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. INFRARED ABSORPTION ⟨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 the *Sample solution* 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 •● (IRA 1-Mar-2014)**:** 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*● (IRA 1-Mar-2014)

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● (IRA 1-Mar-2014) *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 disodium hydrogen 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● (IRA 1-Mar-2014) *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 16*● (RB 1-Oct-2014) for the relative retention times.]● (IRA 1-Mar-2014)

Suitability requirements

Resolution: •NLT 1.3 between bupropion hydrochloride related compound F and bupropion hydrochloride related compound C, *System suitability solution*● (IRA 1-Mar-2014)

Tailing factor: NMT 1.9, *Standard solution*

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

•● (IRA 1-Mar-2014)

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.• (IRA 1-Mar-2014)

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

Instrumental conditions

(See *Spectrophotometry and Light-Scattering* ⟨851⟩.)

Mode: UV-Vis

Analytical wavelength: *298* nm

•• (IRA 1-Mar-2014)

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.• (IRA 1-Mar-2014)

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 *Acceptance Table 2* in ⟨711⟩.

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 concentrated 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 •• (IRA 1-Mar-2014)); 900 mL, deaerated

Apparatus 1: 50 rpm

Times: 1, 2, 4, and 6 h

•• (IRA 1-Mar-2014)

Buffer: 3.45 g of monobasic sodium phosphate monohydrate in 996 mL of water. Add 4.0 mL of triethylamine, and adjust with phosphoric acid to a pH of 2.80. •• (IRA 1-Mar-2014)

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• (IRA 1-Mar-2014)

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.• (IRA 1-Mar-2014)

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 *Acceptance Table 2* in ⟨711⟩.

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 *Spectrophotometry and Light-Scattering* ⟨851⟩.)

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 *Acceptance Table 2* in ⟨711⟩.● (IRA 1-Mar-2014)

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 *Spectrophotometry and Light-Scattering* ⟨851⟩.)
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.● (IRA 1-Mar-2014)
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 *Acceptance Table 2* in ⟨711⟩.

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 concentrated 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 monohydrate 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.● (IRA 1-Mar-2014)
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 *Acceptance Table 2* in ⟨711⟩.

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 concentrated 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.);● (IRA 1-Mar-2014) 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 *Spectrophotometry and Light-Scattering* ⟨851⟩.)
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.● (IRA 1-Mar-2014)
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 *Acceptance Table 2* in ⟨711⟩.

•**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 *Spectrophotometry and Light-Scattering* ⟨851⟩.)
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*):

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

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 *Acceptance Table 2* in ⟨711⟩.● (IRA 1-Mar-2014)

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.● (IRA 1-Mar-2014)
Sample solution: Pass a portion of the solution under test through a suitable filter, and dilute with *Medium*, if necessary.
Instrumental conditions
(See *Spectrophotometry and Light-Scattering* ⟨851⟩.)
Mode: UV-Vis
Analytical wavelength: 252 nm
●● (IRA 1-Mar-2014)
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.● (IRA 1-Mar-2014)
Tolerances: See *Table 9*.

Table 9

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 *Acceptance Table 2* in ⟨711⟩.
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.● (IRA 1-Mar-2014)
Sample solution: Pass a portion of the solution under test through a suitable filter, and dilute with *Medium*, if necessary.
Instrumental conditions
(See *Spectrophotometry and Light-Scattering* ⟨851⟩.)
Mode: UV-Vis
Analytical wavelength: 298 nm
●● (IRA 1-Mar-2014)
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.● (IRA 1-Mar-2014)
Tolerances: See *Table 10*.

Table 10

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 *Acceptance Table 2* in ⟨711⟩.
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 (see *Reagents, Indicators, and Solutions—Buffer Solutions*); 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● (IRA 1-Mar-2014)
Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.
Instrumental conditions
(See *Spectrophotometry and Light-Scattering* ⟨851⟩.)
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.● (IRA 1-Mar-2014)
Tolerances: See *Table 11*.

●**Table 11**

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

● (IRA 1-Mar-2014)
The percentages of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) dissolved at the times specified conform to *Acceptance Table 2* in ⟨711⟩.
●**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 0.2 M 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 *Spectrophotometry and Light-Scattering* ⟨851⟩.)
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*):

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

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

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

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

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 12*.

Table 12

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 *Acceptance Table 2* in ⟨711⟩.
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 *Spectrophotometry and Light-Scattering* ⟨851⟩.)

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 13*.

Table 13

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 *Acceptance Table 2* in ⟨711⟩.

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 *Spectrophotometry and Light-Scattering* ⟨851⟩.)
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 14*.

Table 14

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 *Acceptance Table 2* in ⟨711⟩.● (IRA 1-Mar-2014)

●**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 *Spectrophotometry and Light-Scattering* ⟨851⟩.)
Mode: UV
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 15*.

Table 15

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 *Acceptance Table 2* in ⟨711⟩.● (RB 1-Oct-2014)

- **UNIFORMITY OF DOSAGE UNITS ⟨905⟩:** Meet the requirements ●(IRA 1-Mar-2014)●

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 16*● (RB 1-Oct-2014) 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 impurity 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 impurity 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 impurity (see •*Table 16*)• (RB 1-Oct-2014)

Acceptance criteria: See •*Table 16*.• (RB 1-Oct-2014)

•**Table 16**• (RB 1-Oct-2014)

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%) 100 mg or less	Acceptance Criteria, NMT (%) 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
R,S,S-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

[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.

•**Table 16**• (RB 1-Oct-2014) *(Continued)*

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%) 100 mg or less	Acceptance Criteria, NMT (%) 150 mg or greater
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.

• (IRA 1-Mar-2014)

ADDITIONAL REQUIREMENTS

Change to read:

- **PACKAGING AND STORAGE:** Preserve in well-closed containers. •Store at controlled room temperature. Protect from light.• (IRA 1-Mar-2014)
- **LABELING:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.

Change to read:

- **USP REFERENCE STANDARDS** ⟨11⟩

  USP Bupropion Hydrochloride RS

  USP Bupropion Hydrochloride Related Compound C RS
  1-(3-Chlorophenyl)-2-•hydroxypropan-1-one.• (IRA 1-Mar-2014)
  $C_9H_9O_2Cl$ 184.62

  USP Bupropion Hydrochloride Related Compound F RS
  •1-(3-Chlorophenyl)-1-hydroxypropan-2-one.• (RB 1-Oct-2014)
  $C_9H_9O_2Cl$ 184.62

- •

  USP 3-Chlorobenzoic Acid RS
  3-Chlorobenzoic acid.
  $C_7H_5ClO_2$ 156.57

• (IRA 1-Mar-2014)