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 to accommodate drug products which were approved with different dissolution conditions and acceptance criteria.

- **Dissolution Test 16** was validated using an ACE 5 C18 brand of L1 column. The typical retention time for bupropion is about 10 min.
- **Dissolution Test 17 and 18** were validated using a Symmetry C8 brand of L7 column. The typical retention time for bupropion is about 2.6 min.

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

Should you have any questions, please contact Heather Joyce, Ph.D., Senior Scientific Liaison (301–998–6792 or hrj@usp.org.)
Bupropion Hydrochloride Extended-Release Tablets

**DEFINITION**

Bupropion Hydrochloride Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of bupropion hydrochloride (C<sub>13</sub>H<sub>18</sub>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<sup>-1</sup> and a weaker band at about 740 cm<sup>-1</sup>, similar to the reference preparation.

**ASSAY**

**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.

**Change to read:**

- **B.** The retention time of the major peak of Standard solution A or Sample solution B (RB 1-Aug-2016) corresponds to supernatant.

**ASSAY**

**Change to read:**

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. Immedi-

ate 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 (RB 1-Aug-2016) 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 20 (RB 1-Jun-2017) for the relative retention times.]**

**Suitability requirements**

**Resolution:** NLT 1.3 between bupropion hydrochloride related compound F and bupropion hydrochloride related compound C, System suitability solution

**Tailing factor:** NMT 1.9, Standard solution

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

**Analysis**

**Samples:** Standard solution and Sample solution A or Sample solution B

Calculate the percentage of the labeled amount of bupropion hydrochloride (C<sub>13</sub>H<sub>18</sub>ClNO · HCl) in the portion of Tablets taken:

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

\(r_u\) = peak response of bupropion hydrochloride from Sample solution A or Sample solution B

\(r_s\) = peak response of bupropion hydrochloride from the Standard solution

\(C_s\) = concentration of USP Bupropion Hydrochloride RS in the Standard solution (mg/mL)

\(C_U\) = nominal concentration of bupropion hydrochloride in Sample solution A or Sample solution B (mg/mL)
Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

**Change to read:**

- **Dissolution (711)**
  
  For products labeled for dosing every 12 h
  
  **Test 1**
  
  Medium: Water; 900 mL
  
  Apparatus 2: 50 rpm
  
  Times: 1, 4, and 8 h
  
  Standard solution: \((L/900)\) mg/mL of USP Bupropion Hydrochloride RS in Medium, where \(L\) is the label claim, in mg/Tablet. Dilute with Medium, if necessary.
  
  Sample solution: Pass a portion of the solution under test through a suitable filter, and dilute with Medium, if necessary.
  
  **Instrumental conditions**
  
  (See Ultraviolet-Visible Spectroscopy (857).)
  
  Mode: UV-Vis
  
  Analytical wavelength: 298 nm
  
  Blank: Medium
  
  **Analysis**
  
  Samples: Standard solution and Sample solution
  
  Determine the percentages of the labeled amount of bupropion hydrochloride \((C_{13}H_{18}ClNO \cdot HCl)\) dissolved.
  
  **Tolerances:** See Table 2.

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25–45</td>
</tr>
<tr>
<td>4</td>
<td>60–85</td>
</tr>
<tr>
<td>8</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of bupropion hydrochloride \((C_{13}H_{18}ClNO \cdot HCl)\) dissolved at the times specified conform to *Dissolution (711), Acceptance Table 2.* (88 1-Aug-2016)

**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* • (88 1-Aug-2016) 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* • (88 1-Aug-2016) in 996 mL of water. Add 4.0 mL of triethylamine, and adjust with phosphoric acid to a pH of 2.80.

Mobile phase: Methanol and Buffer (35:65)

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

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

Chromatographic system

(See Chromatography (621), System Suitability.)

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

The percentages of the labeled amount of bupropion hydrochloride \((C_{13}H_{18}ClNO \cdot HCl)\) dissolved at the
Test 5: If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 5.

Medium: Water; 900 mL.
Apparatus 2: 50 rpm
Times: 1, 3, and 6 h
Standard solution: (L/900) mg/mL of USP Bupropion Hydrochloride RS in Medium, where L is the label claim, in mg/Tablet. Dilute with Medium, if necessary.
Sample solution: Pass a portion of the solution under test through a suitable filter, and dilute with Medium, if necessary.

Instrumental conditions (See Ultraviolet-Visible Spectroscopy (857).)
Mode: UV-Vis
Analytical wavelength: 298 nm
Cell: 0.5 cm
Blank: Medium

Analysis
Samples: Standard solution and Sample solution
Determine the percentages of the labeled amount of bupropion hydrochloride (C_{13}H_{18}ClNO·HCl) dissolved.

Tolerances: See Table 5.

Table 5

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

The percentages of the labeled amount of bupropion hydrochloride (C_{13}H_{18}ClNO·HCl) dissolved at the times specified conform to •Dissolution (711), Acceptance Table 2. (88 1-Aug-2016)

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• (88 1-Aug-2016) 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• (88 1-Aug-2016) in 996 mL of water. Add 4.0 mL of triethylamine, and adjust with phosphoric acid to a pH of 2.80.
Mobile phase: Methanol and Buffer (45:55)
Standard solution: (L/900) mg/mL of USP Bupropion Hydrochloride RS in Medium, where L is the label claim, in mg/Tablet
Sample solution: Use portions of the solution under test, and pass through a nylon filter of 0.45-µm pore size.
Chromatographic system (See Chromatography (621), System Suitability.)

Mode: LC
Detector: UV 298 nm
Column: 4.6-mm × 15-cm; packing L1
Flow rate: 1 mL/min
Injection volume: 20 µL

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

Analysis
Samples: Standard solution and Sample solution
Determine the percentages of the labeled amount of bupropion hydrochloride (C_{13}H_{18}ClNO·HCl) dissolved.

Tolerances: See Table 6.

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>4</td>
<td>45–70</td>
</tr>
<tr>
<td>6</td>
<td>NLT 70</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of bupropion hydrochloride (C_{13}H_{18}ClNO·HCl) dissolved at the times specified conform to •Dissolution (711), Acceptance Table 2. (88 1-Aug-2016)

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• (88 1-Aug-2016) to 6000 mL of water, adding 18 g of sodium hydroxide, mixing, and adjusting with either diluted sodium hydroxide or hydrochloric acid to a pH of 1.5); 900 mL.
Apparatus 1: 50 rpm
Times: 1, 2, 4, and 8 h
Standard solution: (L/1000) mg/mL of USP Bupropion Hydrochloride RS in Medium, where L is the label claim, in mg/Tablet
Sample solution: Pass a portion of the solution under test through a suitable filter.

Instrumental conditions (See Ultraviolet-Visible Spectroscopy (857).)
Mode: UV-Vis
Analytical wavelength: 298 nm
Blank: Medium

Analysis
Samples: Standard solution and Sample solution
Determine the percentages of the labeled amount of bupropion hydrochloride (C_{13}H_{18}ClNO·HCl) dissolved.

Tolerances: See Table 7.

Table 7

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

The percentages of the labeled amount of bupropion hydrochloride (C_{13}H_{18}ClNO·HCl) dissolved at the times specified conform to •Dissolution (711), Acceptance Table 2. (88 1-Aug-2016)
Bupropion

Test 10: If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 10.
Medium: Water; 900 mL
Apparatus 2: 50 rpm
Times: 1, 2, 4, and 8 h
Standard solution: (L/900) mg/mL of USP Bupropion Hydrochloride RS in Medium, where L is the label claim, in mg/Tablet
Sample solution: Pass a portion of the solution under test through a suitable filter.
Instrumental conditions
(See Ultraviolet-Visible Spectroscopy (857).)
Mode: UV-Vis
Analytical wavelength: 298 nm
Cell: 0.5 cm
Blank: Medium
System suitability
Sample: Standard solution
Suitability requirements
Relative standard deviation: NMT 2.0%
Analysis
Samples: Standard solution and Sample solution
Calculate the percentage of the labeled amount of bupropion hydrochloride (C₁₃H₁₈ClNO·HCl) dissolved at each time point (i):

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

\[\begin{align*}
A_i &= \text{absorbance of bupropion hydrochloride from the Sample solution at time point } i \\
A_S &= \text{absorbance of bupropion hydrochloride from the Standard solution} \\
C_i &= \text{concentration of USP Bupropion Hydrochloride RS in the Standard solution (mg/mL)} \\
V &= \text{volume of Medium, 900 mL} \\
L &= \text{label claim (mg/Tablet)}
\end{align*}\]

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 (C₁₃H₁₈ClNO·HCl) dissolved at the times specified conform to *Dissolution (711), Acceptance Table 2.*

*Test 17: If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 17.
Medium: 0.1 N hydrochloric acid, pH 1.5 (prepared by transferring 50 mL of hydrochloric acid to 6 L of water containing 18 g of sodium hydroxide, mixing, and adjusting with either diluted sodium hydroxide or diluted hydrochloric acid to a pH of 1.5), 900 mL, deaerated
Apparatus 1: 50 rpm
Times: 1, 2, 4, and 8 h
Buffer: To each liter of water add 6.8 g of monobasic potassium phosphate. Adjust with phosphoric acid to a pH of 3.0.
Mobile phase: Methanol and Buffer (60:40)
Standard solution: (L/900) mg/mL of USP Bupropion Hydrochloride RS in Medium, where L is the label claim, in mg/Tablet. Sonication may be used to promote dissolution.
Sample solution: Pass a portion of the solution under test through a suitable filter. [NOTE—A 0.45-µm nylon membrane filter may be suitable.]
Chromatographic system
(See Chromatography (621), System Suitability.)
Mode: LC
Detector: UV 298 nm
Column: 4.6-mm 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
Relative standard deviation: NMT 2.0%
Analysis
Samples: Standard solution and Sample solution
Calculate the concentration (C) of bupropion hydrochloride (C₁₃H₁₈ClNO·HCl) in the sample withdrawn from the vessel at time point i:

\[
\text{Result}_i = (r_i/r_S) \times C_i
\]

\[\begin{align*}
r_i &= \text{peak response of bupropion from the Sample solution at time point } i \\
r_S &= \text{peak response of bupropion from the Standard solution} \\
C_i &= \text{concentration of USP Bupropion Hydrochloride RS in the Standard solution (mg/mL)}
\end{align*}\]

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

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

\[
\text{Result}_i = \left(\frac{(C_i \times (V - (2 \times V_i)) + (C_i \times (C_i \times V_i))) \times (1/L) \times 100}{(C_i \times (V - (3 \times V_i))) + (C_i \times (C_i \times V_i))) \times (1/L) \times 100} \right)
\]

\[
\text{Result}_i = \left(\frac{(C_i \times (V - (4 \times V_i))) + (C_i \times (C_i \times V_i))) \times (1/L) \times 100}{(C_i \times (V - (5 \times V_i))) + (C_i \times (C_i \times V_i))) \times (1/L) \times 100} \right)
\]

\[
\text{Result}_i = \left(\frac{(C_i \times (V - (6 \times V_i))) + (C_i \times (C_i \times V_i))) \times (1/L) \times 100}{(C_i \times (V - (7 \times V_i))) + (C_i \times (C_i \times V_i))) \times (1/L) \times 100} \right)
\]

\[\begin{align*}
C &= \text{concentration of bupropion hydrochloride in the portion of the sample withdrawn at time point } i \text{ (mg/mL)} \\
V &= \text{volume of Medium, 900 mL} \\
L &= \text{label claim (mg/Tablet)} \\
V_i &= \text{volume of Sample solution withdrawn at each time point (mL)}
\end{align*}\]

Tolerances: See Table 9.

<table>
<thead>
<tr>
<th>Time Point (i)</th>
<th>Time (h)</th>
<th>Amount Dissolved (for Tablets that contain 100 mg of bupropion hydrochloride) (%)</th>
<th>Amount Dissolved (for Tablets that contain 150 mg or 200 mg of bupropion hydrochloride) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>20-40</td>
<td>15-35</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>40-60</td>
<td>35-55</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>60-85</td>
<td>55-80</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>NLT 85</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>
The percentages of the labeled amount of bupropion hydrochloride (C_{13}H_{18}ClNO \cdot HCl) dissolved at the times specified conform to Dissolution (711), Acceptance Table 2. (RB 1-Aug-2016)

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 Bupro- pion Hydrochloride RS in Medium, where \(L\) is the label claim, in mg/Tablet. Dilute with Medium, if necessary.

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

Instrumental conditions

(See Ultraviolet-Visible Spectroscopy (857).)

Mode: UV-Vis

Analytical wavelength: 252 nm

Blank: Medium

Analysis

Samples: Standard solution and Sample solution

Determine the percentages of the labeled amount of bupropion hydrochloride (C_{13}H_{18}ClNO \cdot HCl) dissolved.

Tolerances: See Table 10.

<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>

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: 2, 4, 8, and 12 h

Standard solution: \((L/900)\) mg/mL of USP Bupro- pion Hydrochloride RS in Medium, where \(L\) is the label claim, in mg/Tablet. Dilute with Medium, if necessary.

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

Instrumental conditions

(See Ultraviolet-Visible Spectroscopy (857).)

Mode: UV-Vis

Analytical wavelength: 298 nm

Cell: 0.5 cm (RB 1-Aug-2016)

Blank: Medium

Analysis

Samples: Standard solution and Sample solution

Determine the percentages of the labeled amount of bupropion hydrochloride (C_{13}H_{18}ClNO \cdot HCl) dissolved.

Tolerances: See Table 11.

<table>
<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>

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 (Add 250 mL of \(7.6 \ g/L\) tribasic sodium phosphate (RB 1-Aug-2016) 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.

Instrumental conditions

(See Ultraviolet-Visible Spectroscopy (857).)

Mode: UV-Vis

Analytical wavelength: 298 nm

Cell: 0.5 cm (RB 1-Aug-2016)

Blank: Medium

Analysis

Samples: Standard solution and Sample solution

Determine the percentages of the labeled amount of bupropion hydrochloride (C_{13}H_{18}ClNO \cdot HCl) dissolved.

Tolerances: See Table 12.

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

The percentages of the labeled amount of bupropion hydrochloride (C_{13}H_{18}ClNO \cdot HCl) dissolved at the times specified conform to Dissolution (711), Acceptance Table 2. (RB 1-Aug-2016)
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 (C13H18ClNO · HCl) in the sample withdrawn from the vessel at time point i:

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

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

\[A_S = \text{absorbance of bupropion hydrochloride from the Acid stage standard solution or Buffer stage standard solution}\]

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

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

\[
\text{Result}_1 = C_1 \times V_S \times (1/L) \times 100
\]

\[
\text{Result}_2 = \left\{ \left[ C_2 \times (V_6 - V_5) \right] + (C_1 \times V_S) \right\} \times (1/L) \times 100
\]

\[
\text{Result}_3 = \left\{ \left[ C_3 \times (V_8 - 2 \times V_7) \right] + (C_2 + C_1) \times V_S \right\} \times (1/L) \times 100
\]

\[
\text{Result}_4 = \left\{ \left[ C_4 \times (V_7 - 3 \times V_6) \right] + (C_3 + C_2 + C_1) \times V_S \right\} \times (1/L) \times 100
\]

\[C_1 = \text{concentration of bupropion hydrochloride in the portion of the sample withdrawn at time point } i \text{ (mg/mL)}\]

\[V_6 = \text{volume of Acid stage medium, 750 mL}\]

\[V_8 = \text{volume of Buffer stage medium, 1000 mL}\]

\[V_S = \text{volume of Sample solution withdrawn from the Acid stage medium or Buffer stage medium (mL)}\]

Tolerances: See Table 13.

<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 (C13H18ClNO · HCl) dissolved at the times specified conform to *Dissolution (711), Acceptance Table 2.* (88:1-Aug-2016)

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:

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

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

\[A_S = \text{absorbance of bupropion hydrochloride from the Standard solution}\]

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

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

\[
\text{Result}_1 = C_1 \times V \times (1/L) \times 100
\]

\[
\text{Result}_2 = \left\{ \left[ C_2 \times (V - V_3) \right] + (C_1 \times V_S) \right\} \times (1/L) \times 100
\]

\[
\text{Result}_3 = \left\{ \left[ C_3 \times (V - 2 \times V_2) \right] + (C_2 + C_1) \times V_S \right\} \times (1/L) \times 100
\]

\[
\text{Result}_4 = \left\{ \left[ C_4 \times (V - 3 \times V_1) \right] + (C_3 + C_2 + C_1) \times V_S \right\} \times (1/L) \times 100
\]

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

\[V = \text{volume of Medium, 900 mL}\]

\[V_S = \text{volume of Sample solution withdrawn from the Medium (mL)}\]

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 25</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>25–50</td>
</tr>
</tbody>
</table>
### Table 14ε (Revised 1-Jun-2017)  (Continued)

<table>
<thead>
<tr>
<th>Time Point (h)</th>
<th>Time Point (1)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<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.* (Revised 1-Aug-2016)

**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**

**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 t:

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

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

\[ A_0 = \text{absorbance of bupropion hydrochloride from Standard solution} \]

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

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

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

\[ \text{Result}_2 = [(C_2 \times V) - (V_0)] \times (1/L) \times 100 \]

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

\[ \text{Result}_4 = [(C_2 + C_1) \times V] \times (1/L) \times 100 \]

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

\[ V = \text{volume of Medium, 900 mL} \]

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

\[ V_0 = \text{volume of Sample solution withdrawn from the Medium (mL)} \]

\[ D = \text{dilution factor for the Sample solution, if needed} \]

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

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

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

\[ \text{Result}_3 = [(C_3 + C_2) \times V] \times (1/L) \times 100 \]

\[ \text{Result}_4 = [(C_3 + C_2 + C_1) \times V] \times (1/L) \times 100 \]

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

### Table 15ε (Revised 1-Jun-2017)

<table>
<thead>
<tr>
<th>Time Point (h)</th>
<th>Time Point (1)</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.* (Revised 1-Aug-2016)

**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 (C₁₃H₁₈ClNO · HCl) in the sample withdrawn from the vessel at time point t:

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

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

\[ A_0 = \text{absorbance from the Standard solution} \]

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

\[ D = \text{dilution factor for the Sample solution, if needed} \]

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

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

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

\[ \text{Result}_3 = [(C_3 + C_2) \times V] \times (1/L) \times 100 \]

\[ \text{Result}_4 = [(C_3 + C_2 + C_1) \times V] \times (1/L) \times 100 \]

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

\[ V = \text{volume of Medium, 900 mL} \]

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8 Bupropion

\[ L = \text{label claim (mg/Tablet)} \]
\[ V_i = \text{volume of Sample solution withdrawn at each time point and replaced with Medium (mL)} \]

Tolerances: See Table 16.

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

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

Test 15: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 15*.

Acid stage

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

**Apparatus 1:** 100 rpm

**Time:** 2 h in Acid stage medium

**Buffer:** 3.5 g/L of monobasic sodium phosphate prepared as follows. Dissolve 3.45 g of monobasic sodium phosphate in 996 mL of water, add 4.0 mL oftriethylamine, 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 dilution.

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

**Chromatographic system:** (See Chromatography (621), System Suitability.)

**Mode:** LC

**Detector:** UV 298 nm

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

**Flow rate:** 1 mL/min

**Injection volume:** 10 μL

**Run time:** NLT 1.5 times the retention time of bupropion

System suitability

**Sample:** Acid stage standard solution

**Suitability requirements**

**Tailing factor:** NMT 2.0

**Relative standard deviation:** NMT 2.0%

**Analysis**

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

Calculate the percentage of the labeled amount of bupropion hydrochloride \((C_{13}H_{18}ClNO \cdot HCl)\) dissolved:

\[
\text{Result} = \frac{r_i}{r_s} \times C_1 \times V \times \left( \frac{1}{1} \right) \times 100
\]

\[ r_o = \text{peak response of bupropion from the Acid stage sample solution} \]
\[ r_s = \text{peak response of bupropion from the Acid stage standard solution} \]
\[ C_1 = \text{concentration of USP Bupropion Hydrochloride RS in the Acid stage standard solution (mg/mL)} \]
\[ V = \text{volume of Acid stage medium, 900 mL} \]
\[ L = \text{label claim (mg/Tablet)} \]

**Buffer stage:** Use fresh Tablets.

**Buffer stage medium:** pH 6.8 tribasic sodium phosphate buffer and 0.5% sodium lauryl sulfate (Dissolve 19 g of tribasic sodium phosphate in 1 L of water, add 7 mL of hydrochloric acid, and adjust with 0.2 N sodium hydroxide or dilute hydrochloric acid to a pH of 6.8. Add 5 g of sodium dodecyl sulfate. To promote dissolution, the resulting solution can be continuously stirred and heated to 41°. 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 \((C_{13}H_{18}ClNO \cdot HCl)\) in the sample withdrawn from the vessel at time point \(i\):

\[
\text{Result}_i = \left( C_1 \times V \times \left( \frac{1}{1} \right) \right) \times 100
\]

\[ r_i = \text{peak response of bupropion from the Buffer stage sample solution at time point } i \]
\[ r_s = \text{peak response of bupropion from the Buffer stage standard solution} \]
\[ C_1 = \text{concentration of USP Bupropion Hydrochloride RS in the Buffer stage standard solution (mg/mL)} \]

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

\[
\text{Result}_i = \left( C_1 \times V \times \left( \frac{1}{1} \right) \right) \times 100
\]

\[ C_1 = \text{concentration of bupropion hydrochloride in the portion of the sample withdrawn at time point } i \text{ (mg/mL)} \]
\[ V = \text{volume of Buffer stage medium, 900 mL} \]
\[ L = \text{label claim (mg/Tablet)} \]
The percentages of the labeled amount of bupropion hydrochloride (C₁₃H₁₈ClNO · HCl) dissolved at the times specified conform to Dissolution (711), Acceptance Table 2.

### Test 16: If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 16.

**Medium:** 0.1 N hydrochloric acid; deaerated; 900 mL

**Apparatus 1:** 75 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 (35:65)

**Standard solution:** 0.17 mg/mL of USP Bupropion Hydrochloride RS in Medium. Sonication may be used to promote dilution.

**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 (Cₜ) of bupropion hydrochloride (C₁₃H₁₈ClNO · HCl) in the sample withdrawn from the vessel at time point (t):  

$$C_t = \frac{(r_s/r_f) \times C_s \times D}{100}$$  

Where:

- $r_s$ = peak response of bupropion from the Sample solution at time point (t)  
- $r_f$ = peak response of bupropion from the Standard solution

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; deaerated; 900 mL

**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

**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

The percentages of the labeled amount of bupropion hydrochloride (C₁₃H₁₈ClNO · HCl) dissolved at the times specified conform to Dissolution (711), Acceptance Table 2.
### 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 (CS) of bupropion hydrochloride (C13H18ClNO·HCl) in the sample withdrawn from the vessel at time point t:

$$\text{Result}_1 = \frac{r_U}{r_S} \times C_S$$

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

$$\text{Result}_3 = \frac{(C_1 \times (V - (3 \times V_S))) + (C_2 + C_3) \times V_S}{(1/L) \times 100}$$

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

$$V = \text{volume of Medium, 900 mL}$$

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

$$V_S = \text{volume of Sample solution withdrawn at each time point (mL)}$$

**Tolerances:** See Table 19.

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

  **System suitability solution B:** 0.0012 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 detector wavelength.]

  **System suitability**

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

  **Suitability requirements**

  **Resolution:** NLT 1.3 between bupropion hydrochloride related compound 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:

  $$\text{Result} = \frac{(r_U/r_S) \times (C_S/C_D) \times 100}{1/F}$$

  $$r_U = \text{peak response of 3-chlorobenzoic acid from Sample solution A or Sample solution B}$$

  $$r_S = \text{peak response of 3-chlorobenzoic acid from System suitability solution B}$$

  $$C_S = \text{concentration of USP 3-Chlorobenzoic Acid RS in System suitability solution B (mg/mL)}$$

  $$C_D = \text{nominal concentration of bupropion hydrochloride in Sample solution A or Sample solution B (mg/mL)}$$

  Calculate the percentage of each other degradation product in the portion of Tablets taken:

  $$\text{Result} = \frac{(r_U/r_S) \times (C_S/C_D) \times (1/F) \times 100}{1/F}$$

### Table 19

<table>
<thead>
<tr>
<th>Time Point</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>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>25–50</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>65–95</td>
</tr>
<tr>
<td>4</td>
<td>16</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of bupropion hydrochloride (C13H18ClNO·HCl) dissolved at the times specified conform to Dissolution (711), Acceptance Table 2. [Note—See Table 20• (DB 1-Jun-2013) for the relative retention times.]

**Uniformity of Dosage Units (905):** Meet the requirements.
Table 20a (8B 1-Jun-2017) (Continued)

<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>3-Chlorobenzoic acid</td>
<td>1.80</td>
<td></td>
<td>0.3</td>
</tr>
<tr>
<td>Bupropion dione</td>
<td>2.25</td>
<td></td>
<td>1.00</td>
</tr>
<tr>
<td>Any unspecified</td>
<td>—</td>
<td></td>
<td>1.00</td>
</tr>
<tr>
<td>Total impurities</td>
<td>—</td>
<td></td>
<td>3.2</td>
</tr>
</tbody>
</table>

<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 amine²</td>
<td>0.38</td>
<td>1.2</td>
<td>0.3</td>
</tr>
<tr>
<td>S,5,5,3-Thi-omorpholine derivative³</td>
<td>0.56</td>
<td>1.1</td>
<td>1.0</td>
</tr>
<tr>
<td>S,5,5,3-Thi-omorpholine derivative³</td>
<td>0.78</td>
<td>1.1</td>
<td>0.5</td>
</tr>
<tr>
<td>Bupropion related compound F</td>
<td>1.00</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>
</tbody>
</table>

<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>2-Amino-1-(3-chlorophenyl)-1-propanone.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(3,5,5,6,5)-6-(3-Chlorophenyl)-6-hydroxy-5-methyl-3-thiomorpholine carboxylic acid.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(3,5,6,6,6)-6-(3-Chlorophenyl)-6-hydroxy-5-methyl-3-thiomorpholine carboxylic acid.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-(3-Chlorophenyl)propane-1,2-dione.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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.
    \[C_6H_6ClO_2 \quad 184.62\]
  - USP Bupropion Hydrochloride Related Compound F RS 1-(3-Chlorophenyl)-1-hydroxypropan-2-one.
    \[C_6H_6ClO_2 \quad 184.62\]
  - USP 3-Chlorobenzoic Acid RS 3-Chlorobenzoic acid.
    \[C_6H_5ClO_2 \quad 156.57\]