

Time (h)	Amount Dissolved, 500-mg Tablet (%)	Amount Dissolved, 1000-mg Tablet (%)
16	NLT 90	NLT 90

The percentages of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) dissolved at the times specified conform to [Dissolution \(711\)](#), [Acceptance Table 2](#).

Test 6: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 6*.

Medium: [pH 6.8 phosphate buffer solution](#); 1000 mL, deaerated

Apparatus 2: 100 rpm, with USP sinker, if necessary

Detector: UV 233 nm

Standard solution: [USP Metformin Hydrochloride RS](#) in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable hydrophilic polyethylene filter of 0.45- μ m pore size. Dilute, if necessary, with *Medium* to a concentration similar to that of the *Standard solution*.

Analysis: Calculate the percentage of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) released at each time point:

$$\text{Result} = \{[(A_U/A_S) \times C_S \times (V - V_S) + (C_{60} \times V_S) + (C_{180} \times V_S) + (C_{600} \times V_S)] \times 100\}/L$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = initial volume of *Medium* in the vessel (mL)

V_S = volume withdrawn from the vessel for previous samplings (mL)

C_{60} = concentration of metformin hydrochloride in *Medium* determined at 1 h (mg/mL)

C_{180} = concentration of metformin hydrochloride in *Medium* determined at 3 h (mg/mL)

C_{600} = concentration of metformin hydrochloride in *Medium* determined at 10 h (mg/mL)

L = label claim (mg/Tablet)

Tolerances: See [Table 7](#).

Table 7

Time (h)	Amount Dissolved, 500-mg Tablet (%)	Amount Dissolved, 750-mg Tablet (%)
1	20–40	20–40
3	45–65	45–65
10	NLT 85	NLT 85

The percentages of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) 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 it meets USP *Dissolution Test 7*.

Medium: Prepare as directed in *Test 1*; 1000 mL.

Apparatus 1: 100 rpm for Tablets labeled to contain 750 mg

Apparatus 2: 50 rpm, with USP sinker, for Tablets labeled to contain 500 mg

Times: 1, 3, and 10 h

Detector: UV 232 nm

Standard solution: [USP Metformin Hydrochloride RS](#) in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45- μm pore size. Dilute, if necessary, with *Medium* to a concentration similar to that of the *Standard solution*.

Analysis: Calculate the percentage of the labeled amount of metformin hydrochloride ($\text{C}_4\text{H}_{11}\text{N}_5 \cdot \text{HCl}$) released at each time point:

$$\text{Result} = \{[(A_U/A_S) \times C_S \times (V - V_S) + (C_{60} \times V_S) + (C_{180} \times V_S) + (C_{600} \times V_S)] \times 100\}/L$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = initial volume of *Medium* in the vessel (mL)

V_S = volume withdrawn from the vessel for previous samplings (mL)

C_{60} = concentration of metformin hydrochloride in *Medium* determined at 1 h (mg/mL)

C_{180} = concentration of metformin hydrochloride in *Medium* determined at 3 h (mg/mL)

C_{600} = concentration of metformin hydrochloride in *Medium* determined at 10 h (mg/mL)

L = label claim (mg/Tablet)

Tolerances: See [Table 8](#).

Table 8

Time (h)	Amount Dissolved, 500-mg Tablet (%)	Amount Dissolved, 750-mg Tablet (%)
1	20–40	20–40
3	45–65	40–60
10	NLT 85	NLT 80

The percentages of the labeled amount of metformin hydrochloride ($\text{C}_4\text{H}_{11}\text{N}_5 \cdot \text{HCl}$) dissolved at the times specified conform to [Dissolution \(711\)](#), [Acceptance Table 2](#).

Test 8: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 8*.

Medium: Prepare as directed in *Test 1*; 1000 mL.

Apparatus 1: 100 rpm for Tablets labeled to contain 750 mg

Apparatus 2: 100 rpm, with sinker, for Tablets labeled to contain 500 mg

Times: 1, 2, 6, and 10 h

Detector: UV 232 nm

Standard solution: [USP Metformin Hydrochloride RS](#) in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45- μm pore size. Dilute, if necessary, with *Medium* to a concentration similar to that of the *Standard solution*.

Analysis: Calculate the percentage of the labeled amount of metformin hydrochloride ($\text{C}_4\text{H}_{11}\text{N}_5 \cdot \text{HCl}$) released at each time point:

$$\text{Result} = \{[(A_U/A_S) \times C_S \times (V - V_S) + (C_{60} \times V_S) + (C_{120} \times V_S) + (C_{360} \times V_S) + (C_{600} \times V_S)] \times 100\}/L$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = initial volume of *Medium* in the vessel (mL)

V_S = volume withdrawn from the vessel for previous samplings (mL)

- C_{60} = concentration of metformin hydrochloride in *Medium* determined at 1 h (mg/mL)
 C_{120} = concentration of metformin hydrochloride in *Medium* determined at 2 h (mg/mL)
 C_{360} = concentration of metformin hydrochloride in *Medium* determined at 6 h (mg/mL)
 C_{600} = concentration of metformin hydrochloride in *Medium* determined at 10 h (mg/mL)
 L = label claim (mg/Tablet)

Tolerances: See [Table 9](#).

Table 9

Time (h)	Amount Dissolved, 500-mg Tablet (%)	Amount Dissolved, 750-mg Tablet (%)
1	20–40	20–40
2	30–50	35–55
6	65–85	75–95
10	NLT 85	NLT 85

The percentages of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) 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 it meets USP *Dissolution Test 9*.

Medium: 0.05 M phosphate buffer, pH 6.8; 1000 mL

Apparatus 1: 100 rpm, for Tablets labeled to contain 750 mg

Apparatus 2: 100 rpm, for Tablets labeled to contain 500 mg

Times: 1, 5, 12, and 20 h for Tablets labeled to contain 500 mg; and 1, 4, 10, and 24 h for Tablets labeled to contain 750 mg

Standard solution: 0.5 mg/mL of [USP Metformin Hydrochloride RS](#) in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45- μ m pore size.

Detector: UV 232 nm

Path length: 0.01 cm, flow cell

Blank: *Medium*

Analysis: Calculate the percentage of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) released at each time point:

$$\text{Result} = \{[(A_U/A_S) \times C_S \times (V - V_S) + (C_1 \times V_S) + (C_2 \times V_S) + (C_3 \times V_S) + (C_4 \times V_S)] \times 100\}/L$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = initial volume of *Medium* in the vessel (mL)

V_S = volume withdrawn from the vessel for previous samplings (mL)

C_1 = concentration of metformin hydrochloride in *Medium* determined at the first time point (mg/mL)

C_2 = concentration of metformin hydrochloride in *Medium* determined at the second time point (mg/mL)

C_3 = concentration of metformin hydrochloride in *Medium* determined at the third time point (mg/mL)

C_4 = concentration of metformin hydrochloride in *Medium* determined at the fourth time point (mg/mL)

L = label claim (mg/Tablet)

Tolerances: See [Tables 10](#) and [11](#).

Table 10. For Tablets Labeled to Contain 500 mg

Time (h)	Amount Dissolved (%)
1	20–40
5	45–65
12	70–90
20	NLT 85

Table 11. For Tablets Labeled to Contain 750 mg

Time (h)	Amount Dissolved (%)
1	20–45
4	45–70
10	70–95
24	NLT 85

The percentages of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) dissolved at the times specified conform to [Dissolution \(711\)](#), [Acceptance Table 2](#).

Test 10: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 10*.

Medium: 0.05 M phosphate buffer (prepared by dissolving 6.8 g of [monobasic potassium phosphate](#) in 250 mL of water, adding 77 mL of [0.2 N sodium hydroxide](#) and 500 mL of water, adjusting with [2 N sodium hydroxide](#) or 2 N hydrochloric acid to pH 6.8, and diluting with water to 1000 mL)

Apparatus 1: 100 rpm for Tablets labeled to contain 750 mg

Apparatus 2: 100 rpm for Tablets labeled to contain 500 mg

Times: 1, 3, and 10 h

Standard solution: ($L/100,000$) mg/mL of [USP Metformin Hydrochloride RS](#) in *Medium*, where L is the label claim, in mg/Tablet. This solution is stable for 72 h at room temperature.

Sample solution: At the times specified, withdraw 10 mL of the solution under test and replace with 10 mL of *Medium* previously equilibrated at $37.0 \pm 0.5^\circ$. Centrifuge at 2500 rpm for 10 min. Dilute a portion of the supernatant with *Medium* to obtain a theoretical concentration of ($L/100,000$) mg/mL, where L is the label claim, in mg/Tablet.

Detector: UV 233 nm

Path length: 1 cm

Blank: *Medium*

Analysis: Calculate the concentration, in mg/mL, of metformin hydrochloride (C_i) at each time point:

$$C_i = (A_i/A_S) \times C_S$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

Calculate the cumulative percentage of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) dissolved (Q_i) at each time point (i):

At $i = 1$:

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

At $i = 3$:

$$Q_3 = [C_3(V - V_S) + (C_1 \times V_S)] \times 100/L$$

At $i = 10$:

$$Q_{10} = [C_{10}(V - 2V_S) + (C_1 + C_3)V_S] \times 100/L$$

V = initial volume of *Medium*, 1000 mL

V_S = sampling volume, 10 mL

L = label claim (mg/Tablet)

Tolerances: See [Table 12](#).

Table 12

Time (h)	Amount Dissolved (%)
1	25–45
3	50–70
10	NLT 85

The percentages of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) dissolved at the times specified conform to [Dissolution \(711\)](#), [Acceptance Table 2](#).

Test 11: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 11*.

Medium: [pH 6.8 phosphate buffer solution](#); 1000 mL

Apparatus 1: 100 rpm for Tablets labeled to contain 750 mg

Apparatus 2: 100 rpm for Tablets labeled to contain 500 mg

Times: 1, 3, and 10 h

Standard solution: 7.5 $\mu\text{g/mL}$ of [USP Metformin Hydrochloride RS](#) in *Medium*

Sample solution: At the times specified, withdraw 10 mL of the solution under test, and pass it through a suitable filter of 0.45- μm pore size, discarding the first 3 mL of filtrate. Dilute 3.0 mL of the filtrate with *Medium* to 200 mL. For Tablets labeled to contain 750 mg, dilute 2.0 mL of the filtrate with *Medium* to 200 mL. Replace the volume of *Medium* taken with the same volume of *Medium* preheated at $37.0 \pm 0.5^\circ$.

Detector: UV 232 nm

Path length: 1 cm

Blank: *Medium*

Analysis: Calculate the percentage of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) dissolved at each time point:

$$Q_i = (A_U/A_S) \times (C_S/L) \times V \times D \times 100$$

At 1 h:

$$\text{Result} = Q_1$$

At 3 h:

$$\text{Result} = Q_3 + [(Q_1 \times 10)/V]$$

At 10 h:

$$\text{Result} = Q_{10} + \{[(Q_1 \times 10)/V] + [(Q_3 \times 10)/V]\}$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

- C_S = concentration of the *Standard solution* (mg/mL)
 L = label claim (mg/Tablet)
 V = volume of *Medium*, 1000 mL
 D = dilution factor of the *Sample solution*

Tolerances: See [Table 13](#).

Table 13

Time (h)	Amount Dissolved (%)
1	25–45
3	50–70
10	NLT 80

The percentages of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) dissolved at the times specified conform to [Dissolution \(711\)](#), [Acceptance Table 2](#).

Test 12: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 12*.

Medium: [pH 6.8 phosphate buffer solution](#); 1000 mL

Apparatus 1: 100 rpm

Times: 1, 4, and 12 h

Standard stock solution: 0.2 mg/mL of [USP Metformin Hydrochloride RS](#) in *Medium*

Standard solution: 0.01 mg/mL of [USP Metformin Hydrochloride RS](#) in water, from the *Standard stock solution*

Sample solution: At the times specified, withdraw 10 mL of the solution under test, and replace with 10 mL of *Medium* previously equilibrated at $37.0 \pm 0.5^\circ$. Pass it through a suitable filter, discarding the first few mL of the filtrate.

For Tablets labeled to contain 500 mg: Dilute 2.0 mL of the filtrate with water to 100 mL.

For Tablets labeled to contain 1000 mg: Dilute 1.0 mL of the filtrate with water to 100 mL.

Detector: UV 232 nm

Blank: Dilute 1 mL of *Medium* with water to 100 mL.

Analysis: Calculate the concentration (C_i), in mg/mL, of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) in the sample withdrawn at each time point (i):

$$\text{Result}_i = (A_U/A_S) \times C_S \times D$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

D = dilution factor of the *Sample solution*

Calculate the percentage of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) dissolved (Q_i) at each time point (i):

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

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

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

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

V = initial volume of *Medium*, 1000 mL

L = label claim (mg/Tablet)

V_S = volume of the *Sample solution* withdrawn, 10 mL

Tolerances: See [Table 14](#).

Table 14

Time Point (<i>i</i>)	Time (h)	Amount Dissolved (%)
1	1	NMT 15
2	4	35–65
3	12	NLT 85

The percentages of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) dissolved at the times specified conform to [Dissolution \(711\)](#), [Acceptance Table 2](#).

Test 13: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 13*.

Medium: [pH 6.8 phosphate buffer solution](#); 1000 mL

Apparatus 1: 100 rpm

Times: 1, 4, 6, and 14 h

Standard stock solution: 0.2 mg/mL of [USP Metformin Hydrochloride RS](#) prepared as follows. Transfer a suitable amount of [USP Metformin Hydrochloride RS](#) into an appropriate volumetric flask. Dissolve by adding *Medium* to fill 50% of the flask volume and dilute with *Medium* to volume.

Standard solution: 0.01 mg/mL of [USP Metformin Hydrochloride RS](#) from *Standard stock solution* in water

Sample stock solution: At the times specified, withdraw 10 mL of the solution under test, and replace with the same volume of *Medium* preheated at $37.0 \pm 0.5^\circ$. Pass a portion of the solution under test through a suitable filter of 0.45- μ m pore size, discard the first few mL, and use the filtrate.

Sample solution

For Tablets labeled to contain 500 mg: Dilute 2 mL of *Sample stock solution* with water to 100 mL.

For Tablets labeled to contain 1000 mg: Dilute 1 mL of *Sample stock solution* with water to 100 mL.

Instrumental conditions

(See [Ultraviolet-Visible Spectroscopy \(857\)](#).)

Mode: UV

Analytical wavelength: 232 nm

Blank

For Tablets labeled to contain 500 mg: Dilute 2 mL of *Medium* with water to 100 mL.

For Tablets labeled to contain 1000 mg: Dilute 1 mL of *Medium* with water to 100 mL.

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution*, *Sample solution*, and *Blank*

Calculate the concentration (C_i), in mg/mL, of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) in the sample withdrawn from the vessel at each time point (*i*):

$$\text{Result}_i = (A_U/A_S) \times C_S \times D$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

D = dilution factor of the *Sample solution*

Calculate the percentage of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) 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 metformin hydrochloride in the portion of sample withdrawn at the specified time point (mg/mL)

V = volume of *Medium*, 1000 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 15](#).

Table 15

Time Point (<i>i</i>)	Time (h)	Amount Dissolved (%)
1	1	NMT 20
2	4	45–65
3	6	65–85
4	14	NLT 85

The percentages of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) dissolved at the times specified conform to [Dissolution \(711\)](#), [Acceptance Table 2](#).

Test 14: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 14*.

Medium: pH 6.8 phosphate buffer solution; 1000 mL

Apparatus 1: 100 rpm for Tablets labeled to contain 750 mg

Apparatus 2: 100 rpm for Tablets labeled to contain 500 mg

Times: 1, 3, and 10 h

Standard solution: 7.5 $\mu\text{g/mL}$ of [USP Metformin Hydrochloride RS](#) in *Medium*

Sample solution: At the times specified, withdraw 10 mL of the solution under test and replace with the same volume of *Medium*. Pass the solution under test through a suitable filter of 10- μm pore size. Pass a portion of the filtered solution through a suitable filter of 0.45- μm pore size, discarding the first few milliliters. Dilute with *Medium* to a concentration similar to that of the *Standard solution*.

Instrumental conditions

Mode: UV

Analytical wavelength: 232 nm

Blank: *Medium*

Analysis

Samples: *Standard solution*, *Sample solution*, and *Blank*

Calculate the concentration (C_i), in mg/mL, of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) in the sample withdrawn from the vessel at each time point (*i*):

$$\text{Result}_i = (A_U/A_S) \times C_S \times D$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of the *Standard solution* ($\mu\text{g/mL}$)

D = dilution factor of the *Sample solution*

Calculate the percentage of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) 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 metformin hydrochloride in the portion of sample withdrawn at the specified time point (mg/mL)

V = volume of *Medium*, 1000 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 16](#).

Table 16

Time Point (<i>i</i>)	Time (h)	Amount Dissolved (%)	
		500 mg Tablets	750 mg Tablets
1	1	30–50	25–45
2	3	55–75	50–70
3	10	NLT 85	NLT 85

The percentages of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) dissolved at the times specified conform to [Dissolution <711>](#), [Acceptance Table 2](#).

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

Medium: [pH 6.8 phosphate buffer solution](#); 1000 mL

Apparatus 1: 100 rpm

Times: 1, 3, and 10 h

Standard solution: 0.015 mg/mL of [USP Metformin Hydrochloride RS](#) in *Medium*. Sonicate as needed.

Sample stock solution: At the times specified, withdraw 10 mL of the solution under test and pass it through a suitable filter.

Sample solution

For Tablets labeled to contain 500 mg: Dilute 3 mL of the *Sample stock solution* with *Medium* to 100 mL.

For Tablets labeled to contain 750 mg: Dilute 2 mL of the *Sample stock solution* with *Medium* to 100 mL.

Instrumental conditions

(See [Ultraviolet-Visible Spectroscopy <857>](#).)

Mode: UV-Vis

Analytical wavelength: UV 232 nm

Path length: 1 cm

Blank: *Medium*

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) in the sample withdrawn from the vessel at each time point (*i*):

$$\text{Result} = (A_U/A_S) \times C_S \times D$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

D = dilution factor for the *Sample solution*

Calculate the percentage of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) dissolved at the specified time point:

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

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

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

C_i = concentration of metformin hydrochloride in the portion of sample withdrawn at the specified time point (mg/mL)

V = volume of *Medium*, 1000 mL

L = label claim (mg/Tablet)

V_S = volume of the *Sample solution* withdrawn at each time point (mL)

Tolerances: See [Table 17](#).

Table 17

Time Point (i)	Time (h)	Amount Dissolved (%)
1	1	25–45
2	3	50–70
3	10	NLT 80

The percentages of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) 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: [pH 6.8 phosphate buffer solution](#); 900 mL, deaerated

Apparatus 1: 100 rpm, with vertical holder described in [Figure 1](#)

Times: 1, 4, and 10 h

Standard solution: 0.044 mg/mL of [USP Metformin Hydrochloride RS](#) in *Medium*. Sonicate as needed.

Sample stock solution: At the times specified, withdraw a suitable amount of solution under test and replace with a suitable amount of *Medium*. Pass the solution under test through a suitable filter and discard the first few milliliters.

Sample solution

For Tablets labeled to contain 500 mg: Dilute 2 mL of the *Sample stock solution* with *Medium* to 25 mL.

For Tablets labeled to contain 1000 mg: Dilute 2 mL of the *Sample stock solution* with *Medium* to 50 mL.

Instrumental conditions

(See [Ultraviolet-Visible Spectroscopy \(857\)](#).)

Mode: UV-Vis

Analytical wavelength: UV 250 nm

Path length: 1 cm

Blank: *Medium*

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Place a vertical sample holder into each basket (see [Figure 1](#)). Place 1 Tablet inside the sample holder, making sure that the Tablets are vertical at the bottom of the baskets.

Calculate the concentration (C_i) of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) in the sample withdrawn from the vessel at each time point (i):

$$\text{Result} = (A_U/A_S) \times C_S \times D$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

D = dilution factor of the *Sample solution*

Calculate the percentage of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) dissolved at each time point (i):

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

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

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

C_i = concentration of metformin hydrochloride in the portion of 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 18](#).

Table 18

Time Point (<i>i</i>)	Time (h)	Amount Dissolved (%)
1	1	NMT 30
2	4	45–70
3	10	NLT 85

The percentages of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) dissolved at the times specified conform to [Dissolution <711>](#), [Acceptance Table 2](#).

▲ Test 21: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 21*.

Medium: pH 7.5 phosphate buffer; 900 mL

Apparatus 2: 75 rpm

Times

For Tablets labeled to contain 500 mg: 2, 8, and 20 h

For Tablets labeled to contain 1000 mg: 1, 6, and 18 h

Standard solution: 0.022 mg/mL of [USP Metformin Hydrochloride RS](#) in *Medium*

Sample stock solution: At the times specified, withdraw 10 mL of the solution under test and pass it through a suitable filter.

Sample solution: Dilute 2 mL of the *Sample stock solution* with *Medium* to 100 mL.

Instrumental conditions

(See [Ultraviolet-Visible Spectroscopy \(857\)](#).)

Mode: UV-Vis

Analytical wavelength: UV 232 nm

Cell length: 1 cm

Blank: *Medium*

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0% for five replicates

Analysis

Samples: *Standard solution, Sample solution, and Blank*

Calculate the concentration (C_i) of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) in the sample withdrawn from the vessel at each time point (i):

$$\text{Result} = (A_U/A_S) \times C_S \times D$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

D = dilution factor for the *Sample solution*

Calculate the percentage of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) dissolved at the specified time point:

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

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

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

C_i = concentration of metformin hydrochloride in the portion of 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 (mL)

Tolerances: See [Tables 19](#) and [20](#).

Table 19. For Tablets Labeled to Contain 500 mg

Time Point (i)	Time (h)	Amount Dissolved (for Tablets that contain 500 mg of metformin hydrochloride) (%)
1	2	NMT 30
2	8	32–62
3	20	NLT 80

Table 20. For Tablets Labeled to Contain 1000 mg

Time Point (i)	Time (h)	Amount Dissolved (for Tablets that contain 1000 mg of metformin hydrochloride) (%)
1	1	NMT 15
2	6	37–67

Time Point (i)	Time (h)	Amount Dissolved (for Tablets that contain 1000 mg of metformin hydrochloride) (%)
3	18	NLT 80

The percentages of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) dissolved at the times specified conform to [Dissolution <711>](#), [Acceptance Table 2](#). ▲ (TBD)

- **UNIFORMITY OF DOSAGE UNITS <905>**: Meet the requirements

IMPURITIES

• ORGANIC IMPURITIES

Mobile phase, Sample solution, and Chromatographic system: Proceed as directed in the Assay.

Analysis: From the chromatogram of the *Sample solution* obtained in the Assay, calculate the percentage of each impurity in the portion of Tablets taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response for each impurity

r_T = sum of all the peak responses

Acceptance criteria

Individual impurities: NMT 0.1%

Total impurities: NMT 0.6%

[NOTE—Disregard any peak less than 0.05%, and disregard any peak observed in the blank.]

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed, light-resistant containers, and 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 Metformin Hydrochloride RS](#)

[USP Metformin Related Compound B RS](#)

1-Methylbiguanide hydrochloride.

$C_3H_9N_5HCl$ 151.60

[USP Metformin Related Compound C RS](#)

N,N-Dimethyl-[1,3,5]triazine-2,4,6-triamine.

$C_5H_{10}N_6$ 154.17

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Not Applicable

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