### Bupropion Hydrochloride Extended-Release Tablets

<table>
<thead>
<tr>
<th>Type of Posting</th>
<th>Revision Bulletin</th>
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<td>Official Date</td>
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<tr>
<td>Expert Committee</td>
<td>Chemical Medicines Monographs 4</td>
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<td>Reason for Revision</td>
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</table>

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 Tests 20, 21, 22, and 23* to accommodate FDA-approved drug products with different dissolution conditions and/or tolerances than the existing dissolution tests. Additionally, the table number within the test for *Organic Impurities* and references to this table number were updated.

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

Should you have any questions, please contact Heather Joyce, 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 (C\(_{13}\)H\(_{18}\)ClNO · 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°
  Flow rate: 1.5 mL/min
  Injection volume: 5 μL

  System suitability
  Samples: System suitability solution and Standard solution
  [Note—See ▲Table 25▲ (RB 1-Feb-2019) 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 · HCl) in the portion of Tablets taken:

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

  \(r_U\) = 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).)

**(Apparatus 1):**

- 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\textsubscript{13}H\textsubscript{18}CINO · 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\textsubscript{13}H\textsubscript{18}CINO · 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):** Water; 900 mL

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

**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\textsubscript{13}H\textsubscript{18}CINO · HCl) dissolved.

**Tolerances:** See Table 3.

<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>40–65</td>
</tr>
<tr>
<td>4</td>
<td>65–90</td>
</tr>
<tr>
<td>6</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of bupropion hydrochloride (C\textsubscript{13}H\textsubscript{18}CINO · 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\textsubscript{13}H\textsubscript{18}CINO · HCl) dissolved.

**Tolerances:** See Table 4.

<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\textsubscript{13}H\textsubscript{18}CINO · 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
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: 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 (C₁₃H₁₈CINΟ · 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>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 (C₁₃H₁₈CINΟ · 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: Water; 900 mL

Apparatus 2: 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 (C₁₃H₁₈CINΟ · 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 (C₁₃H₁₈CINΟ · 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/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 (C₁₃H₁₈CINΟ · HCl) dissolved.

Tolerances: See Table 6.
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 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

The percentages of the labeled amount of bupropion hydrochloride (C₁₅H₁₈CINO · HCl) dissolved at the times specified conform to Dissolution (711), Acceptance Table 2.

Tolerances: See Table 8.

<table>
<thead>
<tr>
<th>Table 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time Point (i)</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
</tbody>
</table>

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 (C₁₅H₁₈CINO · HCl) dissolved at each time point (i):

\[
\text{Result, } i = (A/A_0) \times C \times V \times (1/L) \times 100
\]

Where:

- \( A_i \) = absorbance of bupropion hydrochloride from the Sample solution at time point \( i \)
- \( A_0 \) = 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 9.

<table>
<thead>
<tr>
<th>Table 9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time Point (i)</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of bupropion hydrochloride (C₁₅H₁₈CINO · HCl) dissolved at each time point (i):

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

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

\[
\text{Result}_3 = ((C_i \times V - 2 \times V_i) + (C_i \times V_i)) \times (1/L) \times 100
\]

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

Where:

- \( C_i \) = 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 at each time point (mL)

Tolerances: See Table 9.

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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 \((C_{13}H_{18}CINO \cdot HCl)\) dissolved at each time point \((i)\):

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

\(A_i\) = 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
\(V\) = volume of Medium, 900 mL
\(L\) = label claim (mg/Tablet)

Tolerances: See Table 10.

### Table 10

<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 or 200 mg of bupropion hydrochloride) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>32–52</td>
<td>25–45</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>50–70</td>
<td>45–65</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>NLT 75</td>
<td>65–85</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>NLT 85</td>
<td>NLT 85</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of bupropion hydrochloride \((C_{13}H_{18}CINO \cdot HCl)\) 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 \((C_{13}H_{18}CINO \cdot HCl)\) 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 \((C_{13}H_{18}CINO \cdot HCl)\) 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 \((C_{13}H_{18}CINO \cdot HCl)\) 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 \((C_{13}H_{18}CINO \cdot HCl)\) 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
6 Bupropion

Revision Bulletin
Official February 1, 2019

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 (C₃₄H₃₅ClNO · HCl) dissolved.

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 (C₃₄H₃₅ClNO · 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 trisodium 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.

Buffer stage standard solution: 0.15 mg/mL of USP Bupropion Hydrochloride RS in Buffer stage medium.

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 (C₃₄H₃₅ClNO · HCl) in the sample withdrawn from the vessel at time point i:

Resultᵢ = (Aᵢ/Aₛ) × Cᵢ

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

Aₛ = absorbance of bupropion hydrochloride from the Acid stage standard solution or Buffer stage standard solution

Cᵢ = 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 (C₃₄H₃₅ClNO · HCl) dissolved at each time point (i):

Resultᵢ = Cᵢ × Vᵢ × (1/L) × 100

Vᵢ = volume of Acid stage medium, 750 mL

L = label claim (mg/Tablet)

Vᵢ = volume of Buffer stage medium, 1000 mL

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

Tolerances: See Table 14.

<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>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 (C₃₄H₃₅ClNO · 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) of bupropion hydrochloride (C13H18ClNO·HCl) in the sample withdrawn from the vessel at time point i:

\[
\text{Result}_i = (A/A_0) \times C_i
\]

\(A_i\) = absorbance of bupropion hydrochloride from the Sample solution at time point i
\(A_0\) = absorbance of bupropion hydrochloride 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 (C13H18ClNO·HCl) dissolved at each time point (i):

\[
\text{Result}_1 = C_i \times V \times (1/L) \times 100
\]
\[
\text{Result}_2 = \left( [(C_i \times (V - V_0)) + (C_i \times V_0)] \times (1/L) \times 100
\]
\[
\text{Result}_3 = \left( [(C_i \times (V - (2 \times V_0))] + [(C_i + C_2 + C_3)] \times V_3)) \times (1/L) \times 100
\]
\[
\text{Result}_4 = \left( [(C_i \times (V - (3 \times V_0))] + [(C_i + C_2 + C_3)] \times V_3)) \times (1/L) \times 100
\]

\(C_i\) = 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 (h)</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:

\[
\text{Result}_1 = (A/A_0) \times C_i
\]

\(A_i\) = absorbance of bupropion hydrochloride from the Sample solution at time point i
\(A_0\) = absorbance of bupropion hydrochloride 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 (C13H18ClNO·HCl) dissolved at each time point (i):

\[
\text{Result}_1 = C_i \times V \times (1/L) \times 100
\]
\[
\text{Result}_2 = \left( [(C_i \times (V - V_0)) + (C_i \times V_0)] \times (1/L) \times 100
\]
\[
\text{Result}_3 = \left( [(C_i \times (V - (2 \times V_0))] + [(C_i + C_2 + C_3)] \times V_3)) \times (1/L) \times 100
\]
\[
\text{Result}_4 = \left( [(C_i \times (V - (3 \times V_0))] + [(C_i + C_2 + C_3)] \times V_3)) \times (1/L) \times 100
\]

\(C_i\) = 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 (h)</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>

The percentages of the labeled amount of bupropion hydrochloride (C13H18ClNO·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) of bupropion hydrochloride (C₈H₁₈CINO · HCl) in the sample withdrawn from the vessel at time point i:

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

Where:
- \( A_i \) = absorbance from the Sample solution at time point i
- \( A_i \) = absorbance from the Standard solution
- \( C_i \) = 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 (C₈H₁₈CINO · HCl) dissolved at each time point (i):

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

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

\[
\text{Result}_3 = \left( \frac{C_i \times V_i + (C_i \times V_j + C_j)}{1/L} \times 100 \right)
\]

\[
\text{Result}_4 = \left( \frac{C_i \times V_i + (C_i \times V_j + C_j + C_k)}{1/L} \times 100 \right)
\]

Where:
- \( C_i \) = concentration of bupropion hydrochloride in the portion of the sample withdrawn at time point i (mg/mL)
- \( V_i \) = volume of Medium, 900 mL
- \( L \) = label claim (mg/Tablet)
- \( V_j \) = 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>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NMT 20</td>
</tr>
<tr>
<td>2</td>
<td>20-45</td>
</tr>
<tr>
<td>3</td>
<td>55-85</td>
</tr>
<tr>
<td>4</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of bupropion hydrochloride (C₈H₁₈CINO · 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
**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**

**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 (C₈H₁₈CINO · HCl) dissolved:

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

Where:
- \( r_i \) = peak response of bupropion from the Acid stage sample solution
- \( r_k \) = peak response of bupropion from the Acid stage standard solution
- \( C_i \) = 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

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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 \((C_{13}H_{18}ClNO \cdot HCl)\) in the sample withdrawn from the vessel at time point \(i\):

\[
\text{Result}_i = \frac{r_i}{r_s} \times C_s
\]

where:
- \(r_i\) = 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 \(i\):

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

\[
\text{Result}_t = \left(\frac{(C_i + C_s)}{V - 2 \times V_s}\right) \times (1/L) \times 100
\]

\[
\text{Result}_4 = \left(\frac{(C_i + V)}{3 \times V_s}\right) \times (1/L) \times 100
\]

\[
\text{Tolerances}
\]

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>
<thead>
<tr>
<th>Time Point (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5–25</td>
</tr>
<tr>
<td>2</td>
<td>25–45</td>
</tr>
<tr>
<td>3</td>
<td>60–85</td>
</tr>
<tr>
<td>4</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 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) of bupropion hydrochloride \((C_{13}H_{18}ClNO \cdot HCl)\) in the sample withdrawn from the vessel at time point \(i\):

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

\[
\text{Result}_t = (C_i + C_s) \times (1/L) \times 100
\]

\[
\text{Result}_4 = (C_i + C_s + C_s) \times (1/L) \times 100
\]

\[
\text{Tolerances}
\]

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

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

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If the product complies with this test, the

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) of bupropion hydrochloride (C_{18}H_{26}CINO · HCl) in the sample withdrawn from the vessel at time point i:

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

\[
r_i = \text{peak response of bupropion from the Sample solution at time point } i
\]

\[
r_s = \text{peak response of bupropion from the Standard solution}
\]

\[
C_i = \text{concentration of USP Bupropion Hydrochloride RS in the Standard solution (mg/mL)}
\]

Calculate the percentage of the labeled amount of bupropion hydrochloride (C_{18}H_{26}CINO · HCl) dissolved at each time point (i):

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

The percentages of the labeled amount of bupropion hydrochloride (C_{18}H_{26}CINO · 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) of bupropion hydrochloride (C_{18}H_{26}CINO · HCl) in the sample withdrawn from the vessel at time point i:

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

\[
A_i = \text{absorbance from the Sample solution at time point } i
\]

\[
A_s = \text{absorbance from the Standard solution}
\]

\[
C_i = \text{concentration of USP Bupropion Hydrochloride RS in the Standard solution (mg/mL)}
\]

\[
D = \text{dilution factor for the Sample solution, if needed}
\]
Calculate the percentage of the labeled amount of bupropion hydrochloride \((C_{13}H_{18}CINO \cdot HCl)\) dissolved at each time point \(i\):

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

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

\[
\text{Result}_3 = [(C_i \times V) + (C_i + C_i) \times V] \times (1/L) \times 100
\]

\[
\text{Result}_4 = [(C_i \times V) + (C_i + C_i + C_i + V)] \times (1/L) \times 100
\]

\(C_i\) = 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 at each time point and replaced with Medium (mL)

Tolerances: See Table 21.

### Table 21

<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 15</td>
<td>NMT 15</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>10–35</td>
<td>10–35</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>50–75</td>
<td>50–75</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 \((C_{13}H_{18}CINO \cdot HCl)\) 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, deaerated

**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 \((C_{13}H_{18}CINO \cdot HCl)\) in the sample withdrawn from the vessel at time point \(i\):

\[
\text{Result}_i = (A_i / A) \times C_i 	imes D
\]

\(A_i\) = absorbance from the Sample solution at time point \(i\)

\(A\) = absorbance from the Standard solution

\(C_i\) = 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 \((C_{13}H_{18}CINO \cdot HCl)\) dissolved at each time point \(i\):

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

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

\[
\text{Result}_3 = [(C_i \times V) + (C_i + C_i) \times V] \times (1/L) \times 100
\]

\[
\text{Result}_4 = [(C_i \times V) + (C_i + C_i + C_i + V)] \times (1/L) \times 100
\]

\(C_i\) = 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 at each time point and replaced with Medium (mL)

Tolerances: See Table 22.

### Table 22

<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>4</td>
<td>NMT 20</td>
<td>NMT 30</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>35–60</td>
<td>50–70</td>
</tr>
<tr>
<td>3</td>
<td>16</td>
<td>NLT 80</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of bupropion hydrochloride \((C_{13}H_{18}CINO \cdot HCl)\) 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°C, 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

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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) of bupropion hydrochloride \((\text{C}_1\text{H}_18\text{ClNO} \cdot \text{HCl})\) in the sample withdrawn from the vessel at time point \(i\):

\[
\text{Result}_1 = \frac{(A_i/N)}{C_i} \times D
\]

\(A_i\) = absorbance from the Acid stage sample solution or Buffer stage sample solution at time point \(i\)

\(A_i\) = absorbance from the Acid stage standard solution or Buffer stage standard solution at time point \(i\)

\(C_i\) = 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 \((\text{C}_1\text{H}_18\text{ClNO} \cdot \text{HCl})\) dissolved in Acid stage medium:

\[
\text{Result}_1 = \frac{C_i \times V_{A}}{L} \times 100
\]

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

\(V_{A}\) = volume of Acid stage medium, 750 mL

\(L\) = label claim (mg/Tablet)

Calculate the percentage of the labeled amount of bupropion hydrochloride \((\text{C}_1\text{H}_18\text{ClNO} \cdot \text{HCl})\) dissolved at each time point \(i\):

\[
\text{Result}_2 = \frac{[(C_i \times V_{A} - V_{A} \cdot V_{SO}) + (C_{i} \times V_{SO})] \times 100}{V_{SO}}
\]

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

\(V_{A}\) = volume of Acid stage medium, 1000 mL

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

\(C_{i}\) = concentration of bupropion hydrochloride in the portion of the sample withdrawn at time point \(i\) (mg/mL)

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

Tolerances: See Table 23.

<table>
<thead>
<tr>
<th>Time Point</th>
<th>Time</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>NMT 15</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>40–60</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of bupropion hydrochloride \((\text{C}_1\text{H}_18\text{ClNO} \cdot \text{HCl})\) 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) of bupropion hydrochloride \((\text{C}_1\text{H}_18\text{ClNO} \cdot \text{HCl})\) dissolved in the sample withdrawn from the vessel at time point \(i\):

\[
\text{Result} = \frac{(A_i/N)}{C_i} \times D
\]

\(A_i\) = absorbance from the Acid stage sample solution or Buffer stage sample solution at time point \(i\)
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 2A (88:1-Feb-2019) 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 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:

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

\( r_U \) = peak response of each other degradation product from Sample solution A or Sample solution B

\( C_S \) = concentration of bupropion hydrochloride from the Standard solution

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

**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
\[ F = \text{relative response factor for each other degradation product (see Table 25)} \]

Acceptance criteria: See Table 25.

<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></td>
<td></td>
<td></td>
<td>100 mg or less</td>
</tr>
<tr>
<td>Total impurities</td>
<td>—</td>
<td>—</td>
<td>3.2</td>
</tr>
</tbody>
</table>

\(^a\) 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\(S\),\(S\),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