Add the following:

▲Alfuzosin Hydrochloride Extended-Release Tablets

DEFINITION

Alfuzosin Hydrochloride Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of alfuzosin hydrochloride ($C_{19}H_{27}N_5O_4 \cdot HCl$).

IDENTIFICATION

- **A. INFRARED ABSORPTION** ⟨**197**⟩. [NOTE—Methods described in *Infrared Absorption* ⟨197K⟩ or ⟨197A⟩ may be used.]

  Sample: Grind 4 Tablets, and add 20 mL of water. [NOTE—When analyzing multi-layer Tablets, isolate the layer containing alfuzosin hydrochloride using a suitable tool.] Add 20 mL of strong ammonia solution. Extract with 20 mL of methylene chloride, and separate the organic layer. Repeat the extraction successively with 20 mL, then with 10 mL of methylene chloride. Wash the combined organic layers with 20 mL of water. Dry the organic solution using a phase separation filter. Take 2.0 mL of the dried organic solution, and mix with 200 mg of finely ground potassium bromide. Evaporate the methylene chloride at 60°, then at 105° for 30 min. Make a disk. Alternatively, evaporate methylene chloride from the dried organic solution at 60°, then at 105° for 30 min. Perform the IR spectrum.

  Acceptance criteria: The maxima of the spectrum obtained from the *Sample* correspond in position and relative intensity to those obtained from USP Alfuzosin Hydrochloride RS, treated in the same manner as the *Sample*, beginning with "Add 20 mL of water."
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **PROCEDURE**

  Solution A: 5.0 mL of perchloric acid in 900 mL of water. Adjust with 2 M sodium hydroxide to a pH of 3.5, and dilute with water to 1000 mL.

  Mobile phase: Acetonitrile, tetrahydrofuran, and *Solution A* (20:1:80)

  Diluent: 0.01 N hydrochloric acid

  Standard stock solution: 0.15 mg/mL of USP Alfuzosin Hydrochloride RS in methanol

  Standard solution: 0.03 mg/mL of USP Alfuzosin Hydrochloride RS in *Diluent* from the *Standard stock solution*

  Sample stock solution: Place a suitable number of Tablets into a suitable volumetric flask to obtain a solution having a concentration of 0.16 mg/mL of alfuzosin hydrochloride. Add 80% of the flask volume of methanol, and stir for at least 1 h using a magnetic stirrer. Add 10% of the flask volume of *Diluent*, mix, and allow it to cool to room temperature. Dilute the resulting suspension with methanol to volume, stir, and allow to settle for 30 min.

  Sample solution: 0.03 mg/mL of alfuzosin hydrochloride in *Diluent* from the *Sample stock solution* supernatant. Pass through a suitable filter.

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

  Mode: LC
  Detector: UV 254 nm
  Column: 4.6-mm × 15-cm; 5-µm packing L1
  Flow rate: 1.5 mL/min
  Injection volume: 20 µL

  System suitability
  Sample: *Standard solution*
  Suitability requirements
  Tailing factor: 0.8–1.5 for alfuzosin
  Relative standard deviation: NMT 2.0%

  Analysis
  Samples: *Standard solution* and *Sample solution*
  Calculate the percentage of alfuzosin hydrochloride ($C_{19}H_{27}N_5O_4 \cdot HCl$) in the portion of Tablets 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 USP Alfuzosin Hydrochloride RS in the *Standard solution* (mg/mL)
  C_U = nominal concentration of the *Sample solution* (mg/mL)

  Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- **DISSOLUTION** ⟨**711**⟩

  Test 1
  Medium: 0.01 N hydrochloric acid; 500 mL
  Apparatus 2: 100 rpm, with Tablet holder (see *Figure 1*)

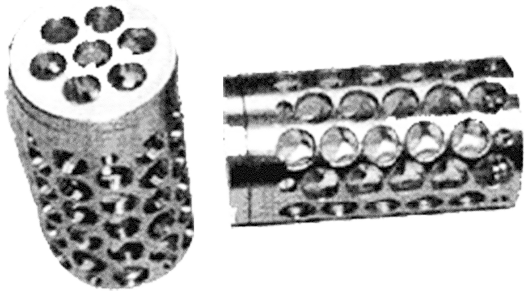

Figure 1. 37.5-mm (l) × 20-mm (d) stainless steel cylinders are used as sample holders. The cylinders contain screw caps drilled with seven 4.5-mm holes. Seven 4.5-mm holes are drilled in the bottom, and 12 longitudinal series of five 5-mm holes are drilled on the cylinders, alternatively starting and ending with one 1.7-mm hole.

  Times: 1, 6, 12, and 20 h
  Sample solution: Pass a portion of the solution under test through a suitable filter.
  Standard solution: (*L*/500) mg/mL of USP Alfuzosin Hydrochloride RS in *Medium*, where *L* is the Tablet label claim in mg

Detector: UV 330 nm
Blank: *Medium*
Path length: 1 cm
Tolerances: See *Table 1*.

Table 1

Level	Time (h)	Amount Dissolved
L1		Each Tablet:
	1	10%–20%
	6	40%–55%
	12	65%–85%
	20	NLT 85%
L2		Average of 12 Tablets complies with L1 and each Tablet:
	1	9%–22%
	6	36%–61%
	12	59%–94%
	20	NLT 77%
L3		Average of 24 Tablets complies with L1, NMT 2 Tablets outside L2, and all Tablets within:
	1	8%–24%
	6	32%–66%
	12	52%–102%
	20	NLT 68%

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.
Medium: 0.01 N hydrochloric acid; 900 mL
Apparatus 2: 100 rpm
Times: 1, 3, 12, and 24 h
Buffer: Dilute 5.0 mL of perchloric acid in 900 mL of water, adjust with diluted sodium hydroxide (0.1 g/mL) to a pH of 3.5 ± 0.5, and dilute with water to 1 L.
Mobile phase: Acetonitrile and *Buffer* (25:75)
Standard stock solution: 0.28 mg/mL of USP Alfuzosin Hydrochloride RS, prepared as follows. In a 200-mL volumetric flask dissolve 55.5 mg of USP Alfuzosin Hydrochloride RS in 5 mL of methanol, sonicate to dissolve, and dilute with *Medium* to volume.
Standard solution: 0.011 mg/mL of USP Alfuzosin Hydrochloride RS in *Medium* from the *Standard stock solution*
Sample solution: Pass a portion of the solution under test through a suitable filter. Replace the portion of solution withdrawn with an equal volume of *Medium*.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 244 nm
Column: 4.6-mm × 15-cm; 5-µm packing L7
Column temperature: 30°
Flow rate: 1.2 mL/min
Injection volume: 20 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Tailing factor: NMT 2.0
Column efficiency: NLT 3000 theoretical plates
Relative standard deviation: NMT 2.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the concentration (C_i) of alfuzosin hydrochloride ($C_{19}H_{27}N_5O_4 \cdot HCl$) in the sample withdrawn from the vessel at each time point (*i*):

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

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 the labeled amount of alfuzosin hydrochloride ($C_{19}H_{27}N_5O_4 \cdot HCl$) 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 alfuzosin 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 2*.

Table 2

Time point (i)	Time (h)	Amount Dissolved
1	1	NMT 20%
2	3	15%–35%
3	12	50%–70%
4	24	NLT 80%

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

Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.
Medium: 0.25% sodium dodecyl sulfate in 0.05 M sodium phosphate buffer, pH 6.8 (2.5 g/L of sodium dodecyl sulfate, 6.9 g/L of monobasic sodium phosphate monohydrate, and 0.83 g/L of sodium hydroxide in water previously de-gassed with helium. Adjust to a pH of 6.8 ± 0.05 with either phosphoric acid or 1 N sodium hydroxide); 900 mL.

Apparatus 1: 100 rpm
Times: 1, 6, 12, and 24 h
Standard stock solution: 1.1 mg/mL of USP Alfuzosin Hydrochloride RS in methanol
Standard solution: 0.011 mg/mL of USP Alfuzosin Hydrochloride RS in *Medium* from the *Standard stock solution*
Sample solution: Pass a portion of the solution under test through a suitable filter.
Instrumental conditions
(See *Spectrophotometry and Light Scattering* ⟨851⟩.)
Mode: UV-Vis
Analytical wavelength: 331 nm, background correction at 490 nm
Blank: Medium
Cell: 1.0 cm
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of alfuzosin hydrochloride ($C_{19}H_{27}N_5O_4 \cdot HCl$) dissolved at each time point (*i*):

$$\text{Result}_i = (A_U/A_S) \times C_S \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Standard solution*
C_S = concentration of the *Standard solution* (mg/mL)
V = volume of *Medium* (mL)
L = label claim (mg/Tablet)
Tolerances: See *Table 3*.

Table 3

Time point (i)	Time (h)	Amount Dissolved
1	1	NMT 15%
2	6	20%–40%
3	12	45%–70%
4	24	NLT 80%

The percentages of the labeled amount of alfuzosin 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*.
Medium: 0.01 N hydrochloric acid; 900 mL
Apparatus 2: 100 rpm
Times: 1, 6, 12, and 20 h
Standard solution: 0.01 mg/mL of USP Alfuzosin Hydrochloride RS in *Medium*
Sample solution: Centrifuge a portion of the solution under test.
Instrumental conditions
(See *Spectrophotometry and Light-Scattering* ⟨851⟩.)
Mode: UV
Analytical wavelength: 245 nm
Blank: Medium
Path length: 0.2 cm
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the concentration (C_i) of alfuzosin hydrochloride ($C_{19}H_{27}N_5O_4 \cdot HCl$) in the sample withdrawn from the vessel at each time point (*i*):

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

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 percentage of the labeled amount of alfuzosin hydrochloride ($C_{19}H_{27}N_5O_4 \cdot HCl$) dissolved at each time point (*i*):

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

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

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

$$\text{Result}_4 = (\{C_4 \times [V - (3 \times V_S)]\} + [(C_3 + C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

C_i = concentration of alfuzosin 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 *Table 4*.

Table 4

Time point (i)	Time (h)	Amount Dissolved
1	1	NMT 30%
2	6	40%–60%
3	12	65%–85%
4	20	NLT 80%

The percentages of the labeled amount of alfuzosin hydrochloride dissolved at the times specified 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*.
Medium: 0.01 N hydrochloric acid; 900 mL
Apparatus 2: 100 rpm
Times: 1, 3, 6, 12, and 20 h
Buffer: Add 1 mL of triethylamine in 1000 mL of water. Adjust with phosphoric acid to a pH of 2.5 ± 0.05. Pass through a suitable filter of 0.45-µm pore size.
Mobile phase: Methanol and *Buffer* (40:60)
Standard stock solution: 0.55 mg/mL of USP Alfuzosin Hydrochloride RS. Prepare by transferring a portion of USP Alfuzosin Hydrochloride RS to a suitable flask. Add methanol to 20% of the flask volume, and sonicate at room temperature to dissolve. Dilute with *Medium* to volume.
Standard solution: 0.011 mg/mL of USP Alfuzosin Hydrochloride RS in *Medium* from the *Standard stock solution.* Pass through a suitable filter of 0.45-µm pore size.
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 245 nm
Column: 4.6-mm × 15-cm; 5-µm packing L1
Flow rate: 1 mL/min
Injection volume: 10 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Tailing factor: NMT 2.0
Column efficiency: NLT 2000 theoretical plates
Relative standard deviation: NMT 2.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the concentration (C_i) of alfuzosin hydrochloride ($C_{19}H_{27}N_5O_4 \cdot HCl$) in the sample withdrawn from the vessel at each time point (*i*):

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

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 the labeled amount of alfuzosin hydrochloride ($C_{19}H_{27}N_5O_4 \cdot HCl$) dissolved at each time point (*i*):

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

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

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

$$\text{Result}_4 = (\{C_4 \times [V - (3 \times V_S)]\} + [(C_3 + C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

$$\text{Result}_5 = (\{C_5 \times [V - (4 \times V_S)]\} + [(C_4 + C_3 + C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

C_i = concentration of alfuzosin 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 *Table 5*.

Table 5

Time point (i)	Time (h)	Amount Dissolved
1	1	NMT 20%
2	3	20%–40%
3	6	35%–55%
4	12	60%–80%
5	20	NLT 80%

The percentages of the labeled amount of alfuzosin hydrochloride dissolved at the times specified conform to *Acceptance Table 2* in ⟨711⟩.● (RB 1-May-2013)

- **UNIFORMITY OF DOSAGE UNITS ⟨905⟩:** Meets the requirements

IMPURITIES

- **ORGANIC IMPURITIES**

Solution A, Mobile phase, Diluent, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.
System suitability stock solution: 0.4 mg/mL of USP Alfuzosin System Suitability Mixture A RS in methanol
System suitability solution: 0.03 mg/mL of USP Alfuzosin System Suitability Mixture A RS in *Diluent* from the *System suitability stock solution*
Standard stock solution: 0.15 mg/mL of USP Alfuzosin Hydrochloride RS in methanol
Standard solution: 0.03 mg/mL of USP Alfuzosin Hydrochloride RS in *Diluent* from the *Standard stock solution*
System suitability
Samples: *System suitability solution* and *Standard solution*
Suitability requirements
Resolution: NLT 1.0 between alfuzosin and the furamide analog, and NLT 1.0 between deacylated alfuzosin and the *N*-formyl analog, *System suitability solution*
Relative standard deviation: NMT 2.0%, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of each impurity in the portion of Tablets taken:

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

r_U = peak response for each impurity from the *Sample solution*
r_S = peak response for alfuzosin from the *Sample solution*
C_S = concentration of USP Alfuzosin Hydrochloride RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of alfuzosin hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 6*.

Table 6

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Deacylated alfuzosin[a]	0.46	0.40
N-Formyl analog[b]	0.50	0.30
Alfuzosin	1.0	—
Furamide analog[c]	1.18	—[d]
Any individual unspecified impurity	—	0.20
Total impurities	—	0.80

[a] N^2-(3-Aminopropyl)-6,7-dimethoxy-N^2-methylquinazoline-2,4-diamine.
[b] *N*-[3-[(4-Amino-6,7-dimethoxyquinazolin-2-yl)(methyl)amino]propyl]formamide.
[c] *N*-[3-[(4-Amino-6,7-dimethoxyquinazolin-2-yl)(methyl)amino]propyl]furan-2-carboxamide.
[d] Furamide analog, a component of USP Alfuzosin System Suitability Mixture A RS, is not a specified impurity.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Protect from light and moisture. 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 Alfuzosin Hydrochloride RS
USP Alfuzosin System Suitability Mixture A RS
Furamide analog: *N*-{3-[(4-Amino-6,7-dimethoxyquinazolin-2-yl)(methyl)amino]propyl}furan-2-carboxamide.
$C_{19}H_{23}N_5O_4$ 385.42
Deacylated alfuzosin: N^2-(3-Aminopropyl)-6,7-dimethoxy-N^2-methylquinazoline-2,4-diamine.
$C_{14}H_{21}N_5O_2$ 291.35
N-Formyl analog: *N*-[3-[(4-Amino-6,7-dimethoxyquinazolin-2-yl)(methyl)amino]propyl]formamide.
$C_{15}H_{21}N_5O_3$ 319.36▲*USP36*