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Prazosin Hydrochloride Capsules

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<https://www.uspnf.com/rb-prazosin-hcl-caps-20230526>.

DEFINITION

Prazosin Hydrochloride Capsules contain an amount of prazosin hydrochloride ($C_{19}H_{21}N_5O_4 \cdot HCl$) equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of prazosin ($C_{19}H_{21}N_5O_4$).

[**CAUTION**—Care should be taken to prevent inhaling particles of prazosin hydrochloride and to prevent it contacting any part of the body.]

IDENTIFICATION

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

ASSAY

• PROCEDURE

Mobile phase: [Methanol](#), [glacial acetic acid](#), and [water](#) (70:1:30). Add 0.2 mL of [diethylamine](#) to 1 L of *Mobile phase*, such that the retention time of prazosin is 6–10 min.

Solution A: To 300 mL of water add 0.85 mL of [hydrochloric acid](#) in a 1000-mL volumetric flask. Dilute with [methanol](#) to volume, and mix. Transfer 300 mL of this solution to a 500-mL volumetric flask, and dilute with [methanol](#) to volume.

Standard stock solution: 0.2 mg/mL of [USP Prazosin Hydrochloride RS](#) in *Solution A*

Standard solution: 0.01 mg/mL of [USP Prazosin Hydrochloride RS](#), prepared as follows. Transfer 5 mL of *Standard stock solution* to a 100-mL volumetric flask, add 45.0 mL of *Solution A*, diluted with [methanol](#) to volume, and mix.

Sample stock solution: Nominally 0.02 mg/mL of prazosin in *Solution A*, prepared as follows. Transfer a portion of the contents of NLT 20 Capsules, equivalent to about 1 mg of prazosin, to a glass-stoppered flask containing 50.0 mL of *Solution A*, and shake by mechanical means for 30 min. Place the flask in an ultrasonic bath for 30 min, cool to room temperature, and pass the contents through a suitable filter of 5- μ m or finer pore size.

Sample solution: Nominally 0.01 mg/mL of prazosin prepared as follows. Transfer 25.0 mL of *Sample stock solution* to a 50-mL volumetric flask, and dilute with [methanol](#) to volume.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 254 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm \times 25-cm; 5- μ m packing [L3](#)

Flow rate: 0.6 mL/min

Injection volume: 5 μ L

Run time: NLT 2 times the retention time of prazosin

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 prazosin ($C_{19}H_{21}N_5O_4$) in the portion of Capsules taken:

$$\text{Result} = (r_u/r_s) \times (C_s/C_u) \times (M_{r1}/M_{r2}) \times 100$$

r_u = peak response of prazosin from the *Sample solution*
 r_s = peak response of prazosin from the *Standard solution*
 C_s = concentration of [USP Prazosin Hydrochloride RS](#) in the *Standard solution* (mg/mL)
 C_u = nominal concentration of prazosin in the *Sample solution* (mg/mL)
 M_{r1} = molecular weight of prazosin, 383.41
 M_{r2} = molecular weight of prazosin hydrochloride, 419.87

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- [Dissolution \(711\)](#).

Test 1

Medium: 0.1 N [hydrochloric acid](#) containing 3% ▲ [sodium dodecyl sulfate](#) ▲ (RB 9-May-2023); 900 mL

Apparatus 1: 100 rpm

Time: 60 min

Standard solution: Known concentration of [USP Prazosin Hydrochloride RS](#) in *Medium*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Determine the percentage of the labeled amount of prazosin ($C_{19}H_{21}N_5O_4$) dissolved, using the procedure in the Assay.

Tolerances: NLT 75% (Q) of the labeled amount of prazosin ($C_{19}H_{21}N_5O_4$) is dissolved.

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

Medium: Prepare as directed in *Test 1*.

Apparatus 1: 10-mesh basket; 100 rpm

Time: 30 min

Buffer: 3.4 g/L of [sodium dihydrogen phosphate](#). Adjust with 10% [sodium hydroxide](#) solution to a pH of 7.5.

Mobile phase: [Methanol](#) and *Buffer* (50:50)

Standard stock solution: 120 µg/mL of [USP Prazosin Hydrochloride RS](#), prepared as follows. In a suitable volumetric flask, dissolve a suitable amount of [USP Prazosin Hydrochloride RS](#) in 20% of the total volume of [methanol](#). Dilute with *Medium* to volume.

Standard solution: ($L/900$) mg/mL of [USP Prazosin Hydrochloride RS](#) in *Medium*, where L is the label claim in mg/Capsule, from *Standard stock solution*

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 254 nm

Column: 4.6-mm × 10-cm; 5-µm packing [L1](#)

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 60 µL

Run time: NLT 2 times the retention time of prazosin

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 3.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of prazosin ($C_{19}H_{21}N_5O_4$) dissolved:

$$\text{Result} = (r_u/r_s) \times (C_s/L) \times V \times (M_{r1}/M_{r2}) \times 100$$

r_u = peak response of prazosin from the *Sample solution*

r_s = peak response of prazosin from the *Standard solution*

C_s = concentration of [USP Prazosin Hydrochloride RS](#) in the *Standard solution* (mg/mL)

L = label claim (mg/Capsule)

V = volume of the *Medium*, 900 mL

M_{r1} = molecular weight of prazosin, 383.41

M_{r2} = molecular weight of prazosin hydrochloride, 419.87

Tolerances: NLT 80% (Q) of the labeled amount of prazosin ($C_{19}H_{21}N_5O_4$) is dissolved.

▲ **Test 3:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

Medium: pH 6.8 phosphate buffer containing 3% [sodium dodecyl sulfate](#) (Dissolve 6.9 g of [sodium phosphate monobasic](#) in 1000 mL of [water](#). Adjust with 2 N [sodium hydroxide](#) to a pH of 6.8. Add 30 g of [sodium dodecyl sulfate](#) to 1000 mL of the resulted solution.); 900 mL, deaerated

Apparatus 2: 100 rpm

Time: 20 min

Mobile phase: [Methanol](#), [water](#), [glacial acetic acid](#), and [diethylamine](#) (670: 330: 10: 0.2)

Standard stock solution A: 0.3 mg/mL of [USP Prazosin Hydrochloride RS](#) in [methanol](#). Sonicate to dissolve if necessary.

Standard stock solution B: 0.024 mg/mL of [USP Prazosin Hydrochloride RS](#) from *Standard stock solution A* in *Medium*

Standard solution: ($L/900$) mg/mL of prazosin from [USP Prazosin Hydrochloride RS](#) from *Standard stock solution B* in *Medium*, where L is the label claim in mg/Capsule

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-μm pore size, discarding the first 3 mL of the filtrate.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; 5-μm packing [L3](#)

Flow rate: 0.8 mL/min

Injection volume: 50 μL

Run time: NLT 1.3 times the retention time of prazosin

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 prazosin ($C_{19}H_{21}N_5O_4$) dissolved:

$$\text{Result} = (r_u/r_s) \times C_s \times V \times (M_{r1}/M_{r2}) \times (1/L) \times 100$$

r_u = peak response of prazosin from the *Sample solution*

r_s = peak response of prazosin from the *Standard solution*

C_s = concentration of [USP Prazosin Hydrochloride RS](#) in the *Standard solution* (mg/mL)

V = volume of the *Medium*, 900 mL

M_{r1} = molecular weight of prazosin, 383.41

M_{r2} = molecular weight of prazosin hydrochloride, 419.87

L = label claim (mg/Capsule)

Tolerances: NLT 80% (Q) of the labeled amount of prazosin ($C_{19}H_{21}N_5O_4$) is dissolved.▲ (RB 9-May-2023)

- **UNIFORMITY OF DOSAGE UNITS (905):** Meet the requirements

IMPURITIES

- **ORGANIC IMPURITIES**

Solution A: 1.93 g of [ammonium acetate](#) in 1000 mL of [water](#). Adjust the solution with [glacial acetic acid](#) to a pH of 5.0.

Solution B: [Acetonitrile](#) and [methanol](#) (75:25)

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	85	15
15.0	85	15
66.0	45	55
75.0	45	55
76.0	85	15
85.0	85	15

Diluent: *Solution A* and *Solution B* (85:15)

Standard stock solution: 0.5 mg/mL of [USP Prazosin Hydrochloride RS](#) in *Diluent*

Standard solution: 0.5 µg/mL of [USP Prazosin Hydrochloride RS](#) from *Standard stock solution* in *Diluent*

Sensitivity solution: 0.05 µg/mL of [USP Prazosin Hydrochloride RS](#) from *Standard solution* in *Diluent*

System suitability stock solution: 0.025 mg/mL each of [USP Prazosin Related Compound D RS](#), [USP Terazosin Related Compound A RS](#), and [USP Terazosin Related Compound C RS](#), prepared as follows. Transfer 12.5 mg of each corresponding Reference Standard to a 500-mL volumetric flask. Add 75 mL of *Solution B* and sonicate. Dilute with *Solution A* to volume.

System suitability solution: 0.1 mg/mL of [USP Prazosin Hydrochloride RS](#) from *Standard stock solution* in *Diluent*, and 0.001 mg/mL each of [USP Prazosin Related Compound D RS](#), [USP Terazosin Related Compound A RS](#), and [USP Terazosin Related Compound C RS](#) in *Diluent* from *System suitability stock solution*

Sample solution: Nominally 0.1 mg/mL of prazosin hydrochloride in *Diluent*, prepared as follows. Transfer a suitable portion of the contents from NLT 20 Capsules to a suitable volumetric flask that doubles the volume of *Diluent* used, add an appropriate amount of *Diluent*, and mix. Centrifuge a portion of the solution. Use the supernatant. [Caution—Do not dilute to volume.]

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; 5-µm packing [L1](#)

Column temperature: 35°

Flow rate: 0.7 mL/min

Injection volume: 15 µL

System suitability

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

Suitability requirements

Resolution: NLT 3.0 between prazosin and terazosin related compound C, *System suitability solution*

Tailing factor: NMT 3.0 for terazosin related compound A, *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 prazosin related compound D, terazosin related compound A, or any unspecified degradation product in the portion of Capsules taken:

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

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

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

C_S = concentration of [USP Prazosin Hydrochloride RS](#) in the *Standard solution* (µg/mL)

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

F = relative response factor (see [Table 2](#))

Acceptance criteria: See [Table 2](#).

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Prazosin related compound D	0.13	0.53	0.2
Terazosin related compound A	0.21	1.0	0.2
Prazosin	1.0	—	—
Terazosin related compound C ^a	1.1	1.0	—
Any unspecified degradation product	—	1.0	0.2
Total degradation products	—	—	1.0

^a For resolution measurement only. Not included in the total degradation products.

ADDITIONAL REQUIREMENTS

- PACKAGING AND STORAGE:** Preserve in well-closed, light-resistant containers. Store at controlled room temperature.
- LABELING:** When more than one test for *Dissolution* is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.

- [USP Reference Standards \(11\)](#)**

[USP Prazosin Hydrochloride RS](#)

[USP Prazosin Related Compound D RS](#)

Furan-2-yl(piperazin-1-yl)methanone.

$C_9H_{12}N_2O_2$ 180.21

[USP Terazosin Related Compound A RS](#)

6,7-Dimethoxy-2-(piperazin-1-yl)quinazolin-4-amine dihydrochloride.

$C_{14}H_{19}N_5O_2 \cdot 2HCl$ 362.26

[USP Terazosin Related Compound C RS](#)

2,2'-(Piperazine-1,4-diy)bis(6,7-dimethoxyquinazolin-4-amine) dihydrochloride.

$C_{24}H_{28}N_8O_4 \cdot 2HCl$ 565.46

Auxiliary Information - Please [check for your question in the FAQs](#) before contacting USP.

Topic/Question	Contact	Expert Committee
PRAZOSIN HYDROCHLORIDE CAPSULES	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: [Chromatographic Database](#)

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