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Dutasteride and Tamsulosin Hydrochloride Capsules

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click https://www.uspnf.com/rb-dutasteride-tamsulosin-hcl-caps-20240426.

DEFINITION

Dutasteride and Tamsulosin Hydrochloride Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of dutasteride ($C_{27}H_{30}F_6N_2O_2$) and NLT 90.0% and NMT 110.0% of the labeled amount of tamsulosin hydrochloride ($C_{20}H_{28}N_2O_5S \cdot HCl$). They may contain butylated hydroxytoluene or another suitable antioxidant.

IDENTIFICATION

• **A.** The retention time of the dutasteride peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay, Procedure 1: Dutasteride*.

• **B.** The UV spectrum of the dutasteride peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay, Procedure 1: Dutasteride*.

• **C.** The retention time of the tamsulosin peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay, Procedure 2: Tamsulosin Hydrochloride*.

• **D.** The UV spectrum of the tamsulosin peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay, Procedure 2: Tamsulosin Hydrochloride*.

ASSAY

• **Procedure 1: Dutasteride**

Buffer: 1.37 g/L of potassium dihydrogen phosphate in water. Adjust with phosphoric acid to a pH of 3.0.

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

Diluent A: Acetonitrile and water (90:10)

Diluent B: Acetonitrile and water (50:50)

Standard solution: 0.02 mg/mL of USP Dutasteride RS in *Diluent A*. Sonicate to dissolve, if necessary.

Sample solution: Nominally 0.02 mg/mL of dutasteride prepared as follows. Take Capsules (NLT 20) and remove the contents, separating the pellets and the soft gelatin capsules. Weigh and transfer the intact soft gelatin capsules into a 500-mL volumetric flask. Add *Diluent B* to 20% of the total volume, and sonicate with shaking until the capsules completely rupture. Add acetonitrile to 50% of the total volume and sonicate for NLT 10 min with shaking at every 3 min for a period of 30 s. Dilute with acetonitrile to volume and mix. Pass the solution through a suitable filter of 0.22-µm pore size. Discard the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

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

Flow rate: 2 mL/min

Injection volume: 100 µL

Run time: NLT 2.5 times the retention time of dutasteride

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 dutasteride ($C_{27}H_{30}F_6N_2O_2$) in the portion of Capsules taken:

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

r_U = peak response of dutasteride from the *Sample solution*

r_S = peak response of dutasteride from the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0%

- **Procedure 2: Tamsulosin Hydrochloride**

Buffer: 2.554 g/L of anhydrous disodium hydrogen phosphate and 0.272 g/L of potassium dihydrogen phosphate in water. Adjust with dilute phosphoric acid to a pH of 7.0.

Mobile phase: Methanol and *Buffer* (55:45)

Standard stock solution: 160 µg/mL of USP Tamsulosin Hydrochloride RS in methanol. Sonicate to dissolve, if necessary.

Standard solution: 8 µg/mL of USP Tamsulosin Hydrochloride RS from *Standard stock solution* in *Mobile phase*

Sample solution: Nominally 8 µg/mL of tamsulosin hydrochloride prepared as follows. Weigh Capsules (NLT 20) and determine the average net content. Open the capsules and remove pellets, and determine weight of the capsules with the soft gelatin capsules. Calculate the average net content of pellets. Accurately weigh and transfer a quantity of pellets equivalent to about 2 mg of tamsulosin hydrochloride to a 250-mL volumetric flask. Add 1 N sodium hydroxide solution to 12% of the total volume and sonicate for NLT 30 min. Add methanol to 28% of the total volume and sonicate for NLT 15 min. Dilute with *Mobile phase* to volume and mix. Pass a portion of the solution through a suitable filter of 0.45-µm pore size. Discard the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 225 nm. For *Identification D*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 35°

Flow rate: 1 mL/min

Injection volume: 50 µL

Run time: NLT 1.5 times the retention time of tamsulosin

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 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 of tamsulosin from the *Sample solution*

r_S = peak response of tamsulosin from the *Standard solution*

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

C_U = nominal concentration of tamsulosin in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0%

OTHER COMPONENTS

- **Content of Butylated Hydroxytoluene (if present in the product)**

Buffer, Mobile phase, and **Diluent A:** Prepare as directed in the *Assay*, *Procedure 1: Dutasteride*.

Standard solution: 7 µg/mL of USP Butylated Hydroxytoluene RS in *Diluent A*. Sonicate to dissolve.

Sample solution: Nominally 7 µg/mL of butylated hydroxytoluene in *Diluent A* prepared as follows. Remove the contents of the Capsules (NLT 20) separating the pellets and soft gelatin capsules. Remove as completely as possible the content of the soft gelatin capsules. Mix the contents, and determine the average net content of the soft gelatin capsules. Accurately weigh and transfer a quantity of the contents of the soft gelatin capsules equivalent to about 0.175 mg of butylated hydroxytoluene to a 25-mL volumetric flask. Add *Diluent A* to 60% of the total volume and sonicate to dissolve. Dilute with *Diluent A* to volume and mix.

Chromatographic system: Proceed as directed in the *Assay*, *Procedure 1: Dutasteride*, except for *Injection volume*.

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 5.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of butylated hydroxytoluene ($C_{15}H_{24}O$) in the portion of Capsules taken:

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

r_U = peak response of butylated hydroxytoluene from the *Sample solution*

r_S = peak response of butylated hydroxytoluene from the *Standard solution*

C_S = concentration of USP Butylated Hydroxytoluene RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of butylated hydroxytoluene in the *Sample solution* (µg/mL)

Acceptance criteria: 85.0%–110.0% of the labeled amount of butylated hydroxytoluene ($C_{15}H_{24}O$)

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

▲Test 1▲ (RB 1-May-2024)

Test for dutasteride

Tier 1

Medium: 10 g/L of cetyltrimethylammonium bromide in 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 75 rpm with a suitable sinker

Time: 45 min

Tier 2

Medium: Dissolve 10 g of cetyltrimethylammonium bromide and 1.6 g of pepsin, purified in 1000 mL of 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 75 rpm with a suitable sinker

Time: 45 min

Buffer and **Mobile phase:** Prepare as directed in the *Assay, Procedure 1: Dutasteride*.

Standard stock solution: 0.22 mg/mL of USP Dutasteride RS in methanol. Sonicate to dissolve.

Standard solution: 0.55 µg/mL of USP Dutasteride RS from *Standard stock solution* in *Medium*

Sample solution: Withdraw and pass about 10 mL of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first few milliliters of the filtrate.

Dissolution procedure: Perform the test using the conditions under *Tier 1*. In the presence of cross-linking repeat the test with new Capsules using the conditions under *Tier 2*.

Chromatographic system: Proceed as directed in the *Assay, Procedure 1: Dutasteride* except for *Detector* and *Injection volume*.

Detector: UV 240 nm

Injection volume: 500 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 dutasteride ($C_{27}H_{30}F_6N_2O_2$) dissolved:

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

r_U = peak response of dutasteride from the *Sample solution*

r_S = peak response of dutasteride from the *Standard solution*

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Capsule)

Tolerances: NLT 80% (Q) of the labeled amount dutasteride ($C_{27}H_{30}F_6N_2O_2$) is dissolved.

Test for tamsulosin hydrochloride

Acid stage medium: 0.1 N hydrochloric acid; 750 mL

Buffer stage medium: Sodium phosphate buffer, pH 6.8 (after 2 h, add 250 mL of 76 g/L sodium phosphate, tribasic, previously heated to 37 ± 0.5°, to the *Acid stage medium* and adjust with either a dilute phosphoric acid or dilute sodium hydroxide solution to a pH of 6.8 ± 0.1); 1000 mL

Apparatus 2: 50 rpm with a suitable sinker

Times: 2 h in *Acid stage medium*; 3 and 7 h in *Buffer stage medium*. The time in the *Buffer stage medium* includes the time in the *Acid stage medium*.

Buffer: Dissolve 6.8 g of ammonium phosphate, dibasic in about 800 mL of water, add 2.0 mL of triethylamine, and adjust with phosphoric acid to a pH of 7.0. Dilute with water to 1000 mL.

Mobile phase: Acetonitrile and *Buffer* (30:70)

Standard stock solution: 0.4 mg/mL of USP Tamsulosin Hydrochloride RS in methanol. Sonicate to dissolve, if necessary.

Acid stage standard solution: 0.5 µg/mL of USP Tamsulosin Hydrochloride RS from *Standard stock solution* in *Acid stage medium*

Buffer stage standard solution: 0.4 µg/mL of USP Tamsulosin Hydrochloride RS from *Standard stock solution* in *Buffer stage medium*

Acid stage sample solution: Withdraw and pass about 10 mL of the solution under test through a suitable filter of 0.45-µm pore size. Discard the first few milliliters of the filtrate. Replace the portion removed with the same volume of *Acid stage medium*.

Buffer stage sample solution: At the specified time points, withdraw and pass about 10 mL of the solution under test through a suitable filter of 0.45-µm pore size. Discard the first few milliliters of the filtrate. Replace the portion removed at each time point with the same volume of *Buffer stage medium*.

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 mL/min

Injection volume: 250 µL

Run time: NLT 1.5 times the retention time of tamsulosin

System suitability

Sample: *Buffer stage standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 5.0%

Analysis

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

Calculate the concentration (C_i) of tamsulosin hydrochloride ($C_{20}H_{28}N_2O_5S \cdot HCl$) in the sample withdrawn from the vessel at each time point (i) as shown in *Table 1*:

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

r_U = peak response of tamsulosin from the *Acid stage sample solution* or *Buffer stage sample solution*

r_S = peak response of tamsulosin from the *Acid stage standard solution* or *Buffer stage standard solution*

C_S = concentration of USP Tamsulosin Hydrochloride RS in the *Acid stage standard solution* or *Buffer stage standard solution* (mg/mL)

Calculate the percentage of the labeled amount of tamsulosin hydrochloride ($C_{20}H_{28}N_2O_5S \cdot HCl$) dissolved at each time point (i) as shown in *Table 1*:

$$\text{Result}_1 = (C_1 \times V_1) \times (1/L) \times 100$$

$$\text{Result}_2 = [(C_2 \times V_2) + (C_1 \times V_S)] \times (1/L) \times 100$$

$$\text{Result}_3 = \{(C_3 \times V_2) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

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

V_1 = volume of the *Acid stage medium*, 750 mL

L = label claim (mg/Capsule)

V_2 = volume of the *Buffer stage medium*, 1000 mL

V_S = volume of the *Acid stage sample solution* or *Buffer stage sample solution* withdrawn at each time point and replaced with *Acid stage medium* or *Buffer stage medium* (mL)

Tolerances: See *Table 1*.

Table 1

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	2	NMT 10
2	3	45–65
3	7	NLT 80

The percentages of the labeled amount of tamsulosin hydrochloride ($C_{20}H_{28}N_2O_5S \cdot HCl$) 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 it meets USP *Dissolution Test 2*.

Test for dutasteride

Tier 1

Medium: Dissolve 10 g of cetyltrimethylammonium bromide in 1 L of 0.1 N hydrochloric acid; 900 mL.

Deaeration, if necessary, is carried out prior to adding cetyltrimethylammonium bromide.

Apparatus 2: 75 rpm with a suitable sinker[1]

Time: 45 min

Tier 2

Medium: Dissolve 10 g of cetyltrimethylammonium bromide in 1 L of 0.1 N hydrochloric acid. Add 1.6 g of pepsin, purified; 900 mL.

Deaeration, if necessary, is carried out prior to adding cetyltrimethylammonium bromide.

Apparatus 2: 75 rpm with a suitable sinker[1]

Time: 45 min

Solution A: Dissolve 1.38 g of sodium phosphate, monobasic in 1000 mL of water. Adjust with phosphoric acid to a pH of 3.0.

Solution B: Acetonitrile

Mobile phase: See *Table 2*.

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	65	35
5	50	50
10	20	80
12	20	80
17	65	35
22	65	35

Standard stock solution: 0.056 mg/mL of USP Dutasteride RS prepared as follows. Transfer a quantity of USP Dutasteride RS to an appropriate volumetric flask, add 4% of the flask volume of acetonitrile. Sonicate to dissolve, if necessary. Dilute with the corresponding *Medium* to volume.

Standard solution: 0.00056 mg/mL of USP Dutasteride RS from the *Standard stock solution* in the corresponding *Medium*

Sample solution: Pass the solution under test through a suitable filter of 2.7-µm pore size, discarding an appropriate volume of filtrate so that a consistent result can be obtained.

Dissolution procedure: If results under the conditions of *Tier 1* do not meet specifications due to cross-linking, proceed with testing new Capsules under the conditions of *Tier 2*.

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: 1.5 mL/min

Injection volume: 200 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 dutasteride ($C_{27}H_{30}F_6N_2O_2$) dissolved:

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

r_U = peak response of dutasteride from the *Sample solution*

r_S = peak response of dutasteride from the *Standard solution*

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

V = volume of *Medium*, 900 mL

L = label claim of dutasteride (mg/Capsule)

Tolerances: NLT 80% (Q) of the labeled amount of dutasteride ($C_{27}H_{30}F_6N_2O_2$) is dissolved.

Test for tamsulosin hydrochloride

Acid stage medium: 0.1 N hydrochloric acid; 750 mL, deaerated, if necessary

Buffer stage medium: 0.05 M sodium phosphate buffer, pH 6.8 (Dissolve 7.1 g of sodium phosphate, dibasic, anhydrous and 4.5 mL of 5 N hydrochloric acid in 1 L of water. Adjust with sodium hydroxide solution or hydrochloric acid to a pH of 6.8.); 1000 mL, deaerated, if necessary

Apparatus 2: 50 rpm

Time

Acid stage: 2 h

Buffer stage: 2.5 and 5 h. The times in the *Buffer stage medium* include the time in the *Acid stage medium*.

Solution A, Solution B, and **Chromatographic system:** Proceed as directed in the *Test for dutasteride*.

Mobile phase: See *Table 3*.

Table 3

Time (min)	Solution A (%)	Solution B (%)
0	65	35
5	50	50
10	20	80
12	20	80
13	65	35
18	65	35

Standard stock solution: 0.4 mg/mL of USP Tamsulosin Hydrochloride RS prepared as follows. Transfer a quantity of USP Tamsulosin Hydrochloride RS to an appropriate volumetric flask, and add 20% of the flask volume of methanol. Sonicate to dissolve, if necessary. Dilute with water to volume.

Standard solution: 0.0004 mg/mL of USP Tamsulosin Hydrochloride RS from the *Standard stock solution* in *Buffer stage medium*

Acid stage sample solution: Withdraw a suitable volume of the solution under test and pass through a suitable filter of 2.7-µm pore size, discarding an appropriate volume of filtrate so that a consistent result can be obtained.

Buffer stage sample solution: After the *Acid stage*, carefully remove the *Acid stage medium* from the vessels, avoiding the loss of test samples, and replace with *Buffer stage medium*. At the specified time points, withdraw a suitable volume of the solution under test. Pass through a suitable filter of 2.7-µm pore size, discarding an appropriate volume of filtrate so that a consistent result can be obtained.

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 5.0%

Analysis

Samples: *Standard solution*, *Acid stage sample solution*, and *Buffer stage sample solution*

Calculate the percentage (Q_A) of the labeled amount of tamsulosin hydrochloride ($C_{20}H_{28}N_2O_5S \cdot HCl$) dissolved in the *Acid stage*:

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

r_U = peak response of tamsulosin from the *Acid stage sample solution*

r_S = peak response of tamsulosin from the *Standard solution*

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

V_A = volume of the *Acid stage medium*, 750 mL

L = label claim of tamsulosin hydrochloride (mg/Capsule)

Calculate the concentration (C_i) of tamsulosin hydrochloride ($C_{20}H_{28}N_2O_5S \cdot HCl$) in the sample withdrawn from the vessel at each time point (i) during the *Buffer stage*:

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

r_U = peak response of tamsulosin from the *Buffer stage sample solution*

r_S = peak response of tamsulosin from the *Standard solution*

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

Calculate the percentage of the labeled amount of tamsulosin hydrochloride ($C_{20}H_{28}N_2O_5S \cdot HCl$) dissolved at each time point (i) during the *Buffer stage*:

$$\text{Result}_1 = [(C_1 \times V_B) \times (1/L) \times 100] + Q_A$$

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

C_i = concentration of tamsulosin hydrochloride in the portion of sample withdrawn at each time point (i) during the *Buffer stage* (mg/mL)

V_B = volume of the *Buffer stage medium*, 1000 mL

L = label claim of tamsulosin hydrochloride (mg/Capsule)

V_S = volume of the *Buffer stage sample solution* withdrawn at each time point during the *Buffer stage*

Tolerances: See *Table 4*.

Table 4

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	2	15–35
2	2.5	40–65
3	5	NLT 80

The percentages of the labeled amount of tamsulosin hydrochloride ($C_{20}H_{28}N_2O_5S \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.▲ (RB 1-May-2024)

• **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements for both dutasteride and tamsulosin hydrochloride

IMPURITIES

Change to read:

• **Organic Impurities, Procedure 1: Dutasteride**

Solution A: 1.37 g/L of potassium dihydrogen phosphate in water. Adjust with phosphoric acid to a pH of 3.0.

Solution B: Acetonitrile and water (90:10)

Mobile phase: See ▲*Table 5*.

Table 5▲ (RB 1-May-2024)

Time (min)	Solution A (%)	Solution B (%)
0	60	40
10	60	40
40	20	80
45	20	80
50	0	100
60	0	100
65	60	40
70	60	40

System suitability stock solution: 0.07 mg/mL of USP Dihydrodutasteride RS in methanol. Sonicate to dissolve.

System suitability solution: 0.7 mg/mL of USP Dutasteride RS and 7 µg/mL of USP Dihydrodutasteride RS prepared as follows. Transfer a quantity of USP Dutasteride RS to a 50-mL volumetric flask. Add *Solution B* to 50% of the total volume and sonicate to dissolve. Add 5.0 mL of the *System suitability stock solution*, dilute with *Solution B* to volume, and mix.

Standard solution: 7 µg/mL of USP Dutasteride RS in *Solution B*. Sonicate to dissolve, if necessary.

Sensitivity solution: 0.35 µg/mL of USP Dutasteride RS from *Standard solution* in *Solution B*

Sample solution: Nominally 0.7 mg/mL of dutasteride prepared as follows. Take Capsules (NLT 20) and remove the contents, separating the pellets and the soft gelatin capsules. Accurately weigh the soft gelatin capsules, and remove the content as completely as possible. Mix and determine the average net content of the soft gelatin capsules. Accurately weigh and transfer a quantity of the contents of the soft gelatin capsules equivalent to about 7 mg of dutasteride to a 10-mL volumetric flask. Add *Solution B* to volume, and mix by shaking.

Chromatographic system

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

Mode: LC

Detector: UV 250 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 50°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Samples: *System suitability solution*, *Standard solution*, and *Sensitivity solution*

Suitability requirements

Resolution: NLT 2.0 between dutasteride and dihydrodutasteride, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual unspecified degradation product in the portion of Capsules taken:

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

r_U = peak response of each individual unspecified degradation product from the *Sample solution*

r_S = peak response of dutasteride from the *Standard solution*

C_S = concentration of USP Dutasteride RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of dutasteride in the *Sample solution* (µg/mL)

Acceptance criteria: The reporting threshold is 0.05%.

Any unspecified degradation product: NMT 1.0%

Total degradation products: NMT 1.5%

Change to read:

• **Organic Impurities, Procedure 2: Tamsulosin Hydrochloride**

Buffer A: 2.554 g/L of sodium phosphate, dibasic, anhydrous, 0.272 g/L of potassium phosphate, monobasic, and 2.0 g/L of sodium 1-decanesulfonate in water. Adjust with a dilute phosphoric acid solution to a pH of 7.0.

Buffer B: 2.554 g/L of sodium phosphate, dibasic, anhydrous and 0.272 g/L of potassium phosphate, monobasic in water. Adjust with a dilute phosphoric acid solution to a pH of 7.0.

Solution A: Methanol, acetonitrile, and *Buffer A* (30:20:50)

Solution B: Acetonitrile and water (60:40)

Mobile phase: See ▲*Table 6*.

Table 6▲ (RB 1-May-2024)

Time (min)	Solution A (%)	Solution B (%)
0	100	0
20	100	0
25	0	100
50	0	100
55	100	0
65	100	0

Diluent: Methanol and *Buffer B* (55:45)

Standard solution: 0.2 µg/mL of USP Tamsulosin Hydrochloride RS in *Diluent*. Sonicate to dissolve, if necessary.

Sensitivity solution: 0.05 µg/mL of USP Tamsulosin Hydrochloride RS from *Standard solution* in *Diluent*.

Sample solution: Nominally 0.1 mg/mL of tamsulosin hydrochloride prepared as follows. Determine the weight of Capsules (NLT 20). Open the capsules and remove the pellets. Determine the weight of the Capsules with the soft gelatin capsules, and calculate the average net content of the pellets. Accurately weigh and transfer a quantity of pellets equivalent to 10 mg of tamsulosin hydrochloride to a 100-mL volumetric flask, add 0.5 N sodium hydroxide solution to 25% of the total volume, and sonicate for NLT 30 min. Add *Diluent* to 30% of the total volume and shake by mechanical means for about 30 min. Dilute with *Diluent* to volume and mix. Pass a portion of the solution through a suitable filter of 0.45-µm pore size. Discard the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 225 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 35°

Flow rate: 1 mL/min

Injection volume: 100 µL

System suitability

Samples: *Standard solution* and *Sensitivity solution*

Suitability requirements

Relative standard deviation: NMT 10.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual unspecified degradation product in the portion of Capsules taken:

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

r_U = peak response of each individual unspecified degradation product from the *Sample solution*

r_S = peak response of tamsulosin from the *Standard solution*

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

C_U = nominal concentration of tamsulosin in the *Sample solution* (µg/mL)

Acceptance criteria: The reporting threshold is 0.05%.

Any unspecified degradation product: NMT 1.0%

Total degradation products: NMT 1.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Store at controlled room temperature.

Add the following:

▲• **Labeling:** The labeling states the *Dissolution* test used only if *Test 1* is not used.▲ (RB 1-May-2024)

• **USP Reference Standards** ⟨11⟩

USP Butylated Hydroxytoluene RS

USP Dihydrodutasteride RS

N-[2,5-Bis(trifluoromethyl)phenyl]-3-oxo-4-aza-5α-androstane-17β-carboxamide.

$C_{27}H_{32}F_6N_2O_2$ 530.56

USP Dutasteride RS

USP Tamsulosin Hydrochloride RS

[1] A suitable sinker is available as part number CAPWST-31 from https://www.qla-llc.com.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
DUTASTERIDE AND TAMSULOSIN HYDROCHLORIDE CAPSULES	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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