Prazosin Hydrochloride Capsules

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Expert Committee	Chemical Medicines Monographs 2
Reason for Revision	Compliance

In accordance with the Rules and Procedures of the 2015–2020 Council of Experts, the Chemical Medicines Monographs 2 Expert Committee has revised the Prazosin Hydrochloride Capsules monograph. The purpose for the revision is to add *Dissolution Test* 2 to accommodate FDA-approved drug products with different dissolution conditions and tolerances than the existing dissolution test in the monograph.

- *Dissolution Test 2* was validated using a Waters XBridge C18 brand of L1 column. The typical retention time for prazosin is about 3 min.

Labeling information has been incorporated to support the inclusion of *Dissolution Test 2*.

The Prazosin Hydrochloride Capsules Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Sujatha Ramakrishna, Principal Scientific Liaison (301-816-8349 or sxr@usp.org).

Revision Bulletin
Official: July 1, 2020

Prazosin Hydrochloride Capsules

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-µm 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 × 25-cm; 5-µm packing L3

Flow rate: 0.6 mL/min

Injection volume: 5 µL

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:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (Mr_1/Mr_2) \times 100$$

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* (µg/mL)

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

Mr_1 = molecular weight of prazosin, 383.41

Mr_2 = molecular weight of prazosin hydrochloride, 419.86

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- **Dissolution** ⟨711⟩

▲Test 1▲ (RB 1-Jul-2020)

Medium: 0.1 N hydrochloric acid containing 3% sodium lauryl sulfate; 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* (µg/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, 419.86

Tolerances: NLT 80% (Q) of the labeled amount of prazosin ($C_{19}H_{21}N_5O_4$) is dissolved. ▲ (RB 1-Jul-2020)

- **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.

Add the following:

▲● **Labeling:** When more than one test for *Dissolution* is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.▲ (RB 1-Jul-2020)

● **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-diyl)bis(6,7-dimethoxyquinazolin-4-amine) dihydrochloride.

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

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