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Sildenafil Tablets

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click www.uspnf.com/rb-sildenafil-tabs-20241227.

DEFINITION
Sildenafil Tablets contain sildenafil citrate equivalent to NLT 90% and NMT 110% of the labeled amount of sildenafil ($C_{22}H_{30}N_6O_4S$).

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K

Solution A: Ammonium hydroxide and water (10:90)

Standard solution: 1.4 mg/mL of USP Sildenafil Citrate RS in *Solution A*

Sample solution: Grind 1 Tablet and add a sufficient amount of *Solution A* to obtain nominally 1 mg/mL of sildenafil. Sonicate for 2 min, shake well, and centrifuge. Use the supernatant.

Analysis: For each of the *Standard solution* and the *Sample solution*, prewash a 6-cc C18 solid phase extraction cartridge with 10 mL of methanol followed by 10 mL of *Solution A*, discarding both washings. Apply 5 mL each of the *Standard solution* and the *Sample solution* to separate prewashed cartridges and draw each solution through the cartridge. Wash each cartridge with 10 mL of water and allow the cartridge to dry under vacuum. Elute the sildenafil from each cartridge with 5 mL of methanol, collecting the eluant in a suitable container. Add about 200 mg of potassium bromide to each container, mix well, and evaporate to dryness. To about 70 mg of each dried mixture, add about 140 mg of potassium bromide and mix.

Acceptance criteria: Meet the requirements

• **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**

Buffer: Dilute 7 mL of triethylamine with water to 1 L. Adjust with phosphoric acid to a pH of 3.0.

Mobile phase: *Buffer*, methanol, and acetonitrile (58:25:17)

Diluent: Acetonitrile and water (90:10)

Standard solution: 0.028 mg/mL of USP Sildenafil Citrate RS in *Mobile phase*

Sample stock solution: Disperse 1 Tablet in at least 5 mL of *Diluent* with the aid of sonication. Once the Tablet is fully dispersed, dilute with *Mobile phase* to 250.0 mL while swirling. Centrifuge and use the supernatant.

Sample solution: Nominally 0.02 mg/mL of sildenafil prepared by diluting a suitable portion of the *Sample stock solution* with *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 290 nm

Column: 3.9-mm × 15-cm; 5-µm packing *L1*

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 1.5 times the retention time of sildenafil

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.3

Relative standard deviation: NMT 3.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of sildenafil ($C_{22}H_{30}N_6O_4S$) 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 sildenafil from the *Sample solution*

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

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

C_U = nominal concentration of sildenafil in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of sildenafil, 474.58

M_{r2} = molecular weight of sildenafil citrate, 666.70

Acceptance criteria: 90%–110%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

▲**Test 1**▲ (RB 1-Jan-2025)

Medium: 0.01 N hydrochloric acid; 900 mL

Apparatus 1: 100 rpm

Time: 15 min

Standard solution: 0.03 mg/mL of USP Sildenafil Citrate RS in *Medium*

Sample solution: A filtered portion of the solution under test, suitably diluted with *Medium*, if necessary

Instrumental conditions

Mode: UV-Vis

Analytical wavelength: Maximum at about 290 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of sildenafil ($C_{22}H_{30}N_6O_4S$) dissolved:

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

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

D = dilution factor for the *Sample solution*, if needed

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

M_{r1} = molecular weight of sildenafil, 474.58

M_{r2} = molecular weight of sildenafil citrate, 666.70

Tolerances: NLT 80% (Q) of the labeled amount of sildenafil ($C_{22}H_{30}N_6O_4S$) is dissolved.

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

Medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 1: 100 rpm

Time: 15 min

Standard solution: 0.03 mg/mL of USP Sildenafil Citrate RS in *Medium*. Sonicate to dissolve, if necessary.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding an appropriate volume of filtrate so that a consistent result can be obtained. Dilute with *Medium* to a concentration similar to that of the *Standard solution*.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: UV

Analytical wavelength: 290 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of sildenafil ($C_{22}H_{30}N_6O_4S$) dissolved:

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

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

D = dilution factor for the *Sample solution*, if needed

V = volume of *Medium*, 500 mL

L = label claim (mg/Tablet)

M_{r1} = molecular weight of sildenafil, 474.58

M_{r2} = molecular weight of sildenafil citrate, 666.70

Tolerances: NLT 80% (Q) of the labeled amount of sildenafil ($C_{22}H_{30}N_6O_4S$) is dissolved.▲ (RB 1-Jan-2025)

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

IMPURITIES

• **Organic Impurities**

Buffer, Mobile phase, Diluent, and **Chromatographic system:** Proceed as directed in the *Assay*, except for *Run time*.

Run time: NLT 3 times the retention time of sildenafil

System suitability solution: A mixture of sildenafil and sildenafil *N*-oxide in *Mobile phase*, prepared as follows. Dissolve 70 mg of USP Sildenafil Citrate RS in 1 mL of a solution of hydrogen peroxide and formic acid (2:1), allow to stand for NMT 10 min, and then dilute with *Mobile phase* to 250.0 mL.

Standard solution: 0.0014 mg/mL of USP Sildenafil Citrate RS in *Mobile phase*

Sensitivity solution: 0.00035 mg/mL of USP Sildenafil Citrate RS in *Mobile phase* from the *Standard solution*

Sample stock solution: Transfer 5 Tablets to a 250-mL volumetric flask and disperse in 25 mL of *Diluent* with the aid of sonication. Dilute with *Mobile phase* to volume. Sonicate, if necessary. Centrifuge and use the supernatant.

Sample solution: Nominally 0.5 mg/mL of sildenafil prepared by diluting a suitable portion of the *Sample stock solution* with *Mobile phase*

System suitability

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

[Note—See *Table 1* for the relative retention times.]

Suitability requirements

Resolution: NLT 2.6 between sildenafil *N*-oxide and sildenafil, *System suitability solution*

Tailing factor: NMT 1.3, *Standard solution*

Relative standard deviation: NMT 3.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any individual degradation product 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 any individual degradation product from the *Sample solution*

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

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

C_U = nominal concentration of sildenafil in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of sildenafil, 474.58

M_{r2} = molecular weight of sildenafil citrate, 666.70

Acceptance criteria: See *Table 1*. Disregard any peak less than 0.05%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Sildenafil	1.0	—
Sildenafil *N*-oxide[a]	1.2	0.20
Any individual degradation product	—	0.20
Total degradation products	—	0.50

[a] 1-{[3-(6,7-Dihydro-1-methyl-7-oxo-3-propyl-1*H*-pyrazolo[4,3-*d*]pyrimidin-5-yl)-4-ethoxyphenyl]sulfonyl}-4-methylpiperazine N^4-oxide.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature.

Add the following:

▲• **Labeling:** The labeling states the *Dissolution* test used only if *Test 1* is not used.▲ (RB 1-Jan-2025)

• **USP Reference Standards** ⟨11⟩

USP Sildenafil Citrate RS

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

Topic/Question	Contact	Expert Committee
SILDENAFIL TABLETS	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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