Bupropion Hydrochloride Extended-Release Tablets

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Expert Committee	Chemical Medicines Monographs 4

In accordance with section 7.04 (c) of the 2015–2020 Rules and Procedures of the Council of Experts and the Pending Monograph Guideline, this is to provide notice that the Chemical Medicines Monographs 4 Expert Committee intends to revise the Bupropion Hydrochloride Extended-Release Tablets monograph.

Based on the supporting data received from a manufacturer awaiting FDA approval, the Expert Committee proposes to add *Dissolution Test 24* to accommodate different dissolution conditions and tolerances. Additionally, the table number within the test for *Organic Impurities* and references to this table number were updated.

The proposed revision is contingent on FDA approval of a product that meets the proposed monograph specifications. The proposed revision will be published as a Revision Bulletin and an official date will be assigned to coincide as closely as possible with the FDA approval of the associated product.

Additionally, minor editorial changes have been made to update the monograph to current *USP* style.

See below for additional information about the proposed text.[1]

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

[1] This text is not the official version of a *USP–NF* monograph and may not reflect the full and accurate contents of the currently official monograph. Please refer to the current edition of the *USP–NF* for official text.

USP provides this text to indicate changes that we anticipate will be made official once the product subject to this proposed revision under the Pending Monograph Program receives FDA approval. Once FDA approval is granted for the associated revision request, a Revision Bulletin will be posted that will include the changes indicated herein, as well as any changes indicated in the product's final approval, combined with the text of the monograph as effective on the date of approval. Any revisions made to a monograph under the Pending Monograph Program that are posted without prior publication for comment in the *Pharmacopeial Forum* must also meet the requirements outlined in the USP Guideline on Use of Accelerated Processes for Revisions to the USP–NF.

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

Change to read:

- **A. ▲SPECTROSCOPIC IDENTIFICATION TESTS** ⟨197⟩**,** *Infrared Spectroscopy***:** 197K▲ (CN 1-May-2020)

  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*▲ (TBD) 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

Table 6 *(continued)*

Time (h)	Amount Dissolved (%)
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*):

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

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 *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
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
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*):

$$\text{Result}_1 = C_1 \times V_A \times (1/L) \times 100$$
$$\text{Result}_2 = \{[C_2 \times (V_B - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$
$$\text{Result}_3 = (\{C_3 \times [V_B - (2 \times V_S)]\} + [(C_2 + C_1) \times V_S]) \times (1/L) \times 100$$
$$\text{Result}_4 = (\{C_4 \times [V_B - (3 \times V_S)]\} + [(C_3 + C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

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 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, deaerated
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*):

$$\text{Result}_2 = [C_2 \times V_B \times (1/L) \times 100] + Q_A$$
$$\text{Result}_3 = [C_3 \times V_B \times (1/L) \times 100] + Q_A$$

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 24:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 24*.

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

Buffer stage medium: pH 6.8 phosphate buffer with 0.5 M sodium chloride (6.8 g/L of monobasic potassium phosphate and 0.9 g/L of sodium hydroxide in water, adjusted with 0.2 M sodium hydroxide or phosphoric acid to a pH of 6.8. Add 29.2 g/L of sodium chloride); 900 mL, deaerated

Apparatus 1: 50 rpm

Times

For Tablets labeled to contain 150 mg of bupropion hydrochloride: 2 h in *Acid stage medium*; 3, 5, 8, and 14 h in *Buffer stage medium*. The time in the *Buffer stage medium* includes the time in the *Acid stage medium*.

For Tablets labeled to contain 300 mg of bupropion hydrochloride: 2 h in *Acid stage medium*; 3, 6, 10, 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. Sonication may be used to promote dissolution. Pass the resulting solution through a suitable filter of 0.45-µm pore size, discarding the first 1 mL of filtrate. Use the solution within 1 h.

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. Sonication may be used to promote dissolution. Pass the resulting solution through a suitable filter of 0.45-µm pore size, discarding the first 1 mL of filtrate.

Acid stage sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first 1 mL of filtrate. Use the solution within 3 h. Remove the remainder of the solution under test from the vessel and proceed with testing in *Buffer stage medium*.

Buffer stage sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first 1 mL of filtrate. Replace the portion removed with the same volume of the appropriate *Buffer stage medium*.

Instrumental conditions

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

Mode: UV

Analytical wavelength: 298 nm

Cell: 0.5 cm

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*:

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

A_U = 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*):

$$\text{Result}_2 = [C_2 \times V_B \times (1/L) \times 100] + Q_A$$
$$\text{Result}_3 = \{[(C_3 \times V_B) + (C_2 \times V_S)] \times (1/L) \times 100\} + Q_A$$
$$\text{Result}_4 = (\{(C_4 \times V_B) + [(C_3 + C_2) \times V_S]\} \times (1/L) \times 100) + Q_A$$
$$\text{Result}_5 = (\{(C_5 \times V_B) + [(C_4 + C_3 + C_2) \times V_S]\} \times (1/L) \times 100) + Q_A$$

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*
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*)	For Tablets Labeled to Contain 150 mg of Bupropion Hydrochloride		For Tablets Labeled to Contain 300 mg of Bupropion Hydrochloride	
	Time (h)	Amount Dissolved (%)	Time (h)	Amount Dissolved (%)
1	2	NMT 10	2	NMT 10
2	3	11–31	3	5–25
3	5	41–61	6	29–49
4	8	64–84	10	58–78
5	14	NLT 80	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*.▲ (TBD)

• **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*▲ (TBD) 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*)▲ (TBD)

Acceptance criteria: See ▲*Table 26*.

Table 26▲ (TBD)

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