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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 \blacktriangle [USP Doxazosin Mesylate RS](#) \blacktriangle (USP 1-Dec-2020) in the *Standard solution* (mg/mL)

C_u = nominal concentration of \blacktriangle doxazosin \blacktriangle (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 \blacktriangle (USP 1-Dec-2020) ($C_{23}H_{25}N_5O_5$) \blacktriangle (USP 1-Dec-2020) dissolved:

$$\blacktriangle \text{Result} = (A_u/A_s) \times C_s \times V \times (M_{r1}/M_{r2}) \times (1/L) \times 100$$

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) \blacktriangle (USP 1-Dec-2020)

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

• [UNIFORMITY OF DOSAGE UNITS \(905\)](#): Meet the requirements

IMPURITIES

Add the following:

\blacktriangle • **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(1H)-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)

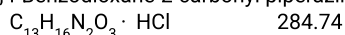
Change to read:

- **USP REFERENCE STANDARDS (11).**

▲ [USP Doxazosin Mesylate RS](#)

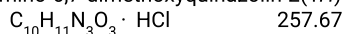
▲ [USP Doxazosin Related Compound A RS](#)

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



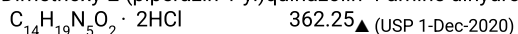
▲ [USP Doxazosin Related Compound G RS](#)

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



▲ [USP Terazosin Related Compound A RS](#)

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



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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