Tamsulosin Hydrochloride Capsules

DEFINITION

Tamsulosin Hydrochloride Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of tamsulosin hydrochloride ($C_{20}H_{28}N_2O_5S \cdot HCl$).

IDENTIFICATION

Delete the following:

•• **A. ULTRAVIOLET ABSORPTION**

Solution A: 8.0 g/L of sodium hydroxide in freshly boiled and cooled water

Analysis: Transfer suitable quantities of Capsule contents, equivalent to 2.5 mg of tamsulosin hydrochloride, into each of two Teflon-lined, screw-cap centrifuge tubes containing approximately 100 glass balls with a diameter of about 5 mm. Add 20 mL of *Solution A* into each of them, heat at 50° for about 10 min, and shake well for 1 h. Add 20 mL of a mixture of acetonitrile and ethyl acetate (3:2) and 5 g of sodium chloride, shake well for 5 min, and centrifuge each tube. Combine the supernatant of the two tubes, and evaporate to dryness under reduced pressure. Dissolve the residue in 2.5 mL of a mixture of acetonitrile and water (1:4), and pass through a membrane filter with a pore size of 0.5 µm or less. Dilute 0.5 mL of the filtrate with water to 50 mL.

Acceptance criteria: The ultraviolet absorption spectrum of the solution obtained exhibits maxima between 222 and 226 nm and between 276 and 281 nm. •(RB 1-Oct-2010)

Change to read:

• ••(RB 1-Oct-2010) 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-2010)

Solution A: Dilute 20 mL of hydrochloric acid with water to 1000 mL.

Solution B: Dissolve 8.7 mL of perchloric acid and 3.0 g of sodium hydroxide in 1900 mL of water. Adjust with 1 N sodium hydroxide to a pH of 2.0, and add sufficient water to make 2000 mL.

Mobile phase: Acetonitrile and *Solution B* (3:7)

Internal standard solution: 0.4 mg/mL of propylparaben in a mixture of acetonitrile and water (3:7)

Standard stock solution: 0.5 mg/mL of USP Tamsulosin Hydrochloride RS in a mixture of acetonitrile and water (3:7)

Standard solution: Transfer 2.0 mL of the *Standard stock solution* to a suitable container, add 5.0 mL of *Internal standard solution,* and add *Mobile phase* to make 40 mL.

Sample solution: Weigh the contents of NLT 20 Capsules. Mix the contents, and transfer a weighed portion of the powder, equivalent to about 1 mg of tamsulosin hydrochloride based on the label claim, into a Teflon-lined, screw-cap centrifuge tube. Place approximately 100 glass balls with a diameter of about 5 mm into the tube, add 20 mL of 0.05 N sodium hydroxide, heat at 50° for 10 min, and shake well for 30 min. Add 15 mL of a mixture of acetonitrile and *Solution A* (2:1) to the solution, and shake well. Add 5.0 mL of the *Internal standard solution,* and shake well. Centrifuge at 1500 rpm for 10 min, and use the supernatant, passing it if necessary through a membrane filter of pore size 0.5 µm or smaller.

Chromatographic system

(See *Chromatography* ⟨621⟩*, System Suitability*.)

Mode: LC

Detector: UV 225 nm

Column: 4.0-mm × 15-cm or 4.6-mm × 15-cm; 5-µm packing L1

Temperature: 40°

Flow rate: 1.0 mL/min for the 4.0-mm column and 1.3 mL /min for the 4.6-mm column. [NOTE—The flow rate can be adjusted as needed to achieve a recommended retention time of approximately 6 min for tamsulosin.]

Injection size: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 12 between tamsulosin and propylparaben. [NOTE—The elution order is tamsulosin hydrochloride followed by propylparaben.]

Relative standard deviation: NMT 2.0%, for the ratios of the peak areas for tamsulosin and the internal standard

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of tamsulosin hydrochloride ($C_{20}H_{28}N_2O_5S \cdot HCl$) in the portion of Capsules taken:

$$\text{Result} = (R_U/R_S) \times (C_S \times V_S/W) \times 100$$

R_U = ratio of the peak areas for tamsulosin and the internal standard from the *Sample solution*

R_S = ratio of the peak areas for tamsulosin and the internal standard from the *Standard solution*

C_S = concentration of USP Tamsulosin Hydrochloride RS in the *Standard stock solution* (mg/mL)

V_S = volume of the *Standard stock solution* taken to prepare the *Standard solution* (mL)

W = amount of tamsulosin hydrochloride, based on the label claim, taken to prepare the *Sample solution* (mg)

Acceptance criteria: 90.0%–110.0%

Add the following:

•• **PROCEDURE 2:** Use this *Procedure* for Capsules labeled to meet the requirements of *Dissolution Test 2*.

Solution B and **Mobile phase:** Proceed as directed for *Procedure 1*.

Buffer: Dissolve 3.4 g of monobasic potassium phosphate in 1 L of water. Adjust with 2 N sodium hydroxide to a pH of 5.80 ± 0.05.

Standard solution: Prepare a solution containing 1.2 mg/mL of USP Tamsulosin Hydrochloride RS in methanol. Dilute with *Buffer* to obtain a solution containing 3.2 µg/mL.

Sample solution: Weigh the contents of NLT 20 Capsules. Mix the contents, and transfer a weighed portion of the Capsule contents, equivalent to 1.6 mg of tamsulosin hydrochloride, into a 100-mL volumetric flask. Add 20 mL of methanol, stir for 30 min, sonicate for 30 min, and stir again for 30 min. Add 40 mL of methanol, sonicate for another 30 min, and stir for another 60 min. Dilute with methanol to volume, mix well, and allow the solution to stand for 5 min. Dilute 5 mL of this solution with *Buffer* to 25 mL, and allow the solution to stand for 5 min. Pass through a PVDF

filter of 0.45-µm pore size, discarding the first 5 mL of the filtrate.
Chromatographic system: Proceed as directed for *Procedure 1*, except to inject 50 µL.
System suitability
Sample: *Standard solution*
Suitability requirements
Relative standard deviation: NMT 2.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of tamsulosin hydrochloride ($C_{20}H_{28}N_2O_5S \cdot HCl$) in the portion of Capsules 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 the *Standard solution* (mg/mL)
C_U = nominal concentration of the *Sample solution* (mg/mL)
Acceptance criteria: 90.0%–110.0%● (RB 1-Oct-2010)

Add the following:

•• **PROCEDURE 3:** Use this *Procedure* for Capsules labeled to meet the requirements of *Dissolution Test 3*.
Solution B and **Mobile phase:** Proceed as directed for *Procedure 1*.
Buffer: Dissolve 6.9 g of monobasic sodium phosphate monohydrate in 1 L of water, and adjust with 5 N sodium hydroxide to a pH of 7.2 ± 0.05.
Standard solution: Prepare a solution containing 0.5 mg/mL of USP Tamsulosin Hydrochloride RS in a mixture of methanol and water (1:1), and dilute a portion of this solution with methanol to obtain a solution containing 0.03 mg/mL.
Sample solution: Weigh the contents of NLT 20 Capsules. Mix the contents, and transfer a weighed portion of the Capsule contents, equivalent to 0.8 mg of tamsulosin hydrochloride, into a 25-mL volumetric flask. Add 5 mL of *Buffer*, shake for 15 min, add 10 mL of methanol, shake for 1 h, and dilute with methanol to volume. Pass through a suitable filter of 0.45-µm pore size.
Chromatographic system: Proceed as directed for *Procedure 1*, except to inject 20 µL.
System suitability, Analysis: Proceed as directed for *Procedure 2.*
Acceptance criteria: 90.0%–110.0%● (RB 1-Oct-2010)

Add the following:

•• **PROCEDURE 4:** For the Capsules labeled to meet the requirements of *Dissolution Test 4*, proceed as directed for *Procedure 1.*● (RB 01-Oct-2010)

Add the following:

•• **PROCEDURE 5:** Use this *Procedure* for Capsules labeled to meet the requirements of *Dissolution Test 5*.
Solution B, Mobile phase, and **Chromatographic system:** Proceed as directed for *Procedure 1*.
Diluent: Methanol and water (75:25)
Standard solution: Prepare a solution containing 0.016 mg/mL of USP Tamsulosin Hydrochloride RS in *Diluent*.
Sample solution: Transfer the contents of 10 Capsules (equivalent to 4 mg of tamsulosin hydrochloride) into a 250-mL volumetric flask. Add 200 mL of *Diluent*, stir, and sonicate simultaneously for at least 2 h. Cool, and dilute with *Diluent* to volume. Pass through a suitable filter.
System suitability and **Analysis:** Proceed as directed for *Procedure 2.*
Acceptance criteria: 90.0%–110.0%● (RB 1-Oct-2010)

Add the following:

•• **PROCEDURE 6:** Use this *Procedure* for Capsules labeled to meet the requirements of *Dissolution Test 6*.
Solution B and **Mobile phase:** Proceed as directed for *Procedure 1*.
Buffer: Dissolve 6.8 g of monobasic potassium phosphate and 0.9 g of sodium hydroxide in 1 L of water. Adjust with sodium hydroxide solution to a pH of 6.8 ± 0.05.
Diluent A: Acetonitrile and *Buffer* (1:1)
Diluent B: Acetonitrile and *Solution B* (1:1)
Standard solution: Prepare a solution containing 0.4 mg/mL of USP Tamsulosin Hydrochloride RS in *Diluent A*, using sonication as necessary. Dilute 2 mL of this solution with *Diluent B* to 100 mL.
Sample solution: Weigh the contents of NLT 20 Capsules. Mix the contents, and transfer a weighed portion of the capsule contents, equivalent to 4 mg of tamsulosin hydrochloride, into a 100-mL volumetric flask. Add 60 mL of *Diluent A*, and sonicate with intermittent shaking to disperse the pellets completely. Cool, and dilute with *Diluent A* to volume. Centrifuge, transfer 5 mL of supernatant solution to a 25-mL volumetric flask, and dilute with *Diluent B* to volume. Pass through a nylon membrane filter of 0.45-µm pore size.
Chromatographic system: Proceed as directed for *Procedure 1*, except to inject 20 µL.
System suitability and **Analysis:** Proceed as directed for *Procedure 2.*
Acceptance criteria: 90.0%–110.0%● (RB 1-Oct-2010)

Add the following:

•• **PROCEDURE 7:** Use this *Procedure* for Capsules labeled to meet the requirements of *Dissolution Test 7*.
Solution B and **Mobile phase:** Proceed as directed for *Procedure 1*.
Buffer: Dissolve 76 g of tribasic sodium phosphate in 1 L of water.
Diluent: 0.1 N hydrochloric acid and *Buffer* (3:1), pH adjusted to 7.0 with diluted hydrochloric acid or sodium hydroxide solution
Standard solution: 0.0016 mg/mL of USP Tamsulosin Hydrochloride RS in *Diluent*
Sample solution: Weigh the contents of NLT 20 Capsules. Mix the contents, and transfer a weighed portion of the Capsule contents, equivalent to 0.4 mg of tamsulosin hydrochloride, into a 250-mL volumetric flask, and dilute with *Diluent* to volume. Stir for 24 h by mechanical means at 40° protected from light. Pass through a suitable filter of 0.45-µm pore size.
Chromatographic system: Proceed as directed for *Procedure 1*, except to inject 50 µL.
System suitability and **Analysis:** Proceed as directed for *Procedure 2.*
Acceptance criteria: 90.0%–110.0%● (RB 1-Oct-2010)

Add the following:

•• **PROCEDURE 8:** Use this *Procedure* for the Capsules labeled to meet the requirements of *Dissolution Test 8*.

Solution B, Mobile phase, and **Chromatographic system:** Proceed as directed for *Procedure 1*.

Standard solution: Prepare a solution containing 1.0 mg/mL of USP Tamsulosin Hydrochloride RS in methanol. Dilute 5 mL of this solution with *Mobile phase* to 20 mL.

Sample solution: Weigh the contents of NLT 20 Capsules. Mix the contents, and transfer a weighed portion of the Capsule contents, equivalent to 2.5 mg of tamsulosin hydrochloride, into a 100-mL volumetric flask. Add 25 mL of 0.1 N sodium hydroxide, and sonicate for 30 min. Add 30 mL of *Mobile phase*, and shake by mechanical means for 30 min. Centrifuge, and pass through a PVDF membrane filter of 0.45-µm pore size, discarding the first few mL of the filtrate.

System suitability and **Analysis:** Proceed as directed for *Procedure 2*.

Acceptance criteria: 90.0%–110.0% ● (RB 1-Oct-2010)

PERFORMANCE TESTS

Change to read:

• **DISSOLUTION** ⟨**711**⟩

●**Test 1**● (RB 1-Oct-2010)

Acid stage medium: Dissolve 2.0 g of sodium chloride in 5.7 mL of hydrochloric acid, and add water to make up to 1000 mL. To 500 mL of this fluid add 1 mL of polysorbate 80 aqueous solution (3 g in 200 mL of water) just before the test; 500 mL.

Buffer stage medium: Phosphate buffer, pH 7.2. ●(Dissolve 6.8 g of monobasic potassium phosphate in 250 mL of water, add 90 mL of 0.2 N sodium hydroxide and 500 mL of water, adjust with 0.2 N sodium hydroxide or 0.2 N hydrochloric acid to a pH of 7.2 ± 0.05, and dilute with water to volume); ● (RB 1-Oct-2010) 500 mL

Apparatus 2: 100 rpm with sinker (see *Figure 2a* in *Dissolution* ⟨711⟩)

Times: 2, 3, and 8 h

Analysis: Perform the test using *Acid stage medium*. At 2 h after the start of the test, withdraw 10.0 mL of the solution under test (T1). Drain the *Acid stage medium* immediately by suction through a tube capped with a 60-mesh stainless wire screen. Rinse the drain tube while adding the *Buffer stage medium* previously warmed, and continue the test. At 3 h after the start of the test (1 h after replacement of the *Medium*), withdraw 10.0 mL of the solution under test (T2), replace the same volume with warmed *Buffer stage medium*, and continue the test. At 8 h after the start of the test (6 h after the replacement of the *Medium*), withdraw 10.0 mL of the solution under test (T3).

Internal standard solution: 0.008 mg/mL of propylparaben in acetonitrile and water (3:7)

Standard solution: Prepare a solution containing 0.5 mg/mL of USP Tamsulosin Hydrochloride RS in acetonitrile and water (3:7). Transfer 4.0 mL of this solution to a 100-mL volumetric flask, and dilute with *Acid stage medium* to volume. Transfer 4.0 mL of this dilution to another 100-mL volumetric flask, and dilute with *Acid stage medium* to volume. This solution has a known concentration (C_S) of about 0.8 µg/mL of tamsulosin hydrochloride. Transfer 10.0 mL of this last dilution to a test tube, and add 2.0 mL of the *Internal standard solution*.

Sample solutions: Add 2.0 mL of the *Internal standard solution* to T1, mix well, and pass through a suitable filter of 0.5-µm pore size, discarding the first 5 mL. Add 1.0 mL of 0.5 N hydrochloric acid and 2.0 mL of *Internal standard solution* to T2, mix well, and pass through a suitable filter of 0.5-µm pore size, discarding the first 5 mL. Add 1.0 mL of 0.5 N hydrochloric acid and 2.0 mL of *Internal standard solution* to T3. Mix well, and pass through a suitable filter of 0.5-µm pore size, discarding the first 5 mL.

Chromatographic system: Proceed as directed in the *Assay*, but using the *Standard solution* described for *Dissolution*, and inject 250 µL instead of 10 µL.

Calculate the ratios (R_{T1}, R_{T2}, R_{T3}, and R_S) of the peak area of tamsulosin to that of the internal standard for all *Sample solutions* and the *Standard solution*. Calculate the percentage of tamsulosin hydrochloride dissolved at each of the following time points.

At 2 h:

$$D_1 = [(C_S \times V)/L] \times (R_{T1}/R_S) \times 100$$

At 3 h:

$$D_2 = [(C_S \times V)/L] \times [(R_{T2}/R_S) + R_{T1}/R_S)] \times 100$$

At 8 h:

$$D_3 = [(C_S \times V)/L] \times [(R_{T3}/R_S) + (R_{T2}/R_S \times V_{T2}/V) + (R_{T1}/R_S)] \times 100$$

C_S = concentration of the *Standard solution*
V = volume of *Medium*, 500 mL
L = Capsule label claim (mg)
V_{T2} = volume of the withdrawn aliquot of T2, 10 mL

Tolerances: See *Table 1*.

Table 1

Time (h)	Amount Dissolved
2	13%–34%
3	47%–68%
8	NLT 80%

The percentages of the labeled amount of tamsulosin hydrochloride dissolved at the times specified conform to *Acceptance Table 2* in ⟨711⟩.

●**Test 2:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Acid stage medium: 0.003% polysorbate 80, pH 1.2 (dilute 8.5 mL of hydrochloric acid with water to 900 mL, add 0.03 mL of polysorbate 80, adjust with 0.2 N sodium hydroxide or 0.2 N hydrochloric acid to a pH of 1.2 ± 0.05, and dilute with water to 1000 mL); 500 mL

Buffer stage medium: Phosphate buffer, pH 7.2 (proceed as directed for *Test 1*); 500 mL

Apparatus 2: 100 rpm, with sinkers.[1]

Times: 2 h for the *Acid stage medium* and 6 h for the *Buffer stage medium*; 8 h total test time

Analysis: Perform the test using *Acid stage medium*. At 2 h after the start of the test, withdraw a sample of the solution under test. Carefully discard the *Acid stage medium* and replace it with the *Buffer stage medium* previously warmed, and continue the test. At 6 h after the replacement of the *Medium*, withdraw a sample of the solution under test.

Standard stock solution: Transfer about 25.0 mg of USP Tamsulosin Hydrochloride RS to a 50-mL volumetric flask. Add 25 mL of methanol. Dilute with *Buffer stage medium* to volume. Sonicate until dissolved.

Standard solution: Dilute the *Standard stock solution* with *Buffer stage medium* to obtain a final concentration of 0.8 µg/mL.

Sample solution: Pass a portion of the solution under test through a suitable filter.

[1] A suitable sinker is available as catalog number CAPWHT-2S from www.qla-llc.com.

Buffer solution: 3.4 g/L of monobasic potassium phosphate in water. Adjust with 2 N sodium hydroxide to a pH of 5.80 ± 0.05.
Mobile phase: Acetonitrile and *Buffer solution* (1:3)
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 225 nm
Column: 4.6-mm × 15-cm, 5-µm packing L1
Flow rate: 1.0 mL/min
Injection size: 50 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Column efficiency: NLT 2000
Tailing factor: NMT 2.0
Relative standard deviation: NMT 2.0%
Calculate the concentration of tamsulosin hydrochloride in the *Medium* at each time point (C_i).
At 2 h:

$$C_1 = (r_U/r_S) \times C_S$$

At 6 h:

$$C_2 = (r_U/r_S) \times C_S$$

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 tamsulosin hydrochloride dissolved at each time point, (Q_i).
At 2 h:

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

At 6 h:

$$Q_2 = (C_1 + C_2) \times (V/L) \times 100$$

V = volume of *Medium* (mL)
L = Capsule label claim (mg)
Tolerances: NMT 25% of the labeled amount of tamsulosin hydrochloride is dissolved in 2 h. NLT 85% of the labeled amount of tamsulosin hydrochloride is dissolved in 8 h.
Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.
Acid stage
Acid stage medium: 0.003% polysorbate 80, pH 1.2 (proceed as directed for *Test 2*); 500 mL
Apparatus 2: 100 rpm, with sinkers
Time: 2 h
Analysis: Pass a portion of the solution under test through a suitable filter. Leave the remaining *Acid stage medium* in the vessel and proceed with the *Buffer stage*.
Tolerances: NMT 10% (Q) of the labeled amount of tamsulosin hydrochloride is dissolved.
Buffer stage
Buffer stage concentrate: 0.1 M phosphate buffer, pH 11.6 (138 g of sodium phosphate monohydrate and 320 mL of 5 N sodium hydroxide in 10 L of water. Adjust with 5 N sodium hydroxide to a pH of 11.6 ± 0.05.)
Buffer stage medium: Add 500 mL of the *Buffer stage concentrate* to the remaining *Acid stage medium* in each vessel. The final pH is about 7.2.
Apparatus 2: 100 rpm, with sinkers
Time: 3 h and 8 h, including the 2 h in the *Acid stage medium*
Sample solution: Pass a portion of the solution under test through a suitable filter.
Standard stock solution: 0.5 mg/mL of USP Tamsulosin Hydrochloride RS in water and methanol (1:1)
Standard solution: Dilute the *Standard stock solution* with *Buffer stage medium* to obtain a final concentration of 0.3 µg/mL.
pH 5.5 buffer solution: 6.8 g/L of monobasic potassium phosphate in water. Adjust with 2 N sodium hydroxide to a pH of 5.5 ± 0.05.
Mobile phase: acetonitrile and *pH 5.5 buffer solution* (2:3)
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 275 nm
Column: 4.6-mm × 15-cm, 5-µm packing L1
Column temperature: 30°
Flow rate: 1 mL/min
Injection size: 100 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Tailing factor: NMT 2.0
Relative standard deviation: NMT 2.5%
Calculate the concentration of tamsulosin hydrocloride dissolved at each time point (C_i).
At 3 h:

$$C_1 = (r_U/r_S) \times C_S$$

At 8 h:

$$C_2 = (r_U/r_S) \times C_S$$

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 tamsulosin hydrochloride dissolved at each time point (Q_i):

$$Q_i = (C_1V_1 + \sum_{i=2}^{n-1} C_iV_S + C_nV) \times (100/L)$$

V_1 = volume of *Acid stage medium*, 500 mL
V_S = volume of sample taken (mL)
C_n = concentration of tamsulosin hydrochloride at each time point
V = volume of *Buffer stage medium*, 1000 mL
L = Capsule label claim (mg)
Tolerances: See *Table 2*.

Table 2

Time (h)	Amount Dissolved
3	65%–85%
8	NLT 80%

The percentages of the labeled amount of tamsulosin hydrochloride dissolved at the times specified conform to *Acceptance Table 2* in ⟨711⟩.
Test 4: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 4*.
Acid stage medium: 0.003% polysorbate 80, pH 1.2 (proceed as directed for *Test 2*); 500 mL
Buffer stage medium: Phosphate buffer, pH 7.2 (proceed as directed for *Test 1*); 500 mL

Apparatus 2: 100 rpm, with sinkers
Times: 2 h for the *Acid stage medium*, 3 h, and 8 h for the *Buffer stage medium* (including the 2 h in the *Acid stage medium*)
Analysis: Perform the test using the *Acid stage medium*. At 2 h after the start of the test, withdraw a sample of the solution under test. Carefully discard the *Acid stage medium*, replace it with the *Buffer stage medium* previously warmed, and continue the test. At 1 h and 6 h after the replacement of the *Medium*, withdraw a sample of the solution under test. Replace the volume of *Medium* withdrawn with the same volume of *Buffer stage medium*, previously warmed.
50 mM sodium perchlorate solution: Dissolve 7.0 g of monohydrate sodium perchlorate in 1 L of water, and add 5 mL of phosphoric acid.
Mobile phase: *50 mM sodium perchlorate solution* and acetonitrile (3:2)
Acid stage standard stock solution: Transfer 20 mg of USP Tamsulosin Hydrochloride RS to a 500-mL volumetric flask, add 25 mL of methanol, and sonicate until dissolved. Dilute with *Acid stage medium* to volume.
Acid stage standard solution: Dilute the *Acid stage standard stock solution* with *Acid stage medium* to obtain a final concentration of about 0.08 µg/mL.
Buffer stage standard stock solution: Transfer 20 mg of USP Tamsulosin Hydrochloride RS to a 250-mL volumetric flask, add 25 mL of methanol, and sonicate until dissolved. Dilute with *Buffer stage medium* to volume.
Buffer stage standard solution: Dilute the *Buffer stage standard stock solution* with *Buffer stage medium* to obtain a final concentration of about 0.8 µg/mL.
Sample solution: Pass a portion of the solution under test through a suitable filter.
Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)
Mode: LC
Detector: UV 230 nm
Analytical column: 3.9-mm × 15-cm, 5-µm packing L1
Guard column: 3-mm × 4-cm, packing L1
Column temperature: 35°
Flow rate: 1.5 mL/min
Injection size: 200 µL
System suitability
Samples: *Acid stage standard solution* and *Buffer stage standard solution*
Suitability requirements
Column efficiency: NLT 1600, *Acid stage standard solution*; NLT 1300, *Buffer stage standard solution*
Relative standard deviation: NMT 3.0%, *Acid stage standard solution*; NMT 1.5%, *Buffer stage standard solution*
Calculate the concentration of tamsulosin hydrocloride dissolved at each time point (C_i).
At 2 h:

$$C_1 = (r_U/r_S) \times C_S$$

At 3 h:

$$C_2 = (r_U/r_S) \times C_S$$

At 8 h:

$$C_3 = (r_U/r_S) \times C_S$$

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 tamsulosin hydrochloride dissolved at each time point (Q_i):

$$Q_i = (C_1V_1 + \sum_{i=2}^{n-1} C_iV_S + C_nV) \times (100/L)$$

V_1 = volume of *Acid stage medium*, 500 mL
V_S = volume of sample taken (mL)
C_n = concentration of tamsulosin hydrochloride at each time point
V = volume of *Buffer stage medium*, 1000 mL
L = Capsule label claim (mg)
Tolerances: See *Table 3*.

Table 3

Time (h)	Amount Dissolved
2	0%–10%
3	45%–68%
8	NLT 80%

The percentages of the labeled amount of tamsulosin hydrochloride dissolved at the times specified in the *Buffer stage* conform to *Acceptance Table 2* in ⟨711⟩.
Test 5: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 5*.
Acid stage medium: 0.003% polysorbate 80, pH 1.2 (proceed as directed for *Test 2*); 500 mL
Buffer stage medium: Phosphate buffer, pH 7.2 (proceed as directed for *Test 1*); 500 mL
Apparatus 2: 50 rpm, with sinkers
Times: 2 h for the *Acid stage medium*, and 3 h and 5 h for the *Buffer stage medium* (including the 2 h in the *Acid stage medium*)
Buffer solution: Dissolve 1.0 g of octanesulfonic acid sodium salt and 1.4 g of monobasic potassium phosphate in 1 L of water. Adjust with potassium hydroxide to a pH of 6.5 ± 0.05.
Mobile phase: *Buffer solution* and acetonitrile (3:2)
Standard stock solution: 0.04 mg/mL of USP Tamsulosin Hydrochloride RS in *Buffer stage medium*
Standard solution: Dilute the *Standard stock solution* with *Buffer stage medium* to obtain a final concentration of 0.8 µg/mL.
Sample solution: Centrifuge a portion of the solution under test at NMT 3000 rpm for NLT 20 min.
Analysis: Perform the test using *Acid stage medium*. At 2 h after the start of the test, withdraw a sample of the solution under test. Carefully discard the *Acid stage medium* replace it with the *Buffer stage medium* previously warmed, and continue the test. At 1 h and 3 h after the replacement of the *Medium*, withdraw a sample of the solution under test. Replace the volume of *Medium* withdrawn with the same volume of *Buffer stage medium*, previously warmed.
Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)

Mode: LC
Detector: UV 225 nm
Column: 3.9-mm × 7.5-cm, 5-µm packing L7
Column temperature: 30°
Flow rate: 1.5 mL/min
Injection size: 100 µL

System suitability
Sample: *Standard solution*
Suitability requirements
Relative standard deviation: NMT 4.0%

Calculate the concentration of tamsulosin hydrocloride dissolved at each time point (C_i).

At 2 h:

$$C_1 = (r_U/r_S) \times C_S$$

At 3 h:

$$C_2 = (r_U/r_S) \times C_S$$

At 5 h:

$$C_3 = (r_U/r_S) \times C_S$$

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 tamsulosin hydrochloride dissolved at each time point (Q_i):

$$Q_i = (C_1V_1 + \sum_{i=2}^{n-1} C_iV_S + C_nV) \times (100/L)$$

V_1 = volume of *Acid stage medium*, 500 mL
V_S = volume of sample taken (mL)
C_n = concentration of tamsulosin hydrochloride at each time point
V = volume of *Buffer stage medium*, 500 mL
L = Capsule label claim (mg)

Tolerances: See *Table 4*.

Table 4

Time (h)	Amount Dissolved
2	15%–35%
3	60%–80%
5	NLT 80%

The percentages of the labeled amount of tamsulosin hydrochloride dissolved at the times specified conform to *Acceptance Table 2* in ⟨711⟩.

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

Acid stage medium: 0.003% polysorbate 80, pH 1.2 (proceed as directed for *Test 2*); 500 mL

Buffer stage medium: Phosphate buffer, pH 7.2 (proceed as directed for *Test 1*); 500 mL

Apparatus 2: 100 rpm, using a 40-mesh basket as a sinker, and the paddle height adjusted at 4.5 cm from the bottom of the vessel

Times: 2 h for the *Acid stage medium*, and 3 h and 8 h for the *Buffer stage medium* (including the 2 h in the *Acid stage medium*)

Analysis: Perform the test using *Acid stage medium*. At 2 h after the start of the test, withdraw a sample of the solution under test. Carefully discard the *Acid stage medium*, replace it with the *Buffer stage medium* previously warmed, and continue the test. At 1 h and 6 h after the replacement of the *Medium*, withdraw a sample of the solution under test. Replace the volume of *Medium* withdrawn with the same volume of *Buffer stage medium*, previously warmed.

Buffer solution: Dissolve 3 g of sodium hydroxide and 8.7 mL of perchloric acid in 1900 mL of water, adjust with 0.5 M sodium hydroxide to a pH of 2.0 ± 0.05, and dilute with water to 2000 mL.

Mobile phase: *Buffer solution* and acetonitrile (7:3)

Standard stock solution: 0.5 mg/mL of USP Tamsulosin Hydrochloride RS in methanol

Acid stage standard solution: Dilute the *Standard stock solution* with *Acid stage medium* to obtain a final concentration of 0.8 µg/mL.

Buffer stage standard solution: Dilute the *Standard stock solution* with *Buffer stage medium* to obtain a final concentration of 0.8 µg/mL.

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

Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 225 nm
Column: 4.6-mm × 15-cm, 3-µm packing L1
Column temperature: 40°
Flow rate: 1.5 mL/min
Injection size: 100 µL

System suitability
Samples: *Acid stage standard solution* and *Buffer stage standard solution*
Suitability requirements
Column efficiency: NLT 7000
Tailing factor: NMT 2.0
Relative standard deviation: NMT 2.0%

Calculate the concentration of tamsulosin hydrocloride dissolved at each time point (C_i).

At 2 h:

$$C_1 = (r_U/r_S) \times C_S$$

At 3 h:

$$C_2 = (r_U/r_S) \times C_S$$

At 8 h:

$$C_3 = (r_U/r_S) \times C_S$$

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 tamsulosin hydrochloride dissolved at each time point (Q_i):

$$Q_i = (C_1V_1 + \sum_{i=2}^{n-1} C_iV_S + C_nV) \times (100/L)$$

V_1 = volume of *Acid stage medium*, 500 mL
V_S = volume of sample taken (mL)
C_n = concentration of tamsulosin hydrochloride at each time point
V = volume of *Buffer stage medium*, 500 mL
L = Capsule label claim (mg)

Tolerances: See *Table 5*.

Table 5

Time (h)	Amount Dissolved
2	0%–20%
3	47%–68%
8	NLT 80%(*Q*)

The percentages of the labeled amount of tamsulosin hydrochloride dissolved at the times specified conform to *Acceptance Table 2* in ⟨711⟩.

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

Acid stage medium: 0.003% polysorbate 80, pH 1.2 (proceed as directed for *Test 2*); 500 mL

Buffer stage medium: Phosphate buffer, pH 7.2 (proceed as directed for *Test 1*); 500 mL, deaerated

Apparatus 2: 100 rpm, with wire helix sinkers

Times: 2 h in the *Acid stage medium*, and 4 h and 12 h in the *Buffer stage medium* (including the 2 h in the *Acid stage medium*)

Standard stock solution: 1 mg/mL of USP Tamsulosin Hydrochloride RS in alcohol

Acid stage standard solution: Dilute the *Standard stock solution* with *Acid stage medium* to obtain a final concentration of about 0.2 µg/mL.

Buffer stage standard solution: Dilute the *Standard stock solution* with *Buffer stage medium* to obtain a final concentration of about 0.8 µg/mL.

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

Analysis: Perform the test using *Acid stage medium*. At 2 h after the start of the test, withdraw a sample of the solution under test. Carefully discard the *Acid stage medium*, replace it with the *Buffer stage medium* previously warmed, and continue the test. At 1 h and 6 h after the replacement of the *Medium*, withdraw a sample of the solution under test. Replace the volume of *Medium* withdrawn with the same volume of *Buffer stage medium*, previously warmed.

Mobile phase A: 2.76 g/L of monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 2.5 ± 0.05.

Mobile phase B: Acetonitrile

Gradient program: See *Table 6*.

Table 6

Time (min)	% Mobile phase A	% Mobile phase B
0	86	14
3	86	14
4.5	30	70
5	86	14

Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)
Mode: LC
Detector: UV 225 nm
Column: 2-mm × 5-cm, packing L1
Column temperature: 30°
Flow rate: 1.5 mL/min
Injection size: 100 µL

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

Suitability requirements
Tailing factor: NMT 1.5
Relative standard deviation: NMT 2.0%

Calculate the concentration of tamsulosin hydrocloride dissolved at each time point (C_i).

At 2 h:

$$C_1 = (r_U/r_S) \times C_S$$

At 4 h:

$$C_2 = (r_U/r_S) \times C_S$$

At 12 h:

$$C_3 = (r_U/r_S) \times C_S$$

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 tamsulosin hydrochloride dissolved at each time point (Q_i):

$$Q_i = (C_1V_1 + \sum_{i=2}^{n-1} C_iV_S + C_nV) \times (100/L)$$

V_1 = volume of *Acid stage medium*, 500 mL
V_S = volume of sample taken (mL)
C_n = concentration of tamsulosin hydrochloride at each time point
V = volume of *Buffer stage medium*, 500 mL
L = Capsule label claim (mg)

Tolerances: See *Table 7*.

Table 7

Time (h)	Amount Dissolved
2	5%–25%
4	46%–66%
12	NLT 80%

The percentages of the labeled amount of tamsulosin hydrochloride dissolved at the times specified conform to *Acceptance Table 2* in ⟨711⟩.

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

Acid stage medium: 0.003% polysorbate 80, pH 1.2 (proceed as directed for *Test 2*); 500 mL

Buffer stage medium: Phosphate buffer, pH 7.2 (proceed as directed for *Test 1*); 500 mL

Apparatus 2: 50 rpm, with sinkers

Times: 2 h in the *Acid stage medium*, and 3 h and 8 h in the *Buffer stage medium* (including the 2 h in the *Acid stage medium*)

Standard stock solution: 0.4 mg/mL of USP Tamsulosin Hydrochloride RS in methanol

Acid stage standard solution: Dilute the *Standard stock solution* with *Acid stage medium* to obtain a final concentration of 0.8 µg/mL.

Buffer stage standard solution: Dilute the *Standard stock solution* with *Buffer stage medium* to obtain a final concentration of 0.8 µg/mL.

Analysis: Perform the test using *Acid stage medium*. At 2 h after the start of the test, withdraw a sample of the solution under test. Carefully discard the *Acid stage medium*, replace it with the *Buffer stage medium* previously warmed, and continue the test. At 1 h and 6 h after the replacement of the *Medium*, withdraw a sample of the solution under test. Replace the volume of *Medium* withdrawn with

the same volume of *Buffer stage medium*, previously warmed.

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

Buffer solution: Dissolve 6.8 g of dibasic ammonium phosphate in 800 mL of water, and add 2 mL of triethylamine. Adjust with phosphoric acid to a pH of 6.5. Dilute with water to 1000 mL.

Mobile phase: *Buffer solution* and acetonitrile (7:3)

Chromatographic system

(See *Chromatography* ⟨621⟩, *System Suitability*.)

Mode: LC

Detector: UV 225 nm

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

Column temperature: 30°

Flow rate: 1.0 mL/min

Injection size: 100 µL

Suitability requirements

Sample: *Buffer stage standard solution*

Column efficiency: NLT 2000 theoretical plates

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Calculate the concentration of tamsulosin hydrocloride dissolved at each time point (C_i).

At 2 h:

$$C_1 = (r_U/r_S) \times C_S$$

At 3 h:

$$C_2 = (r_U/r_S) \times C_S$$

At 8 h:

$$C_3 = (r_U/r_S) \times C_S$$

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 tamsulosin hydrochloride dissolved at each time point (Q_i):

$$Q_i = (C_1V_1 + \sum_{i=2}^{n-1} C_iV_S + C_nV) \times (100/L)$$

V_1 = volume of *Acid stage medium*, 500 mL
V_S = volume of sample taken (mL)
C_n = concentration of tamsulosin hydrochloride at each time point
V = volume of *Buffer stage medium*, 500 mL
L = Capsule label claim (mg)

Tolerances: See *Table 8*.

Table 8

Time (h)	Amount Dissolved
2	0%–10%
3	50%–70%
8	NLT 80%

The percentages of the labeled amount of tamsulosin hydrochloride dissolved at the times specified conform to *Acceptance Table 2* in ⟨711⟩. ● (RB 1-Oct-2010)

Change to read:

• **UNIFORMITY OF DOSAGE UNITS ⟨905⟩:** Meet the requirements

Procedure for content uniformity

●[NOTE—Use the following *Procedure for content uniformity* if *Procedure 1* is used in the *Assay*. For all other formulations, proceed as directed in the test for *Uniformity of Dosage Units* ⟨905⟩.]● (RB 1-Oct-2010)

Solution A, Solution B, Mobile phase, and **Standard stock solution:** Prepare as directed in the *Assay*, ●*Procedure 1*.● (RB 1-Oct-2010)

Internal standard solution: 0.16 mg/mL of propylparaben in a mixture of acetonitrile and water (3:7)

Standard stock solution 1: Transfer 5.0 mL of the *Standard stock solution* to a 25-mL volumetric flask, and dilute with a mixture of acetonitrile and water (3:7) to volume.

Standard solution: Transfer 4.0 mL of *Standard stock solution 1* to a suitable container. Add 5.0 mL of the *Internal standard solution,* and add the *Mobile phase* to make 40 mL.

Sample solution: Place the content of 1 Capsule into a Teflon-lined, screw-cap centrifuge tube. Place approximately 100 glass balls with a diameter of about 5 mm into the tube, add 20 mL of 0.05 N sodium hydroxide, heat at 50° for 10 min, and shake well for 30 min. Add 15 mL of a mixture of acetonitrile and *Solution A* (2:1) to the solution, and shake well. Add 5.0 mL of the *Internal standard solution,* and shake well. Centrifuge at 1500 rpm for 10 min, and use the supernatant, passing it if necessary through a membrane filter of pore size 0.5 µm or smaller.

Chromatographic system: Proceed as directed in the *Assay*, ●*Procedure 1*,● (RB 1-Oct-2010) except to inject 25 µL.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of tamsulosin hydrochloride ($C_{20}H_{28}N_2O_5S \cdot HCl$) in the Capsule taken:

$$\text{Result} = (R_U/R_S) \times (C_S \times V_S/L) \times 100$$

R_U = ratio of the peak areas for tamsulosin and the internal standard from the *Sample solution*
R_S = ratio of the peak areas for tamsulosin and the internal standard from the *Standard solution*
C_S = concentration of USP Tamsulosin Hydrochloride RS in *Standard stock solution 1* (mg/mL)
V_S = volume of *Standard stock solution 1* taken to prepare the *Standard solution* (mL)
L = Capsule label claim (mg)

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in tight containers. Store at controlled room temperature.

Add the following:

●• **LABELING:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.● (RB 1-Oct-2010)

• **USP REFERENCE STANDARDS ⟨11⟩**

USP Tamsulosin Hydrochloride RS

(–)-(*R*)-5-[2-[[2-(*o*-Ethoxyphenoxy)ethyl]amino]propyl]-2-methoxybenzenesulfonamide monohydrochloride.

$C_{20}H_{28}N_2O_5S \cdot HCl$ 444.97