Bupropion Hydrochloride Extended-Release Tablets

Type of Posting: Notice of Intent to Revise
Posting Date: 27–December–2019
Targeted Official Date: To Be Determined, Revision Bulletin
Expert Committee: Chemical Medicines Monographs 4

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

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

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

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

See below for additional information about the proposed text.¹

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

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

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

**DEFINITION**

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

**IDENTIFICATION**

**Change to read:**

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197K (CN 1-May-2020)
- **Sample:** Crush 1 Tablet using a mortar and pestle. Prepare an approximate 1% (w/w) dispersion of the sample in potassium bromide.
- **Acceptance criteria:** The Sample shows strong bands at about 1690, 1560, and 1240 cm\(^{-1}\) and a weaker band at about 740 cm\(^{-1}\), similar to the reference preparation.
- **B.** The retention time of the major peak of Sample solution A or Sample solution B corresponds to that of the Standard solution, as obtained in the Assay.

**ASSAY**

**Change to read:**

- **PROCEDURE**
  - **Diluent 1:** Methanol and 0.001 N hydrochloric acid (20:80)
  - **Solution A:** Acetonitrile, trifluoroacetic acid, and water (10: 0.04: 90)
  - **Solution B:** Acetonitrile, trifluoroacetic acid, and water (95: 0.03: 5)
  - **Mobile phase:** See Table 1.

<table>
<thead>
<tr>
<th>Time</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 Standard stock solution A in 0.001 N hydrochloric acid
- **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
  - **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:
    \[ \text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_S}{C_U} \right) \times 100 \]
    
    \[ r_U = \text{peak response of bupropion hydrochloride from Sample solution A or Sample solution B} \]
    
    \[ r_S = \text{peak response of bupropion hydrochloride from the Standard solution} \]
    
    \[ C_S = \text{concentration of USP Bupropion Hydrochloride RS in the Standard solution (mg/mL)} \]
    
    \[ C_U = \text{nominal concentration of bupropion hydrochloride in Sample solution A or Sample solution B (mg/mL)} \]

- **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
2 Bupropion

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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$_{18}$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: 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 Water; 900 mL

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. Dilute with Medium, if necessary.

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

Chromatographic system

(See Chromatography (621), System Suitability.)

Mode: LC

Detector: UV 298 nm

Column: 4.6-mm × 15-cm; packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: Standard solution

Suitability requirements

Column efficiency: NLT 2000 theoretical plates

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: Standard solution and Sample solution

Determine the percentages of the labeled amount of bupropion hydrochloride (C$_{13}$H$_{18}$CINO·HCl) dissolved.

Tolerances: See Table 3.

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$_{13}$H$_{18}$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$_{13}$H$_{18}$CINO·HCl) dissolved.

Tolerances: See Table 4.

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$_{13}$H$_{18}$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

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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\textsubscript{13}H\textsubscript{18}ClNO·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\textsubscript{13}H\textsubscript{18}ClNO·HCl) dissolved at the times specified conform to Dissolution (711), Acceptance Table 2.

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

Medium: 0.1 N hydrochloric acid, pH 1.5 (prepared by transferring 50 mL of hydrochloric acid to 6000 mL of water, adding 18 g of sodium hydroxide, mixing, and adjusting with either diluted sodium hydroxide or hydrochloric acid to a pH of 1.5); 900 mL, deaerated
Apparatus 1: 50 rpm
Times: 1, 2, 4, and 6 h
Buffer: 3.45 g of monobasic sodium phosphate in 996 mL of water. Add 4.0 mL of triethylamine, and adjust with phosphoric acid to a pH of 2.80.
Mobile phase: Methanol and Buffer (45:55)
Standard solution: (L/900) mg/mL of USP Bupropion Hydrochloride RS in Medium, where L is the label claim, in mg/Tablet
Sample solution: Use portions of the solution under test, and pass through a nylon filter of 0.45-μm pore size.

Chromatographic system
(See Chromatography (621), System Suitability.)
Mode: LC
Detector: UV 298 nm
Column: 4.6-mm × 15-cm; packing L1
Flow rate: 1 mL/min
Injection volume: 20 μL

System suitability
Sample: Standard solution
Suitability requirements
Column efficiency: NLT 2000 theoretical plates
Tailing factor: NMT 2.0
Relative standard deviation: NMT 2.0%

Analysis
Samples: Standard solution and Sample solution
Determine the percentages of the labeled amount of bupropion hydrochloride (C\textsubscript{13}H\textsubscript{18}ClNO·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>
</tbody>
</table>

The percentages of the labeled amount of bupropion hydrochloride (C\textsubscript{13}H\textsubscript{18}ClNO·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, deaerated
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\textsubscript{13}H\textsubscript{18}ClNO·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\textsubscript{13}H\textsubscript{18}ClNO·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
Blank: Medium

System suitability
Sample: Standard solution

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>

Table 6 (continued)

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

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\textsubscript{13}H\textsubscript{18}ClNO·HCl) dissolved at the times specified conform to Dissolution (711), Acceptance Table 2.

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>
</tbody>
</table>
4 Bupropion

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

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

\(A_i\) = absorbance of bupropion hydrochloride from the Sample solution at time point \(i\)
\(A_f\) = 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>3</td>
<td>4</td>
<td>55-85</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of bupropion hydrochloride \((C_{13}H_{18}CNO \cdot HCl)\) 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 sample withdrawn at time point \(i\) through a suitable filter of 10-µm pore size.

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

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

\(r_i\) = peak response of bupropion from the Sample solution at time point \(i\)
\(r_f\) = 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 \((C_{13}H_{18}CNO \cdot HCl)\) dissolved at each time point \((i)\):

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

\(C_i\) = 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 (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 80</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

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

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

Medium: Water, degassed; 900 mL

Apparatus 1: 50 rpm
Times: 1, 2, 4, and 8 h
Standard stock solution: 0.56 mg/mL of USP Bupropion Hydrochloride RS in Medium

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

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

### Bupropion

**Instrumental conditions**
(See Ultraviolet-Visible Spectroscopy (857).)

- **Mode:** UV-Vis
- **Analytical wavelength:** 298 nm
- **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 \((i)\):  
    \[
    \text{Result, } \% = (A/A_i) \times C_i \times V \times (1/L) \times 100
    \]
  - \(A_i\) = absorbance of bupropion from the Sample solution at time point \(i\)
  - \(A_s\) = absorbance of bupropion from the Standard solution
  - \(C_i\) = 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 10.

#### Table 10

<table>
<thead>
<tr>
<th>Time Point ((h))</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
- **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

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6 Bupropion

Test 11: The absorbance of bupropion hydrochloride from the Dissolution Test 11 indicates that it meets USP 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

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 (C₁₅H₁₈ClNO · HCl) dissolved
Tolerances: See Table 12.

### 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 (C₁₅H₁₈ClNO · 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. 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 (C₁₅H₁₈ClNO · HCl) in the sample withdrawn from the vessel at time point i:

\[
\text{Result}_i = \left( \frac{A_i}{A_{i\text{r}}} \right) \times C_i
\]

where

- \(A_i\) = absorbance of bupropion hydrochloride from the Sample solution at time point i
- \(A_{i\text{r}}\) = absorbance of bupropion hydrochloride from the Acid stage standard solution or Buffer stage standard solution

\(C_i\) = concentration of bupropion hydrochloride in the Acid stage medium or Buffer stage medium (mg/mL)

Calculate the percentage of the labeled amount of bupropion hydrochloride (C₁₅H₁₈ClNO · HCl) dissolved at each time point i:

\[
\text{Result}_i = \left( \frac{C_i \times V_i \times (1/L)}{900} \right) \times 100
\]

**Tolerances**: See Table 14.

### Table 14

<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 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 (C₁₅H₁₈ClNO · 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: 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 (C₁₅H₁₈ClNO · HCl) in the sample withdrawn from the vessel at time point i:

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Result\textsubscript{i} = (A\textsubscript{i}/A\textsubscript{j}) × C\textsubscript{i}

A\textsubscript{i} = absorbance of bupropion hydrochloride from the Sample solution at time point \(i\)
A\textsubscript{j} = absorbance of bupropion hydrochloride from the Standard solution
C\textsubscript{i} = concentration of USP Bupropion Hydrochloride RS in the Standard solution (mg/mL)

Calculate the percentage of the labeled amount of bupropion hydrochloride (C\textsubscript{13}H\textsubscript{18}CINO · HCl) dissolved at each time point (\(i\)):

Result\textsubscript{1} = C\textsubscript{1} × V × (1/L) × 100
Result\textsubscript{2} = ([C\textsubscript{2} × (V - V\textsubscript{2})] + [C\textsubscript{1} × V\textsubscript{2}]) × (1/L) × 100
Result\textsubscript{3} = ([C\textsubscript{2} × (V - 2 × V\textsubscript{2})] + [C\textsubscript{1} + C\textsubscript{2} × V\textsubscript{2}]) × (1/L) × 100
Result\textsubscript{4} = ([C\textsubscript{2} × (V - 3 × V\textsubscript{2})] + [C\textsubscript{1} + C\textsubscript{2} + C\textsubscript{3} × V\textsubscript{2}]) × (1/L) × 100

C\textsubscript{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\textsubscript{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 (C\textsubscript{13}H\textsubscript{18}CINO · 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 (C\textsubscript{13}H\textsubscript{18}CINO · HCl) in the sample withdrawn from the vessel at time point \(i\):

Result\textsubscript{1} = (A\textsubscript{1}/A\textsubscript{j}) × C\textsubscript{1}

A\textsubscript{1} = absorbance of bupropion hydrochloride from the Sample solution at time point \(i\)
A\textsubscript{j} = absorbance of bupropion hydrochloride from the Standard solution
C\textsubscript{1} = concentration of USP Bupropion Hydrochloride RS in the Standard solution (mg/mL)

Calculate the percentage of the labeled amount of bupropion hydrochloride (C\textsubscript{13}H\textsubcript{18}CINO · HCl) dissolved at each time point (\(i\)):

Result\textsubscript{1} = C\textsubscript{1} × V × (1/L) × 100
Result\textsubscript{2} = ([C\textsubscript{2} × (V - V\textsubscript{2})] + [C\textsubscript{1} × V\textsubscript{2}]) × (1/L) × 100
Result\textsubscript{3} = ([C\textsubscript{2} × (V - 2 × V\textsubscript{2})] + [C\textsubscript{1} + C\textsubscript{2} × V\textsubscript{2}]) × (1/L) × 100
Result\textsubscript{4} = ([C\textsubscript{2} × (V - 3 × V\textsubscript{2})] + [C\textsubscript{1} + C\textsubscript{2} + C\textsubscript{3} × V\textsubscript{2}]) × (1/L) × 100

C\textsubscript{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\textsubscript{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>

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 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 (C\textsubscript{13}H\textsubscript{18}CINO · HCl) in the sample withdrawn from the vessel at time point \(i\):

Result\textsubscript{1} = (A\textsubscript{1}/A\textsubscript{j}) × C\textsubscript{1}

A\textsubscript{1} = absorbance of bupropion hydrochloride from the Sample solution at time point \(i\)
A\textsubscript{j} = absorbance of bupropion hydrochloride from the Standard solution
C\textsubscript{1} = concentration of USP Bupropion Hydrochloride RS in the Standard solution (mg/mL)
Bupropion

Result, \( t \) = \((A/A_t) \times C_t \times D\)

\( A_t \) = absorbance from the Sample solution at time point \( t \)
\( A_i \) = absorbance from the Standard solution
\( C_t \) = 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\(_{18}\)H\(_{26}\)ClNO · HCl) dissolved at each time point (\( t \)):

\[
\text{Result, } t = C_t \times V \times (1/L) \times 100
\]

\[
\text{Result, } i = [(C_t \times V) + (C_i \times V_i)] \times (1/L) \times 100
\]

\[
\text{Result, } s = [(C_t \times V) + [(C_i + C_s) \times V_s]] \times (1/L) \times 100
\]

\( C_t \) = concentration of bupropion hydrochloride in the portion of the sample withdrawn at time point \( t \) (mg/mL)
\( V = \text{volume of Medium, } 900 \text{ mL}
\( L = \text{label claim (mg/Tablet)}
\( V_s = \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 (( i ))</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>SS-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 (C\(_{18}\)H\(_{26}\)ClNO · 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 3.5 g of monobasic sodium phosphate in 996 mL of water, add 4.0 mL of triethylamine, and adjust with phosphoric acid to a pH of 2.8.

Mobile phase: Methanol and Buffer (45:55)

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

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

Chromatographic system

(See Chromatography (621), System Suitability.)

Mode: LC

Detector: UV 298 nm

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

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 1.5 times the retention time of bupropion

System suitability

Sample: Acid stage standard solution

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: Acid stage standard solution and Acid stage sample solution

Calculate the percentage of the labeled amount of bupropion hydrochloride (C\(_{18}\)H\(_{26}\)ClNO · HCl) dissolved:

\[
\text{Result} = (r_v/r_r) \times C_t \times V \times (1/L) \times 100
\]

\( r_v \) = peak response of bupropion from the Acid stage sample solution

\( r_r \) = peak response of bupropion from the Acid stage standard solution

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

\( V = \text{volume of Acid stage medium, } 900 \text{ 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°. Allow the solution to cool to 37° before use. Do not allow the temperature to fall below 36.5° before beginning the test.); 900 mL

Apparatus 1: 100 rpm

Times: 1, 2, 4, and 8 h

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

Mobile phase: Acetonitrile and Buffer (60:40)

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

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

Chromatographic system: Proceed as directed under the Acid stage.

System suitability

Sample: Buffer stage standard solution

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: Buffer stage standard solution and Buffer stage sample solution

Calculate the concentration (\( C \)) of bupropion hydrochloride (C\(_{18}\)H\(_{26}\)ClNO · HCl) in the sample withdrawn from the vessel at time point \( t \):

\[
\text{Result, } t = (r_v/r_r) \times C_t
\]

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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

Table 18

<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>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 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)

Detector: UV 298 nm

Column: 4.6-mm x 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 (C₁₃H₁₈ClNO · HCl) in the sample withdrawn from the vessel at time point i:

Result = (rᵢ/rₛ) × Cₛ × D

Test 18:

<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>NLT 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 (C₁₃H₁₈ClNO · HCl) dissolved at the times specified conform to Dissolution (711), Acceptance Table 2.
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 (C13H18ClNO · HCl) in the sample withdrawn from the vessel at time point i:

Resulti = (ri/ri) × Ci

ri = peak response of bupropion from the Sample solution at time point i
ri = peak response of bupropion from the Standard solution
Ci = 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 ():

Resulti = Ci × V × (1/L) × 100

Result1 = ((C1 × (V – V2)) + (C1 × V2)) × (1/L) × 100

Result2 = ((C2 + C3) × V2) × (1/L) × 100

Result3 = ((C2 × (V – (2 × V3))) + (C2 + C3) × V3) × (1/L) × 100

Result4 = ((C2 × (V – (3 × V4))) + (C2 + C3 + C4) × V4) × (1/L) × 100

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

Tolerances: See Table 20.

Table 20 (continued)

<table>
<thead>
<tr>
<th>Time Point (h)</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>
</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 20: If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 20.

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

Apparatus 1: 75 rpm

Times: 2, 4, 8, and 16 h

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

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

Instrumental conditions
(See Ultraviolet-Visible Spectroscopy (857).)

Mode: UV-Vis

Analytical wavelength: 298 nm

Blank: Medium

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

Resulti = (Ai/Ai) × Ci × D

Ai = absorbance from the Sample solution at time point i
Ai = absorbance from the Standard solution
Ci = 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 (C13H18ClNO · HCl) dissolved at each time point ():

Resulti = Ci × V × (1/L) × 100

Result1 = (C1 × (V + V2)) + (C1 × V2) × (1/L) × 100

Result2 = ((C2 + C3) × V2) × (1/L) × 100

Result3 = ((C2 × (V – (2 × V3))) + (C2 + C3) × V3) × (1/L) × 100

Result4 = ((C2 × (V – (3 × V4))) + (C2 + C3 + C4) × V4) × (1/L) × 100

Ci = 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 = volume of Sample solution withdrawn at each time point (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>55–80</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 \((C_{17}H_{18}CINO \cdot HCl)\) 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 \((C)\) of bupropion hydrochloride \((C_{17}H_{18}CINO \cdot HCl)\) in the sample withdrawn from the vessel at time point \(i\):

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

\(A_i\) = 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 \((C_{17}H_{18}CINO \cdot HCl)\) dissolved at each time point (i):

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

\[
\text{Result}_2 = \left[ (C_i \times V) + (C_i \times V_2) \right] \times (1/L) \times 100
\]

\[
\text{Result}_3 = \left[ (C_i \times V) + (C_i + C_s) \times V_3 \right] \times (1/L) \times 100
\]

\(C_i\) = 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 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 \((C_{17}H_{18}CINO \cdot HCl)\) 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

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 \((C_{17}H_{18}CINO \cdot HCl)\) in the sample withdrawn from the vessel at time point \(i\):

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

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

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12 Bupropion

\[ A_i = \text{absorbance from the Acid stage standard solution or Buffer stage standard solution at time point } i \]

\[ C_i = \text{concentration of USP Bupropion Hydrochloride RS in the Acid stage standard solution or Buffer stage standard solution (mg/mL)} \]

\[ D = \text{dilution factor, if needed} \]

Calculate the percentage of the labeled amount of bupropion hydrochloride (\(C_{11}\)H\(_{18}\)CINO · HCl) dissolved in Acid stage medium:

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

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

\[ V_A = \text{volume of Acid stage medium, 750 mL} \]

\[ L = \text{label claim (mg/Tablet)} \]

Calculate the percentage of the labeled amount of bupropion hydrochloride (\(C_{11}\)H\(_{18}\)CINO · HCl) dissolved at each time point (i):

\[ \text{Result}_1 = (C_i \times V_A - V_{sa}) \times (1/L) \times 100 \]

\[ \text{Result}_2 = (C_i \times V_A - V_{sa} - V_{sb}) \times (1/L) \times 100 \]

\[ \text{Result}_3 = (C_i \times V_A - V_{sa} + V_{sb}) + (C_i \times V_{sa}) \times (1/L) \times 100 \]

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

\[ V_A = \text{volume of Buffer stage medium, 1000 mL} \]

\[ V_{sa} = \text{volume of Acid stage sample solution withdrawn at time point } 1 \text{ (mL)} \]

\[ L = \text{label claim (mg/Tablet)} \]

\[ V_{sb} = \text{volume of Buffer stage sample solution withdrawn at each time point (mL)} \]

**Tolerances:** See Table 23.

<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 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 (\(C_{11}\)H\(_{18}\)CINO · 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 (\(C_{11}\)H\(_{18}\)CINO · HCl) in the sample withdrawn from the vessel at time point i:

\[ \text{Result}_1 = A_i \times A_i \times C_i \]

\[ A_i = \text{absorbance from the Acid stage sample solution or Buffer stage sample solution at time point } i \]

\[ A_i = \text{absorbance from the Acid stage standard solution or Buffer stage standard solution at time point } i \]

\[ C_i = \text{concentration of USP Bupropion Hydrochloride RS in the Acid stage standard solution or Buffer stage standard solution (mg/mL)} \]

Calculate the percentage of the labeled amount of bupropion hydrochloride (\(C_{11}\)H\(_{18}\)CINO · HCl) dissolved in Acid stage medium (Q):

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

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

\[ V_A = \text{volume of Acid stage medium, 900 mL} \]

\[ L = \text{label claim (mg/Tablet)} \]

Calculate the percentage of the labeled amount of bupropion hydrochloride (\(C_{11}\)H\(_{18}\)CINO · HCl) dissolved at each time point (i):

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

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

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

\[ V_b = \text{volume of Buffer stage medium, 900 mL} \]

\[ L = \text{label claim (mg/Tablet)} \]

\[ Q_a = \text{percentage of the labeled amount of bupropion hydrochloride dissolved in the Acid stage medium} \]

**Tolerances:** See Table 24.

<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 15</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
<td>50-75</td>
</tr>
<tr>
<td>3</td>
<td>16</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

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

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

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

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

**Apparatus 1:** 50 rpm

**Times**

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

For Tablets labeled to contain 300 mg of bupropion hydrochloride: 2 h in Acid stage medium; 3, 6, 10, and 16 h in Buffer stage medium. The time in the Buffer stage medium includes the time in the Acid stage medium.

**Acid stage standard solution:** $(L)/900$ mg/mL of USP Bupropion Hydrochloride RS in Acid stage medium, where $L$ is the label claim, in mg/Tablet. Sonication may be used to promote dissolution. Pass the resulting solution through a suitable filter of 0.45-µm pore size, discarding the first 1 mL of filtrate. Use the solution within 1 h.

**Buffer stage standard solution:** $(L)/900$ mg/mL of USP Bupropion Hydrochloride RS in Buffer stage medium, where $L$ is the label claim, in mg/Tablet. Sonication may be used to promote dissolution. Pass the resulting solution through a suitable filter of 0.45-µm pore size, discarding the first 1 mL of filtrate.

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

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

**Instrumental conditions**

(See Ultraviolet-Visible Spectroscopy (857).)

**Mode:** UV

**Analytical wavelength:** 298 nm

**Cell:** 0.5 cm

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

**System suitability**

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

**Suitability requirements**

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

**Analysis**

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

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

$$C_i = \left( \frac{A_i}{A_o} \right) \times C_o$$

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

$$\text{Result}_1 = C_i \times V_o \times (1/L) \times 100$$

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

$$\text{Result}_j = \left( \frac{C_j \times V_j \times (1/L) \times 100 + Q_o}{V_o} \right)$$

Where:

- $C_j$ = concentration of bupropion hydrochloride in the portion of the sample withdrawn at time point $j$ (mg/mL)
- $V_j$ = volume of Acid stage medium, 900 mL
- $L$ = label claim (mg/Tablet)
- $Q_o$ = percentage of the labeled amount of bupropion hydrochloride dissolved in the Acid stage medium
- $V_o$ = volume of Sample solution withdrawn at each time point and replaced with Medium (mL)

**Tolerances:** See Table 25.

### Table 25

<table>
<thead>
<tr>
<th>Time Point ($j$)</th>
<th>For Tablets Labeled to Contain 150 mg of Bupropion Hydrochloride</th>
<th>For Tablets Labeled to Contain 300 mg of Bupropion Hydrochloride</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Time ($h$)</td>
<td>Amount Dissolved (%)</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>NMT 10</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>11–31</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>41–61</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>64–84</td>
</tr>
<tr>
<td>5</td>
<td>14</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

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C238075-M10524-CHM42015, rev. 00 20191227
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 USP 3-Chlorobenzoic Acid RS in methanol

System suitability solution B: 0.012 mg/mL of USP Bupropion Hydrochloride Related Compound C RS, 0.02 mg/mL of USP Bupropion Hydrochloride Related Compound F RS, and 0.0012 mg/mL of USP 3-Chlorobenzoic Acid RS in methanol

System suitability solution B: 0.0012 mg/mL of 3-Chlorobenzoic Acid RS in methanol

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

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

System suitability solution 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

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

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

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

**System suitability**

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

[NOTE—See Table 26 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:

\[
\text{Result} = \left( \frac{r_u}{r_s} \right) \times \left( \frac{C_s}{C_u} \right) \times 100
\]

where:

- \( r_u \) = 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:

\[
\text{Result} = \left( \frac{r_u}{r_s} \right) \times \left( \frac{C_s}{C_u} \right) \times (1/F) \times 100
\]

where:

- \( F \) = relative response factor for each other degradation product (see Table 26)

Acceptance criteria: See Table 26.

<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>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>S, S, S-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>S, R, R-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</td>
<td>1.0</td>
<td>—</td>
<td>—</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>
<tr>
<td>Total impurities</td>
<td>—</td>
<td>—</td>
<td>3.2</td>
</tr>
</tbody>
</table>

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

<sup>b</sup> (35,55,65)-6-(3-Chlorophenyl)-6-hydroxy-5-methyl-3-thiomorpholine carboxylic acid.

<sup>c</sup> (35,5R,6R)-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)-2-hydroxypropan-1-one.

C<sub>9</sub>H<sub>13</sub>Cl 184.62

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### Notice of Intent to Revise

**Official: To Be Determined**

<table>
<thead>
<tr>
<th>USP Bupropion Hydrochloride Related Compound F RS</th>
<th>USP 3-Chlorobenzoic Acid RS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-(3-Chlorophenyl)-1-hydroxypropan-2-one.</td>
<td>3-Chlorobenzoic acid.</td>
</tr>
<tr>
<td>C₉H₈O₂Cl 184.62</td>
<td>C₇H₅ClO₂ 156.57</td>
</tr>
</tbody>
</table>