Oxybutynin Chloride Extended-Release Tablets

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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 ($C_{22}H_{31}NO_3 \cdot HCl$).

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▲ (RB 1-Oct-2019)

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 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

Column: 4.6-mm × 15-cm; packing L11

Flow rate: 1.5 mL/min

Injection volume: 50 µL

System suitability

Sample: *System suitability solution*

[NOTE—The relative retention times for oxybutynin and oxybutynin related compound A are about 1.0 and 1.6, respectively.]

Suitability requirements

Resolution: NLT 1.5 between oxybutynin and oxybutynin related compound A

Tailing factor: Greater than 0.75 and NMT 2.5 for each peak

Relative standard deviation: NMT 3% for each compound for six replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of oxybutynin chloride ($C_{22}H_{31}NO_3 \cdot HCl$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Oxybutynin Chloride RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of oxybutynin chloride in the *Sample solution* (mg/mL)

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°. 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%▲ (RB 1-Oct-2019)

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°

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 dropwise to a pH of 3.5, and mix well.

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 solution: 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°

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 ($C_{22}H_{31}NO_3 \cdot HCl$) 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%
24	NLT 75%

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 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 ($C_{22}H_{31}NO_3 \cdot HCl$) dissolved at each time point (C_{T2}, C_{T4}, C_{T8}, C_{T16}):

$$C_i = (r_U/r_S) \times (C_S/L) \times V \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Working standard solution*

C_S = concentration of the *Working standard solution* (mg/mL)

L = label claim (mg/Tablet)

V = volume of *Medium*, 250 mL

C_{T2} = percentage dissolved at 2 h, C_2

C_{T4} = percentage dissolved at 4 h, $C_2 + C_4$

C_{T8} = percentage dissolved at 8 h, $C_2 + C_4 + C_8$

C_{T16} = percentage dissolved at 16 h, $C_2 + C_4 + C_8 + C_{16}$

Tolerances: See *Tables 3* and *4*.

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

Time (h)	Amount Dissolved
2	0%–10%
4	10%–30%
8	40%–65%
16	NLT 80%

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

Time (h)	Amount Dissolved
2	0%–10%
4	10%–30%
8	35%–65%
16	NLT 75%

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 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°, 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: 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 amount, in mg, of oxybutynin chloride ($C_{22}H_{31}NO_3 \cdot HCl$) dissolved at each time interval:

$$\text{Result} = (r_U/r_S) \times (C_S/L) \times V$$

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of the *Standard solution* (mg/mL)
L = label claim (mg/Tablet)
V = volume of *Medium*, 50 mL

Calculate the percentage of the labeled amount of oxybutynin dissolved:

$$\text{Result} = \Sigma(\text{amount dissolved at current time interval} + \text{amount dissolved at previous time intervals}) \times 100/L$$

Tolerances: See *Table 5*.

Table 5

Time (h)	Amount Dissolved
4	NMT 25%
10	40%–65%
24	NLT 75%

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 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, 12 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
Samples: *Standard solution* and *Sample solution*
Calculate the concentration (C_i) in mg/mL of oxybutynin chloride ($C_{22}H_{31}NO_3 \cdot HCl$) at each time point (*i*):

$$C_i = (r_U/r_S) \times C_S$$

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

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

At $i = 1$

$$Q_1 = (C_1 \times V/L) \times 100$$

At $i = 2$ to n

$$\frac{\left(C_1 \times 900\right) + \sum_{j=2}^{n-1} C_j V_S + C_n \times \left[900 - \left(n-2\right)V_S\right] \times 100}{L}$$

i = 1, 2, ..., n
j = 2, 3, ..., 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 2 through n–1 (mg/mL)
V_S = sampling volume (mL)
L = label claim (mg/Tablet)

Tolerances: See *Table 6*.

Table 6

Time (h)	Amount Dissolved
2	NMT 10%
4	10%–40%
6	40%–75%
14	NLT 85%

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):

$$\text{Result}_i = (r_U/r_S) \times C_S$$

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = 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):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$
$$\text{Result}_2 = [(C_2 \times V) + (C_1 \times V_S)] \times (1/L) \times 100$$
$$\text{Result}_3 = \{(C_3 \times V) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$
$$\text{Result}_4 = \{(C_4 \times V) + [(C_3 + C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

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 7

Time (h)	Amount Dissolved
2	NMT 10%
8	30%–50%
12	55%–75%
24	NLT 85%

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 ($C_{22}H_{31}NO_3 \cdot HCl$) 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 *Diluent* from *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 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 ($C_{22}H_{31}NO_3 \cdot HCl$) in the sample withdrawn from the vessel at each time point (*i*) shown in *Table 8*:

$$C_i = (r_U/r_S) \times C_S$$

r_U = peak response of oxybutynin from the *Sample solution*
r_S = peak response of oxybutynin from the *Standard solution*
C_S = concentration of USP Oxybutynin Chloride RS in 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 shown in *Table 8*:

$$\text{Result}_1 = C_1 \times V \times D \times (1/L) \times 100$$
$$\text{Result}_2 = (C_2 + C_1) \times V \times D \times (1/L) \times 100$$
$$\text{Result}_3 = (C_1 + C_2 + C_3) \times V \times D \times (1/L) \times 100$$

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*.

Table 8

Time (h)	Amount Dissolved (%)
4	NMT 20
10	35–60
24	NLT 80

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 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 ($C_{22}H_{31}NO_3 \cdot HCl$) dissolved in the *Acid stage medium*:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (1/L) \times 100$$

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Oxybutynin Chloride RS in the *Standard solution* (mg/mL)
V = volume of the *Acid stage medium*, 900 mL
L = label claim (mg/Tablet)

Calculate the concentration (C_i) of oxybutynin chloride ($C_{22}H_{31}NO_3 \cdot HCl$) in the sample withdrawn from the vessel at each time point *i* during the buffer stage:

$$C_i = (r_i/r_S) \times C_S$$

r_i = peak response from the *Sample solution* at time point *i*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Oxybutynin Chloride RS in 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* during the buffer stage:

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$
$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$
$$\text{Result}_3 = (\{C_3 \times [V - (2 \times V_S)]\} + [(C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

C_i = concentration of oxybutynin chloride in the *Sample solution* withdrawn at time point *i* (mg/mL)
V = volume of the *Buffer stage medium*, 900 mL
L = label claim (mg/Tablet)
V_S = volume of the *Sample solution* withdrawn at each time point *i* during the buffer stage (mL)

Tolerances: See *Tables 9* and *10*.

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

Time (h)	Amount Dissolved (%)
2	NMT 10
4	15–35
8	40–70
16	NLT 70

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

Time (h)	Amount Dissolved (%)
2	NMT 10
6	35–60
10	60–85
16	NLT 80

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 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

Tablet Strength (mg)	Volume of Standard stock solution (mL)	Final Volume (mL)
5	5.0	100.0
10	10.0	100.0
15	15.0	100.0

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 ($C_{22}H_{31}NO_3 \cdot HCl$) dissolved at each time point (C_{T2}, C_{T4}, C_{T8}, C_{T16}):

$$C_i = (r_U/r_S) \times (C_S/L) \times V \times 100$$

C_i = percentage of oxybutynin chloride in the *Sample solution* withdrawn at time point *i*
r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Oxybutynin Chloride RS in the *Standard solution* (mg/mL)
L = label claim (mg/Tablet)
V = volume of *Medium*, 250 mL
C_{T2} = percentage dissolved at 2 h, C_{T2}
C_{T4} = percentage dissolved at 4 h, $C_{T2} + C_{T4}$
C_{T8} = percentage dissolved at 8 h, $C_{T2} + C_{T4} + C_{T8}$
C_{T16} = percentage dissolved at 16 h, $C_{T2} + C_{T4} + C_{T8} + C_{T16}$

Tolerances: See *Table 12*.

Table 12

Time (h)	Amount Dissolved (%)
2	NMT 10
4	5–25
8	34–59
16	NLT 80

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 13

Time (h)	Amount Dissolved (%)
2	0–10
4	10–30
8	46–66
16	NLT 80

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

Change to read:

- **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▲ (RB 1-Oct-2019) *Assay* procedure.

Impurity standard solution: 1 µg/mL of USP Oxybutynin Related Compound A RS in ▲the corresponding ▲ (RB 1-Oct-2019) *Diluent* from the ▲corresponding▲ (RB 1-Oct-2019) *Impurity stock solution*

Analysis

Samples: *Impurity standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = 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