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Doxazosin Tablets

DEFINITION

Doxazosin Tablets contain an amount of Doxazosin Mesylate equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of doxazosin ($C_{23}H_{25}N_5O_5$).

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*.

Add the following:

▲• **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Dec-2020)

ASSAY

Change to read:

• **Procedure**

Buffer: Transfer 3.4 g of monobasic potassium phosphate into a 1-L flask, and add 800 mL of water and 4.0 mL of triethylamine to dissolve. Adjust with phosphoric acid to a pH of 4.5, and dilute with water to volume.

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

Diluent: Methanol and 0.1 N hydrochloric acid (90:10)

Standard solution: 0.049 mg/mL of USP Doxazosin Mesylate RS in *Diluent*. ▲Sonicate to dissolve as needed.▲ (USP 1-Dec-2020)

Sample stock solution: ▲Nominally (*L*/25) mg/mL of doxazosin prepared as follows, where *L* is the label claim in mg/Tablet.▲ (USP 1-Dec-2020)

Transfer 10 Tablets, whole or ground, into a 250-mL volumetric flask, add 10 mL of water, and sonicate until the Tablets are disintegrated. Add 150 mL of *Diluent*, sonicate for 30 min, and dilute with *Diluent* to volume.

Sample solution: Nominally 0.04 mg/mL of doxazosin in *Diluent* from *Sample stock solution*. ▲For Tablets labeled to contain 1 mg, use the corresponding *Sample stock solution* directly. Centrifuge a portion of the solution and use the filtrate.▲ (USP 1-Dec-2020)

Chromatographic system

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

Mode: LC

Detector: UV 245 nm. ▲For *Identification B*, use a diode array detector in the range of 200–400 nm.▲ (USP 1-Dec-2020)

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

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

▲**Run time:** NLT 1.6 times the retention time of doxazosin▲ (USP 1-Dec-2020)

System suitability

Sample: *Standard solution*

Suitability requirements

▲▲ (USP 1-Dec-2020)

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 doxazosin ($C_{23}H_{25}N_5O_5$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

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

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

C_S = concentration of ▲USP Doxazosin Mesylate RS▲ (USP 1-Dec-2020) in the *Standard solution* (mg/mL)

C_U = nominal concentration of ▲doxazosin▲ (USP 1-Dec-2020) in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of doxazosin, 451.48

M_{r2} = molecular weight of doxazosin mesylate, 547.58

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Medium: 0.01 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Standard solution: A known concentration of USP Doxazosin Mesylate RS in *Medium*.

Sample solution: Pass a portion of the solution under test through a suitable filter. Dilute with *Medium* as needed.

Instrumental conditions

Mode: UV

Analytical wavelength: 246 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of doxazosin ▲▲ (USP 1-Dec-2020) ($C_{23}H_{25}N_5O_5$) ▲▲ (USP 1-Dec-2020) dissolved:

$$\text{▲Result} = (A_U/A_S) \times C_S \times V \times (M_{r1}/M_{r2}) \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

M_{r1} = molecular weight of doxazosin, 451.48

M_{r2} = molecular weight of doxazosin mesylate, 547.58

L = label claim of doxazosin (mg/Tablet)▲ (USP 1-Dec-2020)

Tolerances: NLT 70% (Q) of the labeled amount of doxazosin ▲▲ (USP 1-Dec-2020) ($C_{23}H_{25}N_5O_5$) ▲▲ (USP 1-Dec-2020) is dissolved.

• **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements

IMPURITIES

Add the following:

▲• **Organic Impurities:** Protect the solutions containing doxazosin from light.

Buffer: 3.4 g/L of monobasic potassium phosphate, prepared by dissolving 3.4 g of monobasic potassium phosphate in 1 L of water

Solution A: Mix 90 mL of acetonitrile with 920 mL of *Buffer*. Add 1 mL of triethylamine and adjust with phosphoric acid to a pH of 3.0.

Solution B: Mix 500 mL of acetonitrile with 500 mL of *Buffer*. Add 1 mL of triethylamine and adjust with phosphoric acid to a pH of 3.0.

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
7.0	100	0
35.0	0	100
45.0	0	100

Time (min)	Solution A (%)	Solution B (%)
45.1	100	0
65.0	100	0

Diluent: Methanol, phosphoric acid, and water (500:1:500)

System suitability solution: 2 µg/mL each of USP Doxazosin Related Compound A RS and USP Doxazosin Related Compound G RS in *Diluent*

Standard stock solution A: 24 µg/mL of USP Doxazosin Mesylate RS in *Diluent*. Sonicate to dissolve as needed.

Standard stock solution B: 25 µg/mL of USP Terazosin Related Compound A RS (equivalent to 20 µg/mL of terazosin related compound A free base) in *Diluent*. Sonicate to dissolve as needed.

Sensitivity solution: 0.6 µg/mL of USP Doxazosin Mesylate RS in *Diluent* from *Standard stock solution A*

Standard solution: 2.4 µg/mL of USP Doxazosin Mesylate RS and 6.25 µg/mL of USP Terazosin Related Compound A RS (equivalent to 5 µg/mL of terazosin related compound A free base) in *Diluent* from *Standard stock solution A* and *Standard stock solution B*. Sonicate to dissolve and pass through a PVDF filter or other suitable filter of 0.45-µm pore size as needed.

Sample solution: Nominally 1 mg/mL of doxazosin prepared as follows. Transfer a nominal amount of 5 mg of doxazosin from NLT 20 finely powdered Tablets to a suitable tube. Add 5 mL of *Diluent*. Vortex and sonicate for 15 min.

[NOTE—If needed, centrifuge the solution and pass the supernatant through a PVDF filter or other suitable filter of 0.45-µm pore size. Discard NLT 3 mL of the filtrate.]

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 25-cm; 5-µm packing L10

Flow rate: 1 mL/min

Injection volume: 30 µL

System suitability

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

[NOTE—See *Table 2* for the relative retention times.]

Suitability requirements

Resolution: NLT 1 between the doxazosin related compound G and doxazosin related compound A peaks, *System suitability solution*

Tailing factor: NMT 1.5 for the doxazosin peak, *Standard solution*

Relative standard deviation: NMT 5.0% for the doxazosin and terazosin related compound A peaks, *Standard solution*

Signal-to-noise ratio: NLT 10 for the doxazosin peak, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of terazosin related compound A free base in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of terazosin related compound A from the *Sample solution*

r_S = peak response of terazosin related compound A from the *Standard solution*

C_S = concentration of USP Terazosin Related Compound A RS in the *Standard solution* (µg/mL)

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

M_{r1} = molecular weight of terazosin related compound A free base, 289.34

M_{r2} = molecular weight of terazosin related compound A, 362.25

Calculate the percentage of any other specified and unspecified impurities in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times (M_{r1}/M_{r2}) \times 100$$

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

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

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

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

F = relative response factor (see *Table 2*)

M_{r1} = molecular weight of doxazosin free base, 451.48

M_{r2} = molecular weight of doxazosin mesylate, 547.58

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Terazosin related compound A[a]	0.20	—	0.5
Doxazosin related compound G[b]	0.26	0.81	0.2
Doxazosin related compound A[c]	0.30	0.64	0.25
Doxazosin related compound D[d]	0.57	0.47	0.25
Doxazosin	1.00	—	—
Doxazosin related compound F[e]	1.36	0.97	0.25
Any unspecified degradation product	—	1.00	0.2
Total impurities	—	—	1.0▲ (USP 1-Dec-2020)

[a] 6,7-Dimethoxy-2-(piperazin-1-yl)quinazolin-4-amine.

[b] 4-Amino-6,7-dimethoxyquinazolin-2(1*H*)-one.

[c] *N*-1,4-Benzodioxane-2-carbonyl piperazine.

[d] 1,4-Benzodioxane-2-carboxylic acid.

[e] *N*,*N*′-Bis(1,4-benzodioxane-2-carbonyl)piperazine.

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in tight containers. ▲Store at controlled room temperature.▲ (USP 1-Dec-2020)

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Doxazosin Mesylate RS

▲ USP Doxazosin Related Compound A RS

N-1,4-Benzodioxane-2-carbonyl piperazine hydrochloride.

$C_{13}H_{16}N_2O_3 \cdot HCl$ 284.74

USP Doxazosin Related Compound G RS

4-Amino-6,7-dimethoxyquinazolin-2(1*H*)-one hydrochloride.

$C_{10}H_{11}N_3O_3 \cdot HCl$ 257.67

USP Terazosin Related Compound A RS

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

$C_{14}H_{19}N_5O_2 \cdot 2HCl$ 362.25▲ (USP 1-Dec-2020)

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

Topic/Question	Contact	Expert Committee
DOXAZOSIN TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Topic/Question	Contact	Expert Committee
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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