Oxybutynin Chloride Extended-Release Tablets

Type of Posting          Revision Bulletin
Posting Date            27–Sep–2019
Official Date           01–Oct–2019
Expert Committee        Chemical Medicines Monographs 3
Reason for Revision     Compliance

In accordance with the Rules and Procedures of the 2015–2020 Council of Experts, the Chemical Medicines Monographs 3 Expert Committee has revised the Oxybutynin Chloride Extended-Release Tablets monograph. The purpose for this revision is to add *Dissolution Test 9* to accommodate FDA-approved drug products with different tolerances than the existing dissolution tests. In addition, *Procedure 2* has been added to the *Assay* to incorporate different *Diluent* and *Sample solution* preparations to accommodate a sponsor’s *Assay* method for this drug product.

- *Dissolution Test 9* was validated using a Hypersil BDS C8 brand of L7 column. The typical retention time for oxybutynin is about 4.5 min.

- *Assay, Procedure 2* was validated using an Inertsil Phenyl brand of L11 column. The typical retention time for oxybutynin is about 5.5 min.

The revision also necessitates an update to the cross-references in the test for *Organic Impurities*.

The Oxybutynin Chloride Extended-Release Tablets Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Behnaz Almasi, Scientific Liaison (301-816-3412 or ba@usp.org).
Oxybutynin Chloride Extended-Release Tablets

**DEFINITION**
Oxybutynin Chloride Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of oxybutynin chloride (C_{22}H_{23}NO_3·HCl).

**IDENTIFICATION**

- **A. INFRARED ABSORPTION (197)**
  - **Standard:** Dissolve 15 mg of USP Oxybutynin Chloride RS in 5 mL of water. Adjust with 0.1 N sodium hydroxide to a pH of between 7 and 8. Extract the solution twice with 10 mL of ether. Combine the extracts, evaporate the ether, and dry under vacuum over silica gel for at least 30 min. Redissolve the dried residue in a small amount of acetone, transfer the solution to an IR salt plate, and evaporate to cast a thin film.
  - **Sample:** Add a quantity of finely powdered Tablets, equivalent to about 15 mg of oxybutynin chloride, to 5 mL of water per Tablet. Mix for 1 min. Adjust with 0.1 N sodium hydroxide to a pH between 7 and 8. Extract the solution twice with 10 mL of ether. Combine the extracts, evaporate the ether, and dry under vacuum over silica gel for at least 30 min. Redissolve the dried residue in a small amount of acetone, transfer the solution to an IR salt plate, and evaporate to cast a thin film.

- **B.** The retention time of the major peak of the Sample solution corresponds to that of the Standard solution, as obtained in the Assay.

**ASSAY**

**Change to read:**

- **PROCEDURE 1**
  - **Diluent:** Use water adjusted with phosphoric acid to a pH of 3.5.
  - **Solution A:** Methanol and acetonitrile (1:1)
  - **Mobile phase:** Acetonitrile, triethylamine, and water (700:3:1300). Adjust with phosphoric acid to a pH of 3.9.
  - **Impurity stock solution:** 0.11 mg/mL of USP Oxybutynin Chloride Related Compound A RS in acetonitrile
  - **Standard stock solution:** 0.37 mg/mL of USP Oxybutynin Chloride RS in acetonitrile
  - **System suitability solution:** Transfer 10 mL of the Standard stock solution and 1 mL of the Impurity stock solution to a 100-mL volumetric flask, and dilute with Diluent to volume.
  - **Standard solution:** 0.1 mg/mL of USP Oxybutynin Chloride RS in Diluent from the Standard stock solution
  - **Sample solution**
    - For Tablets that contain 5 mg of oxybutynin chloride: Place 10 Tablets in a 500-mL volumetric flask, add 150 mL of Solution A, and stir for at least 4 h or until dissolved. Dilute with Diluent to volume. Mix thoroughly, centrifuge, and use the clear supernatant.
    - For Tablets that contain 10 mg or more of oxybutynin chloride: Place 10 Tablets in a 1000-mL volumetric flask, add 300 mL of Solution A, and stir for at least 4 h or until dissolved. Dilute with Diluent to volume. If necessary, make a further dilution with Diluent to obtain a solution having a final concentration equivalent to 0.1 mg/mL of oxybutynin chloride. Mix thoroughly, centrifuge, and use the clear supernatant.
  - **Chromatographic system**
    - (See Chromatography (621), System Suitability.)
    - **Mode:** LC
    - **Detector:** UV 220 nm
  - **Analysis**
    - **Acceptance criteria:** 90.0%–110.0%

  **Add the following:**

- **PROCEDURE 2:** Use Procedure 2 for Tablets labeled to meet the requirements of USP Dissolution Test 9.
  - **Mobile phase, Chromatographic system, System suitability and Analysis:** Proceed as directed in Assay Procedure 1.
  - **Diluent:** Methanol and water (80:20)
  - **Impurity stock solution:** 0.11 mg/mL of USP Oxybutynin Related Compound A RS in methanol. Sonicate to dissolve, if necessary.
  - **Standard stock solution:** 0.37 mg/mL of USP Oxybutynin Chloride RS in Diluent. Sonicate to dissolve, if necessary.
  - **System suitability solution:** Transfer 10 mL of the Standard stock solution and 1 mL of the Impurity stock solution to a 100-mL volumetric flask, and dilute with Diluent to volume.
  - **Standard solution:** 0.1 mg/mL of USP Oxybutynin Chloride RS in Diluent from the Standard stock solution
  - **Sample solution**
    - Nominally 0.1 mg/mL of oxybutynin chloride prepared as follows. Place 10 Tablets in an appropriate volumetric flask, add 60% of the flask volume of Diluent, and sonicate for at least 60 min with intermittent shaking. Maintain the temperature of the sonicator between 20 and 25°C. Dilute with Diluent to volume. Mix thoroughly, centrifuge, and use the clear supernatant. Further dilute with Diluent as needed. [Note—Centrifuging at 6000 rpm for 10 min may be suitable.]
  - **Acceptance criteria:** 90.0%–110.0%
### Performance Tests

**Change to read:**

- **Dissolution (711)**
  
  **Test 1**
  
  **Medium:** Simulated gastric fluid without enzyme; 50 mL
  
  **Apparatus 7:** See Drug Release (724), 30 cycles/min; 2–3-cm amplitude, at 37.0 ± 0.5°C
  
  **Times:** 4, 10, and 24 h
  
  **Solution A:** 4.83 g/L of monobasic sodium phosphate in water. Add 2.3 mL/L of triethylamine, and adjust with phosphoric acid to a pH of 2.2 ± 0.2.
  
  **Mobile phase:** Acetonitrile and Solution A (7:13)
  
  **Solution B:** To 1 L of water add phosphoric acid to a pH of 2.2 ± 0.2.
  
  **Standard stock solutions:** 250, 300, and 350 µg/mL of USP Oxybutynin Chloride RS in acetonitrile
  
  **Standard solutions:** Prepare a series of dilutions of the Standard stock solutions in Solution B having final concentrations similar to those expected in the Sample solution.
  
  **System suitability:** Use a medium range Standard solution of USP Oxybutynin Chloride RS.
  
  **Sample solution:** Use portions of the solution under test.
  
  If the solution is cloudy, centrifuge at 2000 rpm for 10 min, and use the supernatant.
  
  **Chromatographic system**
  
  (See Chromatography (621), System Suitability.)
  
  **Mode:** LC
  
  **Detector:** UV 230 nm
  
  **Column:** 4.6-mm × 5-cm; packing L11
  
  **Column temperature:** 35°C
  
  **Flow rate:** 1.5 mL/min
  
  **Injection volume:** 50 µL
  
  **System suitability**
  
  **Sample:** System suitability solution
  
  **Suitability requirements**
  
  **Tailing factor:** Greater than 0.5 and less than 2.5
  
  **Relative standard deviation:** NMT 2.0%
  
  **Analysis**
  
  **Samples:** Standard solutions and Sample solution
  
  Construct a calibration curve by plotting the peak response versus concentration of the Standard solutions. A weighing factor, 1/𝑥, is applied to the regression line of the calibration curve to enhance the accuracy of the low standard concentrations.
  
  Determine the percentage of oxybutynin chloride (C₂₂H₂₅NO₃··HCl) dissolved in each interval from a linear regression analysis of the calibration curve.
  
  **Tolerances:** See Tables 1 and 2.

| Table 1. For Tablets Labeled to Contain 5 or 10 mg of Oxybutynin Chloride |
|-------------------------------------------------|-----------------|
| Time (h) | Amount Dissolved |
| 4 | NMT 20% |
| 10 | 34.5%–59.5% |
| 24 | NLT 80% |

| Table 2. For Tablets Labeled to Contain 15 mg of Oxybutynin Chloride |
|-------------------------------------------------|-----------------|
| Time (h) | Amount Dissolved |
| 4 | NMT 20% |
| 10 | 34.5%–59.5% |

The percentages of the labeled amount of oxybutynin chloride (C₂₂H₂₅NO₃··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 the product meets USP Dissolution Test 2.

**Acid stage medium:** Simulated gastric fluid, without enzymes, pH 1.2 ± 0.05; 250 mL (first row)

**Buffer stage medium:** Simulated gastric fluid, without enzymes, pH 6.8 ± 0.1; 250 mL (rows 2–4)

**Apparatus 3:** 25 dips/min; 20-mesh polypropylene screen on top and bottom; 30 s drip time

**Times:** 2 h in the Acid stage medium (first row); 4, 8, and 16 h (corresponding to 2, 6, and 14 h after changing the medium) in the Buffer stage medium (rows 2–4)

**Solution A:** Transfer 1 mL of triethylamine to 1000 mL of water. Adjust with phosphoric acid to a pH of 3.50 ± 0.05.

**Mobile phase:** Acetonitrile and Solution A (4:1)

**Standard stock solution:** 0.2 mg/mL of USP Oxybutynin Chloride RS in Acid stage medium.

**Working standard solution:** Transfer 5.0 mL of the Standard stock solution for Tablets labeled to contain 5 mg, transfer 10 mL for Tablets labeled to contain 10 mg, or transfer 15 mL for Tablets labeled to contain 15 mg to a 100-mL volumetric flask. Dilute with Buffer stage medium to volume.

**Sample solution:** Centrifuge a portion of the solution under test at approximately 3000 rpm for 10 min. Use the supernatant.

**Chromatographic system**

(See Chromatography (621), System Suitability.)

**Mode:** LC

**Detector:** UV 203 nm

**Column:** 4.6-mm × 25-cm; packing L7

**Flow rate:** 1.5 mL/min

**Injection volume:** 25 µL

**System suitability**

**Sample:** Working standard solution

**Suitability requirements**

**Tailing factor:** NMT 2.0%

**Relative standard deviation:** NMT 3.0%

**Analysis**

**Samples:** Working standard solution and Sample solution

Calculate the percentage of the labeled amount of oxybutynin chloride (C₂₂H₂₅NO₃··HCl) dissolved at each time point (Cₖ₆, C₄₆, C₇₄, C₉₆):

\[ C_i = \frac{r_i}{r_0} \times \frac{(C_i/L) \times V \times 100}{L} \]

\( r_0 \) = peak response from the Sample solution

\( r_i \) = peak response from the Working standard solution

\( C_i \) = concentration of the Working standard solution (mg/mL)

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

\( V \) = volume of Medium, 250 mL

\( C_{172} \) = percentage dissolved at 2 h, \( C_2 \)

\( C_{174} \) = percentage dissolved at 4 h, \( C_4 + C_2 \)

\( C_{178} \) = percentage dissolved at 8 h, \( C_8 + C_4 + C_2 \)

\( C_{1716} \) = percentage dissolved at 16 h, \( C_8 + C_4 + C_2 + \sum C_i \)
Tolerances: See Tables 3 and 4.

**Table 3. For Tablets Labeled to Contain 5 or 10 mg of Oxybutynin Chloride**

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>0%–10%</td>
</tr>
<tr>
<td>4</td>
<td>10%–30%</td>
</tr>
<tr>
<td>8</td>
<td>40%–65%</td>
</tr>
<tr>
<td>16</td>
<td>NLT 80%</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of oxybutynin chloride \((\text{C}_22\text{H}_{31}\text{NO}_3 \cdot \text{HCl})\) 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 the product meets USP Dissolution Test 3.

**Medium:** Simulated gastric fluid without enzyme; 50 mL

**Apparatus 7:** See Drug Release (724). Use acrylic rods. 30 dips/min, 37.0 ± 0.5 \(^\circ\)C, 10 s drip time. Dip time interval: row 1, 1 h; row 2, 3 h; row 3, 6 h; row 4, 5 h; row 5, 9 h.

**Times:** 4, 10, and 24 h

**pH 2.3 phosphate buffer:** 3.4 g/L of monobasic potassium phosphate in water. Adjust with phosphoric acid or 2 N potassium hydroxide to a pH of 2.30 ± 0.05.

**Standard solution:** \((L/200)\) mg/mL of USP Oxybutynin Chloride 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 nylon filter of 0.45-µm pore size, discarding the first few mL.

**Mobile phase:** pH 2.3 phosphate buffer and acetonitrile \((7:3)\)

**Chromatographic system**

(See Chromatography (621), System Suitability.)

**Mode:** LC

**Detector:** UV 220 nm

**Column:** 4.6-mm × 15-cm; packing L10

**Flow rate:** 1.0 mL/min

**Injection volume:** 20 µL

**System suitability**

**Sample:** Standard solution

**Suitability requirements**

**Tailing factor:** NMT 2.0

**Relative standard deviation:** NMT 2.0%

**Analysis**

Calculate the amount, in mg, of oxybutynin chloride \((\text{C}_22\text{H}_{31}\text{NO}_3 \cdot \text{HCl})\) dissolved at each time interval:

\[
\text{Result} = (r_u/r_s) \times (C_u/L) \times V
\]

**Tolerances:** See Table 5.

**Table 4. For Tablets Labeled to Contain 15 mg of Oxybutynin Chloride**

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>0%–10%</td>
</tr>
<tr>
<td>4</td>
<td>10%–30%</td>
</tr>
<tr>
<td>8</td>
<td>35%–65%</td>
</tr>
<tr>
<td>16</td>
<td>NLT 75%</td>
</tr>
</tbody>
</table>

**Table 5**

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>NMT 25%</td>
</tr>
<tr>
<td>10</td>
<td>40%–65%</td>
</tr>
<tr>
<td>24</td>
<td>NLT 75%</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of oxybutynin chloride \((\text{C}_22\text{H}_{31}\text{NO}_3 \cdot \text{HCl})\) dissolved at the times specified conform to Dissolution (711), Acceptance Table 2.

**Test 4:** If the product complies with this test, the labeling indicates that the product meets USP Dissolution Test 4.

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

**Buffer stage medium:** pH 6.0 sodium phosphate buffer with 0.2% of sodium lauryl sulfate; 900 mL

**Apparatus 2:** 50 rpm, with sinkers. [NOTE—A suitable sinker is available as catalog number CAPWHT-2S from www.QLA-LLC.com.]

**Times:** 2 h in the Acid stage medium; 4, 6, and 14 h (corresponding to 2, 4, T2 h after changing the medium) in the Buffer stage medium

**Standard solution:** \((L/1000)\) mg/mL of USP Oxybutynin Chloride RS in Buffer stage medium, where \(L\) is the label claim, in mg/Tablet

**Sample solution:** Pass a portion of the solution under test through a suitable PVDF filter of 0.45-µm pore size.

**pH 3.5 phosphate buffer:** 6.94 g/L of monobasic potassium phosphate in water. Adjust with diluted phosphoric acid to a pH of 3.50 ± 0.05.

**Mobile phase:** pH 3.5 phosphate buffer and acetonitrile \((1:1)\)

**Chromatographic system**

(See Chromatography (621), System Suitability.)

**Mode:** LC

**Detector:** UV 210 nm

**Column:** 4.6-mm × 15-cm; packing L7

**Flow rate:** 1.0 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**

Calculate the concentration \((C)\) in mg/mL of oxybutynin chloride \((\text{C}_22\text{H}_{31}\text{NO}_3 \cdot \text{HCl})\) at each time point \((i)\):

\[
C_i = (r_u/r_s) \times C_u
\]

\[
r_u = \text{peak response from the Sample solution}
\]

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

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If the product complies with this test, the labeling

Test 5:

= label claim (mg/Tablet)

\[Q_i = (C_i \times V/L) \times 100\]

At \(i = 2\) to \(n\)

\[
\left( C_j \times 900 \right) + \sum_{j=i}^{n-1} \left( \frac{1}{2} C_j V_s + C_{n-1} \times [900 - (n - 2) V_s] \times 100 \right)
\]

\(i = 1, 2, \ldots, n\)

\(j = 2, 3, \ldots, n-1\)

\(C_i\) = concentration of oxybutynin chloride in the Sample solution at time point \(i\) (mg/mL)

\(C_j\) = concentration of oxybutynin chloride in the Sample solution at time point \(j\) through \(n-1\) (mg/mL)

\(V_s\) = sampling volume (mL)

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

**Tolerances:** See Table 6.

<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>4</td>
<td>10%–40%</td>
</tr>
<tr>
<td>6</td>
<td>40%–75%</td>
</tr>
<tr>
<td>14</td>
<td>NLT 85%</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of oxybutynin chloride (C\(_{22}H_{31}NO_3\cdot HCl\)) dissolved at the times specified conform to Dissolution (711), Acceptance Table 2.

**Test 5:** If the product complies with this test, the labeling indicates that the product meets USP Dissolution Test 5.

**Medium:** Acetate buffer pH 4.5, prepared as follows.

Transfer 2.99 g of sodium acetate to a 1000-mL volumetric flask, dissolve in 700 mL of water, adjust with glacial acetic acid to a pH of 4.5, and dilute with water to volume; 900 mL.

**Apparatus 2:** 75 rpm

**Times:** 2, 8, 12, and 24 h

**Standard stock solution:** 0.28 mg/mL of USP Oxybutynin Chloride RS in acetonitrile. Use sonication, if necessary.

**Standard solution:** (L/900) mg/mL of USP Oxybutynin Chloride RS in Medium, where \(L\) is the label claim, in mg/Tablet, from the Standard stock solution

**Sample solution:** Pass a portion of the solution under test through a suitable PVDF filter of 0.45-µm pore size, discarding the first few mL of the filtrate. Replace the portion of solution withdrawn with an equal volume of Medium.

**pH 3.5 phosphate buffer:** 6.94 g/L of monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 3.50 ± 0.05.

**Mobile phase:** pH 3.5 phosphate buffer and acetonitrile (1:1)

**Chromatographic system**

(See Chromatography (621), System Suitability.)

**Mode:** LC

**Detector:** UV 210 nm

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

**Flow rate:** 1.0 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% for six replicate injections

**Analysis**

**Samples:** Standard solution and Sample solution

Calculate the concentration (\(C_i\)), in mg/mL, of oxybutynin chloride (C\(_{22}H_{31}NO_3\cdot HCl\)) in the sample withdrawn from the vessel at each point (\(i\)):

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

\(r_i\) = peak response from the Sample solution

\(r_s\) = peak response from the Standard solution

\(C_i\) = concentration of the Standard solution (mg/mL)

Calculate the percentage of the labeled amount of oxybutynin chloride (C\(_{22}H_{31}NO_3\cdot HCl\)) dissolved at each time point (\(i\)):

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

\[\text{Result}_{2} = [(C_i \times V) + (C_i \times V_2)] \times (1/L) \times 100\]

\[\text{Result}_{3} = [(C_i \times V) + (C_i + C_2) \times V_3] \times (1/L) \times 100\]

\[\text{Result}_{4} = [(C_i \times V) + (C_i + C_2 + C_3) \times V_4] \times (1/L) \times 100\]

\(C_i\) = concentration of oxybutynin chloride in the portion of the sample withdrawn at the specified time point (mg/mL)

\(V\) = volume of Medium, 900 mL

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

\(V_s\) = volume of the Sample solution withdrawn at each time point and replaced with Medium (mL)

**Tolerances:** See Table 7.

<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>8</td>
<td>30%–50%</td>
</tr>
<tr>
<td>12</td>
<td>55%–75%</td>
</tr>
<tr>
<td>24</td>
<td>NLT 85%</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of oxybutynin chloride (C\(_{22}H_{31}NO_3\cdot HCl\)) 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 the product meets USP Dissolution Test 6.

**Medium:** Simulated gastric fluid without enzyme; 50 mL

**Apparatus 7:** See Drug Release (724); each Tablet is glued to a suitable rod with water insoluble glue. At the end of each specified test interval, the systems are transferred to the next row of new tubes containing 50 mL of fresh Medium, 30 cycles/min; 2–3 cm amplitude.

**Times:** 4, 10, and 24 h
Calculate the percentage of the labeled amount of oxybutynin chloride (C$_{22}$H$_{25}$NO$_3$·HCl) dissolved by using the following method.

**Buffer:** 4.83 g/L of monobasic sodium phosphate in water. Add 2.3 mL/L of triethylamine, and adjust with phosphoric acid to a pH of 2.2 ± 0.2.

**Mobile phase:** Acetonitrile and Buffer (25:75)

**Diluent:** To 1 L of water add phosphoric acid dropwise to a pH of 3.5 and mix well.

**Standard stock solution:** 0.5 mg/mL of USP Oxybutynin Chloride RS in acetonitrile

**Standard solution:** 0.05 mg/mL of USP Oxybutynin Chloride RS in acetonitrile

**Sample solution:** Pass a portion of the solution under test through a suitable PVDF filter of 0.45-µm pore size, discarding the first few milliliters of the filtrate. Dilute with Diluent, if necessary, to obtain a solution with a concentration similar to that of the Standard solution.

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

**Mode:** LC

**Detector:** UV 230 nm

**Column:** 4.6-mm × 5-cm; 5-µm packing L11

**Column temperature:** 35°

**Flow rate:** 1.5 mL/min

**Injection volume:** 50 µL

**System suitability**

**Sample:** Standard solution

**Suitability requirements**

- **Tailing factor:** 0.5–2.5
- **Relative standard deviation:** NMT 2.0%

**Analysis**

**Samples:** Standard solution and Sample solution

Calculate the concentration ($C_i$), in mg/mL, of oxybutynin chloride (C$_{22}$H$_{25}$NO$_3$·HCl) in the sample withdrawn from the vessel at each time point $i$ shown in Table 8:

$$C_i = \left(\frac{r_i}{r_3}\right) \times C_3$$

$C_3$ = concentration of oxybutynin chloride (C$_{22}$H$_{25}$NO$_3$·HCl) in the sample withdrawn from the vessel at each time point $i$ shown in Table 8.

Calculate the percentage of the labeled amount of oxybutynin chloride (C$_{22}$H$_{25}$NO$_3$·HCl) dissolved at each time point shown in Table 8:

\[\text{Result}_0 = C_i \times V \times D \times (1/L) \times 100\]
\[\text{Result}_1 = (C_i + C_j) \times V \times D \times (1/L) \times 100\]
\[\text{Result}_3 = (C_i + C_j + C_3) \times V \times D \times (1/L) \times 100\]

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

$V$ = volume of Medium, 50 mL

$D$ = dilution factor for the Sample solution

$L$ = label claim (mg/Tablet)

**Tolerances:** See Table 8.

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### Table 8 (continued)

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>35–60</td>
</tr>
<tr>
<td>24</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of oxybutynin chloride (C$_{22}$H$_{25}$NO$_3$·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 the product meets USP Dissolution Test 7.

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

**Buffer stage medium:** pH 6.0 sodium phosphate buffer with 0.2% of sodium lauryl sulfate; 900 mL

**Apparatus 2:** 50 rpm, with sinkers. [Note—A suitable sinker is available as catalog number CAPWHT-2S from www.QLA-LLC.com.]

**Times:** 2 h in the Acid stage medium; 4, 8, and 16 h (corresponding to 2, 6, 14 h after changing the medium) in the Buffer stage medium for 5 mg Tablets and 6, 10, 16 h (corresponding to 4, 8, 14 h after changing the medium) in the Buffer stage medium for 10 mg and 15 mg Tablets.

**Procedure:** After 2 h in the Acid stage medium, withdraw a sample from the solution, and filter. Replace the Acid stage medium with the Buffer stage medium, and run the test for the times specified.

**Buffer:** 6.94 g/L of monobasic potassium phosphate in water. Adjust with diluted phosphoric acid to a pH of 3.50 ± 0.05.

**Mobile phase:** Acetonitrile and Buffer (1:1)

**Standard solution:** 0.01 mg/mL of USP Oxybutynin Chloride RS in Buffer stage medium

**Sample solution:** Pass a portion of the solution under test through a suitable PVDF filter of 0.45-µm pore size.

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

**Mode:** LC

**Detector:** UV 210 nm

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

**Flow rate:** 1.0 mL/min

**Injection volume:** 10 µL

**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 percentage of the labeled amount of oxybutynin chloride (C$_{22}$H$_{25}$NO$_3$·HCl) dissolved in the Acid stage medium:

$$\text{Result} = \left(\frac{r_i}{r_3}\right) \times C_i \times V \times (1/L) \times 100$$

$C_i$ = peak response from the Sample solution

$C_3$ = peak response from the Standard solution

$L$ = label claim (mg/Tablet)

**Relative standard deviation:** NMT 2.0%

**Tolerances:** See Table 8.


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

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

\[ C_s = \text{concentration of USP Oxybutynin Chloride RS in the Standard solution (mg/mL)} \]

Calculate the percentage of the labeled amount of oxybutynin chloride \((C_{22H8N5O3\cdot HCl})\) dissolved at each time point \(i\) during the buffer stage:

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

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

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

\[ C_i = \text{concentration of oxybutynin chloride in the Sample solution withdrawn at time point } i \](mg/mL)

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

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

\[ V_i = \text{volume of the Sample solution withdrawn at each time point } i \text{ during the buffer stage (mL)} \]

Tolerances: See Tables 9 and 10.

### Table 9. For Tablets Labeled to Contain 5 mg of Oxybutynin Chloride

<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>4</td>
<td>15–35</td>
</tr>
<tr>
<td>8</td>
<td>40–70</td>
</tr>
<tr>
<td>16</td>
<td>NLT 70</td>
</tr>
</tbody>
</table>

### Table 10. For Tablets Labeled to Contain 10 and 15 mg of Oxybutynin Chloride

<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>6</td>
<td>35–60</td>
</tr>
<tr>
<td>10</td>
<td>60–85</td>
</tr>
<tr>
<td>16</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of oxybutynin chloride \((C_{22H8N5O3\cdot HCl})\) 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 the product meets USP Dissolution Test 8.

**Acid stage medium:** Simulated gastric fluid, without enzymes, pH 1.2; 250 mL (first row)

**Buffer stage medium:** Simulated intestinal fluid, without enzymes, pH 6.8; 250 mL (rows 2–4)

**Apparatus 3:** 25 dips/min; 20-mesh polypropylene screen on top and bottom; 30 s drip time

**Times:** 2 h in the Acid stage medium (first row); 4, 8, and 16 h (corresponding to 2, 6, and 14 h after changing the medium) in the Buffer stage medium (rows 2–4)

**Buffer:** 4.83 g/L of monobasic sodium phosphate in water. Add 2.3 mL/L of triethylamine, and adjust with diluted phosphoric acid to a pH of 4.0.

**Mobile phase:** Acetonitrile and Buffer (35:65)

**Standard stock solution:** 0.2 mg/mL of USP Oxybutynin Chloride RS in Acid stage medium

**Standard solution:** Transfer volume of the Standard stock solution specified in Table 11 to a 100-mL volumetric flask and dilute with Buffer stage medium to volume.

### Table 11

<table>
<thead>
<tr>
<th>Tablet Strength (mg)</th>
<th>Volume of Standard stock solution (mL)</th>
<th>Final Volume (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>5.0</td>
<td>100.0</td>
</tr>
<tr>
<td>10</td>
<td>10.0</td>
<td>100.0</td>
</tr>
<tr>
<td>15</td>
<td>15.0</td>
<td>100.0</td>
</tr>
</tbody>
</table>

**Sample solution:** Pass a portion of the solution under test through a suitable PVDF filter of 0.45-μm pore size, discarding the first few milliliters.

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

**Mode:** LC

**Detector:** UV 230 nm

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

**Column temperature:** 35°

**Flow rate:** 1.5 mL/min

**Injection volume:** 50 µL

**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 total percentage of the labeled amount of oxybutynin chloride \((C_{22H8N5O3\cdot HCl})\) dissolved at each time point \((C_{T2}, C_{T4}, C_{T6}, C_{T8})\):

\[
C_i = \left( \frac{r_i}{r_s} \right) \times \left( \frac{C_i}{L} \right) \times V \times 100
\]

\[ C_i = \text{percentage of oxybutynin chloride in the Sample solution withdrawn at time point } i \]

\[ r_i = \text{peak response from the Sample solution} \]

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

\[ C_s = \text{concentration of USP Oxybutynin Chloride RS in the Standard solution (mg/mL)} \]

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

\[ V = \text{volume of Medium, 250 mL} \]

\[ C_{T2} = \text{percentage dissolved at 2 h, } C_{T2} \]

\[ C_{T4} = \text{percentage dissolved at 4 h, } C_{T4} + C_{T6} \]

\[ C_{T8} = \text{percentage dissolved at 8 h, } C_{T8} + C_{T6} \]

\[ C_{T16} = \text{percentage dissolved at 16 h, } C_{T16} \]

Tolerances: See Table 12.

### 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>4</td>
<td>5–25</td>
</tr>
<tr>
<td>8</td>
<td>34–59</td>
</tr>
<tr>
<td>16</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

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C226832-M59502-CHM32015, rev. 00 20190927
The percentages of the labeled amount of oxybutynin chloride \( (C_{22}H_{31}NO_3 \cdot HCl) \) dissolved at the times specified conform to Dissolution (711), Acceptance Table 2.

▲ Test 9: If the product complies with this test, the labeling indicates that the product meets USP Dissolution Test 9, Acid stage medium, Buffer stage medium, Apparatus 3, Times, Solution A, Mobile phase, Standard stock solution, Working standard solution, Sample solution, Chromatographic system, System suitability, and Analysis: Proceed as directed in Test 2. Tolerances: See Table 13.

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>0–10</td>
</tr>
<tr>
<td>4</td>
<td>10–30</td>
</tr>
<tr>
<td>8</td>
<td>46–66</td>
</tr>
<tr>
<td>16</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of oxybutynin chloride \( (C_{22}H_{31}NO_3 \cdot HCl) \) dissolved at the times specified conform to Dissolution (711), Acceptance Table 2.▲ (RB 1-Oct-2019)

▲ Uniformity of Dosage Units (905): Meet the requirements

**IMPURITIES**

*Organic Impurities* Diluent, Solution A ▲ (if Assay, Procedure 1 is used) ▲ (RB 1-Oct-2019) Mobile phase, Impurity stock solution, System suitability solution, Sample solution, Chromatographic system, and System suitability:

Proceed as directed in the corresponding Assay procedure.

**Impurity standard solution:** 1 µg/mL of USP Oxybutynin Related Compound A RS in the corresponding Diluent from the corresponding Impurity stock solution

**Analysis** Samples: Impurity standard solution and Sample solution Calculate the percentage of each impurity in the portion of Tablets taken:

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

\( r_i \) = peak response of each impurity from the Sample solution

\( r_s \) = peak response from the Impurity standard solution

\( C_s \) = concentration of USP Oxybutynin Related Compound A RS in the Standard solution (mg/mL)

\( C_U \) = nominal concentration of the Sample solution (mg/mL)

[Note—Disregard any peak less than 0.1%.

**Acceptance criteria**

Individual impurities: NMT 1% of oxybutynin related compound A is found.

Total impurities: NMT 2%

**ADDITIONAL REQUIREMENTS**

*Packaging and Storage:* Preserve in tight containers. Store at controlled room temperature.

*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 Oxybutynin Chloride RS
USP Oxybutynin Related Compound A RS
Phenylcyclohexylglycolic acid.

\( C_{14}H_{18}O_3 \) 234.30

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