyl-3-thiomorpholine carboxylic acid.

[d] 1-(3-Chlorophenyl)propane-1,2-dione.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature. Protect from light.
- **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **USP Reference Standards** ⟨11⟩

USP Bupropion Hydrochloride RS

USP Bupropion Hydrochloride Related Compound C RS

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

$C_9H_9O_2Cl$ 184.62

USP Bupropion Hydrochloride Related Compound F RS

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

$C_9H_9O_2Cl$ 184.62

USP 3-Chlorobenzoic Acid RS

3-Chlorobenzoic acid.

$C_7H_5ClO_2$ 156.57

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