**Bupropion Hydrochloride Extended-Release Tablets**

**Type of Posting**  
Revision Bulletin

**Posting Date**  
27–Oct–2017

**Official Date**  
01–Nov–2017

**Expert Committee**  
Chemical Medicines Monographs 4

**Reason for Revision**  
Compliance

In accordance with the Rules and Procedures of the 2015-2020 Council of Experts, the Chemical Medicines Monographs 4 Expert Committee has revised the Bupropion Hydrochloride Extended-Release Tablets monograph. The purpose for the revision is to add Dissolution Test 19 to accommodate drug products which were approved with different dissolution conditions and acceptance criteria.

Minor editorial changes have been made to update the monograph to the current USP style.

The Bupropion Hydrochloride Extended-Release Tablets Revision Bulletin supersedes the currently official monograph. The Revision Bulletin will be incorporated into the Second Supplement to *USP 41–NF 36*.

Should you have any questions, please contact Heather Joyce, Ph.D., Senior Scientific Liaison (301–998–6792 or hrj@usp.org).
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 (C13H18ClNO · 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 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>
<thead>
<tr>
<th>Time (min)</th>
<th>Solution A (%)</th>
<th>Solution B (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>90</td>
<td>10</td>
</tr>
<tr>
<td>3.4</td>
<td>87</td>
<td>13</td>
</tr>
<tr>
<td>10.0</td>
<td>15</td>
<td>85</td>
</tr>
<tr>
<td>10.1</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>13.0</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>13.2</td>
<td>90</td>
<td>10</td>
</tr>
<tr>
<td>19.0</td>
<td>90</td>
<td>10</td>
</tr>
</tbody>
</table>

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°C
Flow rate: 1.5 mL/min
Injection volume: 5 µL
System suitability
Samples: System suitability solution and Standard solution

[Note—See *Table 21* (BB 3-Nov-2017) 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 (C13H18ClNO · HCl) in the portion of Tablets taken:

\[ \text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_U}{C_S} \right) \times 100 \]

\[ r_U = \text{peak response of bupropion hydrochloride from Sample solution A or Sample solution B} \]
\[ r_S = \text{peak response of bupropion hydrochloride from the Standard solution} \]
\[ C_S = \text{concentration of USP Bupropion Hydrochloride RS in the Standard solution} \text{ (mg/mL)} \]
\[ C_U = \text{nominal concentration of bupropion hydrochloride in Sample solution A or Sample solution B (mg/mL)} \]
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>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25–45</td>
</tr>
<tr>
<td>4</td>
<td>60–85</td>
</tr>
<tr>
<td>8</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

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.)

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

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>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>35–55</td>
</tr>
<tr>
<td>3</td>
<td>65–85</td>
</tr>
<tr>
<td>6</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

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: \((L/1000)\) 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 (821), 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>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25–50</td>
</tr>
<tr>
<td>2</td>
<td>45–70</td>
</tr>
<tr>
<td>4</td>
<td>NLT 70</td>
</tr>
<tr>
<td>6</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

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>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20–45</td>
</tr>
<tr>
<td>2</td>
<td>35–55</td>
</tr>
<tr>
<td>4</td>
<td>55–85</td>
</tr>
<tr>
<td>8</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

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 \( i \):

\[
\text{Result}_i = \left( \frac{A_i}{A_S} \right) \times C_i \times V \times \left( \frac{1}{L} \right) \times 100
\]

\( A_i \): absorbance of bupropion hydrochloride from the Sample solution at time point \( i \)

\( A_S \): absorbance of bupropion hydrochloride from the Standard solution

\( C_i \): 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>
<thead>
<tr>
<th>Time Point ( i )</th>
<th>Time ( h )</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>20-40</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>35-60</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>55-85</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

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

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

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

Apparatus 1: 50 rpm

Times: 1, 2, 4, and 8 h

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

Mobile phase: Methanol and Buffer (60:40)

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

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

Chromatographic system

(See Chromatography (621), System Suitability.)

Mode: LC

Detector: UV 298 nm

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

Flow rate: 1 mL/min

Injection volume: 25 µL

Run time: NLT 1.5 times the retention time of bupropion

System suitability

Sample: Standard solution

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: Standard solution and Sample solution

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

\[
\text{Result}_i = \left( \frac{r_i}{r_S} \right) \times C_i
\]

\( r_i \): peak response of bupropion from the Sample solution at time point \( i \)

\( r_S \): peak response of bupropion from the Standard solution

\( C_i \): 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 \( i \):

\[
\text{Result}_1 = C_i \times V \times \left( \frac{1}{L} \right) \times 100
\]

\( \text{Result}_2 = \left( \left[ C_i \times (V - V_S) \right] + \left[ C_i \times V_S \right] \right) \times \left( \frac{1}{L} \right) \times 100
\]

\( \text{Result}_3 = \left( \left[ C_i \times (V - 2 \times V_S) \right] + \left[ C_i \times 2 \times V_S \right] \right) \times \left( \frac{1}{L} \right) \times 100
\]

\( \text{Result}_4 = \left( \left[ C_i \times (V - 3 \times V_S) \right] + \left[ C_i \times 3 \times V_S \right] \right) \times \left( \frac{1}{L} \right) \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>
<thead>
<tr>
<th>Time Point ( i )</th>
<th>Time ( h )</th>
<th>Amount Dissolved (for Tablets that contain 100 mg of bupropion hydrochloride) (%)</th>
<th>Amount Dissolved (for Tablets that contain 150 mg or 200 mg of bupropion hydrochloride) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>20-40</td>
<td>15-35</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>40-60</td>
<td>35-55</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>60-85</td>
<td>55-80</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>NLT 85</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>
The percentages of the labeled amount of bupropion hydrochloride (C_{13}H_{18}ClNO \cdot HCl) dissolved at the times specified conform to Dissolution (711), Acceptance Table 2. · (RB 1-Nov-2017)

**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, 8, 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:** 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

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>NMT 20</td>
</tr>
<tr>
<td>4</td>
<td>20-45</td>
</tr>
<tr>
<td>8</td>
<td>65-90</td>
</tr>
<tr>
<td>16</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of bupropion hydrochloride (C_{13}H_{18}ClNO \cdot HCl) dissolved at the times specified conform to Dissolution (711), Acceptance Table 2. · (RB 1-Jun-2017)

**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.

### 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

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15-35</td>
</tr>
<tr>
<td>2</td>
<td>25-50</td>
</tr>
<tr>
<td>4</td>
<td>40-65</td>
</tr>
<tr>
<td>8</td>
<td>65-90</td>
</tr>
<tr>
<td>12</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of bupropion hydrochloride (C_{13}H_{18}ClNO \cdot HCl) dissolved at the times specified conform to Dissolution (711), Acceptance Table 2. · (RB 1-Nov-2017)

**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:** 1, 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.

### 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

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15-35</td>
</tr>
<tr>
<td>2</td>
<td>25-50</td>
</tr>
<tr>
<td>4</td>
<td>40-65</td>
</tr>
<tr>
<td>8</td>
<td>65-90</td>
</tr>
<tr>
<td>12</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of bupropion hydrochloride (C_{13}H_{18}ClNO \cdot HCl) dissolved at the times specified conform to Dissolution (711), Acceptance Table 2. · (RB 1-Nov-2017)
Bupropion

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·HCl) dissolved at each time point:

The percentages of the labeled amount of bupropion hydrochloride (C$_{13}$H$_{18}$ClNO·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) of bupropion hydrochloride (C$_{13}$H$_{18}$ClNO·HCl) in the sample withdrawn from the vessel at time point i:

Result, = ($A_i/A_L$) × $C_L$

$A_i$ = absorbance of bupropion hydrochloride from the Sample solution at time point i
$A_L$ = absorbance of bupropion hydrochloride from the Acid stage standard solution or Buffer stage standard solution
$C_L$ = 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·HCl) dissolved at each time point (i):

Result$_1$ = $C_i$ × $V_i$ × (1/L) × 100

Result$_2$ = $([C_i × (V_i - V_3)] + (C_i × V_3))$ × (1/L) × 100

Result$_3$ = $([C_i × (V_i - (2 × V_3))] + [(C_i + C_2) × V_3])$ × (1/L) × 100

Result$_4$ = $([C_i × (V_i - (3 × V_3))] + [(C_i + C_2 + C_3) × V_3])$ × (1/L) × 100

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

$V_i$ = volume of Acid stage medium, 750 mL
$L$ = label claim (mg/Tablet)
$V_3$ = volume of Buffer stage medium, 1000 mL
$V_3$ = volume of Sample solution withdrawn from the Acid stage medium or Buffer stage medium (mL)

Tolerances: See Table 13.

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>NMT 10</td>
</tr>
<tr>
<td>3</td>
<td>10–30</td>
</tr>
<tr>
<td>8</td>
<td>60–90</td>
</tr>
<tr>
<td>16</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of bupropion hydrochloride (C$_{13}$H$_{18}$ClNO·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

<table>
<thead>
<tr>
<th>Time Point (h)</th>
<th>Time (b)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>NMT 10</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>10–30</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>55–85</td>
</tr>
<tr>
<td>4</td>
<td>16</td>
<td>NLT 75</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of bupropion hydrochloride (C$_{13}$H$_{18}$ClNO·HCl) dissolved at the times specified conform to Dissolution (711), Acceptance Table 2.
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) of bupropion hydrochloride (C₁₃H₁₈ClNO·HCl) in the sample withdrawn from the vessel at time point i:

\[ \text{Result}_i = \left( \frac{A_i}{A_S} \right) \times C_S \]

\( A_i \) = 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 (C₁₃H₁₈ClNO·HCl) dissolved at each time point (i):

\[ \text{Result}_1 = \frac{C_i \times V}{(1/L) \times 100} \]

\[ \text{Result}_2 = \left( \left[ C_S \times (V - V_i) \right] + (C_i \times V_i) \right) \times (1/L) \times 100 \]

\[ \text{Result}_3 = \left( \left[ C_S \times (V - (2 \times V_i)) \right] + \left[ (C_2 + C_3) \times V_j \right] \right) \times (1/L) \times 100 \]

\[ \text{Result}_4 = \left( \left[ C_4 \times (V - (3 \times V_i)) \right] + \left[ (C_2 + C_5) \times V_i \right] \right) \times (1/L) \times 100 \]

\( C_i \) = 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)
\( V_i \) = volume of Sample solution withdrawn from the Medium (mL)

Tolerances: See *Table 15.*

<table>
<thead>
<tr>
<th>Time Point (i)</th>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>NMT 25</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>25-50</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>60-85</td>
</tr>
<tr>
<td>4</td>
<td>12</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of bupropion hydrochloride (C₁₃H₁₈ClNO·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) of bupropion hydrochloride (C₁₃H₁₈ClNO·HCl) in the sample withdrawn from the vessel at time point i:

\[ \text{Result}_i = \left( \frac{A_i}{A_S} \right) \times C_S \]

\( A_i \) = 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 (C₁₃H₁₈ClNO·HCl) dissolved at each time point (i):

\[ \text{Result}_1 = \frac{C_i \times V}{(1/L) \times 100} \]

\[ \text{Result}_2 = \left( \left[ C_S \times (V - V_i) \right] + (C_i \times V_i) \right) \times (1/L) \times 100 \]

\[ \text{Result}_3 = \left( \left[ C_S \times (V - (2 \times V_i)) \right] + \left[ (C_2 + C_3) \times V_j \right] \right) \times (1/L) \times 100 \]

\[ \text{Result}_4 = \left( \left[ C_4 \times (V - (3 \times V_i)) \right] + \left[ (C_2 + C_5) \times V_i \right] \right) \times (1/L) \times 100 \]

\( C_i \) = 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)
\( V_i \) = volume of Sample solution withdrawn from the Medium (mL)

Tolerances: See *Table 16.*

<table>
<thead>
<tr>
<th>Time Point (i)</th>
<th>Time (h)</th>
<th>Amount Dissolved (150 mg/Tablet) (%)</th>
<th>Amount Dissolved (300 mg/Tablet) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>NMT 25</td>
<td>NMT 25</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>30-55</td>
<td>25-45</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>65-90</td>
<td>60-80</td>
</tr>
<tr>
<td>4</td>
<td>12</td>
<td>NLT 80</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

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C191670-M10524-CHM42015, Rev. 0 20171027
The percentages of the labeled amount of bupropion hydrochloride (C₁₃H₁₈ClNO \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-Visible
Analytical wavelength: 252 nm
Blank: Medium

Analysis

Samples: Standard solution and Sample solution
Calculate the concentration (C) of bupropion hydrochloride (C₁₃H₁₈ClNO \cdot HCl) in the sample withdrawn from the vessel at time point i:

\[ \text{Result}_1 = \left( \frac{A_i}{A_s} \right) \times C_i \times D \]

\[ A_i = \text{absorbance from the Sample solution at time point i} \]
\[ A_s = \text{absorbance from the Standard solution} \]
\[ C_i = \text{concentration of USP Bupropion Hydrochloride RS in the Standard solution (mg/mL)} \]
\[ D = \text{dilution factor for the Sample solution, if needed} \]

Calculate the percentage of the labeled amount of bupropion hydrochloride (C₁₃H₁₈ClNO \cdot HCl) dissolved at each time point (i):

\[ \text{Result}_1 = C_i \times V \times (1/L) \times 100 \]

\[ \text{Result}_2 = \left( (C_2 \times V) + (C_i \times V) \right) \times (1/L) \times 100 \]

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

\[ C_i = \text{concentration of bupropion hydrochloride in the portion of the sample withdrawn at time point i (mg/mL)} \]
\[ V = \text{volume of Medium, 900 mL} \]
\[ L = \text{label claim (mg/Tablet)} \]
\[ V_i = \text{volume of Sample solution withdrawn at each time point and replaced with Medium (mL)} \]

Tolerances: See Table 17.

<table>
<thead>
<tr>
<th>Time Point (h)</th>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>NMT 20</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>20-45</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>55-85</td>
</tr>
<tr>
<td>4</td>
<td>16</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of bupropion hydrochloride (C₁₃H₁₈ClNO \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 (C₁₃H₁₈ClNO \cdot HCl) dissolved:

\[ \text{Result} = \left( \frac{r_o}{r_i} \times C_i \right) \times V \times (1/L) \times 100 \]

\[ r_o = \text{peak response of bupropion from the Acid stage sample solution} \]
\[ r_i = \text{peak response of bupropion from the Acid stage standard solution} \]
\[ C_i = \text{concentration of USP Bupropion Hydrochloride RS in the Acid stage standard solution (mg/mL)} \]
\[ V = \text{volume of Acid stage medium, 900 mL} \]
\[ L = \text{label claim (mg/Tablet)} \]

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°C. Allow the solution to cool to 37°C before use. Do not allow the temperature to fall below 36.5°C 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) of bupropion hydrochloride (C₁₃H₁₈ClNO·HCl) in the sample withdrawn from the vessel at time point i:

Result₁ = (rᵢ/rₛ) × Cₛ

where:

rᵢ = peak response of bupropion from the Buffer stage sample solution at time point i
rₛ = peak response of bupropion from the Buffer stage standard solution
Cₛ = concentration of USP Bupropion Hydrochloride RS in the Buffer stage standard solution (mg/mL)

Calculate the percentage of the labeled amount of bupropion hydrochloride (C₁₃H₁₈ClNO·HCl) dissolved at each time point (i):

Result₂ = (Cₛ × (V - Vₛ)) + (Cⁱ × Vₛ) / (1/L) × 100

Result₃ = ((Cᵢ × (V - (2 × Vₛ))) / Vₛ) × (1/L) × 100

Result₄ = ((Cᵢ × (V - (3 × Vₛ))) / Vₛ) × (1/L) × 100

Table 18a

<table>
<thead>
<tr>
<th>Time Point (f)</th>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>5-25</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>25-45</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>60-85</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>NLT 85</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of bupropion hydrochloride (C₁₃H₁₈ClNO·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.

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, 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°C
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) of bupropion hydrochloride (C₁₃H₁₈ClNO·HCl) in the sample withdrawn from the vessel at time point i:

Result = (rᵢ/rₛ) × Cₛ × D

where:

rᵢ = peak response of bupropion from the Sample solution at time point i
rₛ = peak response of bupropion from the Standard solution
Cₛ = concentration of USP Bupropion Hydrochloride RS in the Standard solution (mg/mL)
D = dilution factor for the Sample solution, if needed

Tolerances
Acid stage: NMT 10%; the percentage of the labeled amount of bupropion hydrochloride (C₁₃H₁₈ClNO·HCl) dissolved at the time specified conforms to Dissolution (711), Acceptance Table 3.
Buffer stage: See Table 18.
Calculate the percentage of the labeled amount of bupropion hydrochloride \((C_{13}H_{18}ClNO \cdot HCl)\) dissolved at each time point \((i)\):  
\[
\text{Result}_1 = C_i \times V \times \left(\frac{1}{L}\right) \times 100
\]
\[
\text{Result}_2 = \left[\left(C_2 \times V\right) + \left(C_1 \times V_i\right)\right] \times \left(\frac{1}{L}\right) \times 100
\]
\[
\text{Result}_3 = \left[\left(C_1 \times V\right) + \left[C_2 + C_3\right] \times V_i\right] \times \left(\frac{1}{L}\right) \times 100
\]
\[
\text{Result}_4 = \left[\left(C_1 \times V\right) + \left[C_2 + C_3 + C_4\right] \times V_i\right] \times \left(\frac{1}{L}\right) \times 100
\]

- \(C_i\): 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>
<thead>
<tr>
<th>Time Point ((i))</th>
<th>Time ((h))</th>
<th>Amount Dissolved ((% ))</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>NMT 10</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>30–60</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>65–88</td>
</tr>
<tr>
<td>4</td>
<td>16</td>
<td>NLT 85</td>
</tr>
</tbody>
</table>

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 x 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 \((C)\) of bupropion hydrochloride \((C_{13}H_{18}ClNO \cdot HCl)\) in the sample withdrawn from the vessel at time point \(i\):  
\[
\text{Result}_i = \left(\frac{r_i}{r_s}\right) \times C_i
\]

- \(r_i\): peak response of bupropion from the Sample solution at time point \(i\)
- \(r_s\): peak response of bupropion from the Standard solution

\(C_i\): 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 \((i)\):  
\[
\text{Result}_i = \left(\frac{C_i \times V \times \left(\frac{1}{L}\right) \times 100}{\text{label claim (mg/Tablet)}}\right)
\]

### Tolerances:
See Table 20.

<table>
<thead>
<tr>
<th>Time Point ((i))</th>
<th>Time ((h))</th>
<th>Amount Dissolved (for Tablets that contain 150 mg of bupropion hydrochloride) ((% ))</th>
<th>Amount Dissolved (for Tablets that contain 300 mg of bupropion hydrochloride) ((% ))</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>NMT 20</td>
<td>NMT 20</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>25–50</td>
<td>25–50</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>65–95</td>
<td>60–85</td>
</tr>
<tr>
<td>4</td>
<td>16</td>
<td>NLT 80</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

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.

**Uniformity of Dosage Units (905):** Meet the requirements
ORGANIC IMPURITIES

**Bupropion**

Official November 1, 2017

Revision Bulletin

0.02 mg/mL of hydrochloride in System suitability stock solution A:

- Diluent 1, Solution A, Solution B, Mobile phase,
- and Hydrochloride 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 solution B: 0.012 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 21 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:

\[
\text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_S}{C_U} \right) \times 100
\]

- \(r_U\) = peak response of each degradation product from Sample solution A or Sample solution B
- \(r_S\) = peak response of 3-chlorobenzoic acid from Sample solution A or Sample 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:

\[
\text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_S}{C_U} \right) \times (1/F) \times 100
\]

**Acceptance criteria:** See Table 21.

### Table 21

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Relative Response Factor</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupropion amine &lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.38</td>
<td>1.2</td>
<td>0.3</td>
</tr>
<tr>
<td>5,5,5-Thiomorpholine derivative&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.56</td>
<td>1.1</td>
<td>1.0</td>
</tr>
<tr>
<td>5,5,5-Thiomorpholine derivative&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.78</td>
<td>1.1</td>
<td>0.5</td>
</tr>
<tr>
<td>Bupropion related compound F</td>
<td>1.71</td>
<td>1.8</td>
<td>1.2</td>
</tr>
<tr>
<td>Bupropion related compound C</td>
<td>1.75</td>
<td>1.7</td>
<td>0.3</td>
</tr>
<tr>
<td>3-Chlorobenzoic acid</td>
<td>1.80</td>
<td>—</td>
<td>0.3</td>
</tr>
<tr>
<td>Bupropion dione derivative&lt;sup&gt;d&lt;/sup&gt;</td>
<td>2.25</td>
<td>1.00</td>
<td>0.4</td>
</tr>
<tr>
<td>Any unspecified degradation product</td>
<td>—</td>
<td>1.00</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Total impurities: 3.2–3.3

<sup>a</sup>2-Amino-1-(3-chlorophenyl)-1-propanone.

<sup>b</sup>(35,55,55)-6-(3-Chlorophenyl)-6-hydroxy-5-methyl-3-thiomorpholine carboxylic acid.

<sup>c</sup>(35,55,55,55)-6-(3-Chlorophenyl)-6-hydroxy-5-methyl-3-thiomorpholine carboxylic acid.

<sup>d</sup>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)-1-hydroxypropan-1-one. C₇H₆O₂Cl = 184.62
  - USP Bupropion Hydrochloride Related Compound F RS
    - (1-(3-Chlorophenyl)-1-hydroxypropan-2-one. C₇H₆O₂Cl = 184.62

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Bupropion

C₉H₇O₂Cl  184.62
USP 3-Chlorobenzoic Acid RS
3-Chlorobenzoic acid.
C₇H₅ClO₂  156.57