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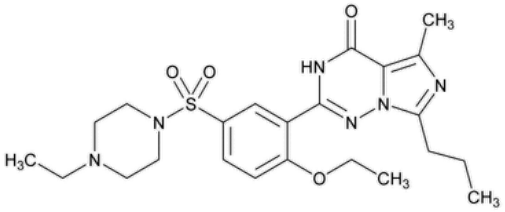
Vardenafil Hydrochloride



• HCl • 3 H_2O

$C_{23}H_{32}N_6O_4S \cdot HCl \cdot 3H_2O$ 579.11

Piperazine, 1-[[3-(1,4-dihydro-5-methyl-4-oxo-7-propylimidazo[5,1-*f*][1,2,4]triazin-2-yl)-4-ethoxyphenyl]sulfonyl]-4-ethyl-, monohydrochloride, trihydrate-;

2-[2-Ethoxy-5-(4-ethyl-piperazine-1-sulfonyl)-phenyl]-5-methyl-7-propyl-3*H*-imidazo[5,1-*f*][1,2,4]triazin-4-one, hydrochloride, trihydrate CAS RN®: 330808-88-3; UNII: 5M8S2CU0TS.

Anhydrous 525.06 CAS RN®: 224785-91-5; UNII: IF61NL91H3.

DEFINITION

Vardenafil Hydrochloride contains NLT 98.0% and NMT 102.0% of vardenafil hydrochloride ($C_{23}H_{32}N_6O_4S \cdot HCl$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

• **C.** Identification Tests—General, *Chloride*⟨191⟩**:** Meets the requirements

ASSAY

• **Procedure**

Protect all solutions containing vardenafil from light.

Buffer: Dissolve 1.3 g of monobasic potassium phosphate and 0.7 g of dibasic sodium phosphate dihydrate in 1 L of water.

Mobile phase: See *Table 1*. Return to original conditions, and re-equilibrate the system.

Table 1

Time (min)	Buffer (%)	Acetonitrile (%)
0	80	20
2	80	20
22	25	75
27	25	75

System suitability solution: 0.5 mg/mL of USP Vardenafil System Suitability RS prepared as follows. Transfer an appropriate quantity of the Reference Standard to a volumetric flask. Add 20% of the flask volume of acetonitrile and dilute with *Buffer* to volume.

Standard solution: 0.15 mg/mL of USP Vardenafil Hydrochloride RS prepared as follows. Transfer an appropriate quantity of USP Vardenafil Hydrochloride RS to a volumetric flask. Add 20% of the flask volume of acetonitrile and dilute with *Buffer* to volume.

Sample solution: 0.15 mg/mL of Vardenafil Hydrochloride prepared as follows. Transfer an appropriate quantity of Vardenafil Hydrochloride to a volumetric flask. Add 20% of the flask volume of acetonitrile and dilute with *Buffer* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 242 nm

Column: 3-mm × 25-cm; 5-µm packing L1

Column temperature: 45°

Flow rate: 0.5 mL/min

Injection volume: 10 µL

System suitability

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

Suitability requirements

Resolution: NLT 5.0 between vardenafil and 7-methyl vardenafil, *System suitability solution*

Relative standard deviation: NMT 0.85%, *Standard solution*

Tailing factor: 0.8–1.5, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of vardenafil hydrochloride ($C_{23}H_{32}N_6O_4S \cdot HCl$) in the portion of Vardenafil Hydrochloride taken:

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

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

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

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

C_U = concentration of Vardenafil Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

• **Organic Impurities**

Protect all solutions containing vardenafil from light.

Buffer, Mobile phase, System suitability solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Diluent: Acetonitrile and *Buffer* (20:80)

Standard stock solution: 0.5 mg/mL of USP Vardenafil Hydrochloride RS prepared as follows. Transfer an appropriate quantity of the Reference Standard to a volumetric flask. Add 20% of the flask volume of acetonitrile and dilute with *Buffer* to volume.

Standard solution: 0.5 µg/mL of USP Vardenafil Hydrochloride RS in *Diluent* from the *Standard stock solution*

Sample solution: 0.5 mg/mL of Vardenafil Hydrochloride prepared as follows. Transfer an appropriate quantity of Vardenafil Hydrochloride to a volumetric flask. Add 20% of the flask volume of acetonitrile and dilute with *Buffer* to volume.

System suitability

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

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

Suitability requirements

Resolution: NLT 5.0 between vardenafil and 7-methyl vardenafil, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Vardenafil Hydrochloride taken:

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

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

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

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

C_U = concentration of Vardenafil Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*. Disregard any impurity peak less than 0.05%.

Table 2

Name		Relative Retention Time	Acceptance Criteria, NMT (%)
7-Methyl vardenafil[a]		0.83	0.15
Vardenafil		1.0	—
Unspecified impurities	Vardenafil acid[b]	0.48	0.10 each
	Vardenafil dimer[c]	1.2	
	Any unspecified individual impurity	—	
Total impurities		—	0.3

[a] 2-{2-Ethoxy-5-[(4-ethylpiperazin-1-yl)sulfonyl]phenyl}-5,7-dimethylimidazo[5,1-*f*][1,2,4]triazin-4(3*H*)-one.

[b] 4-Ethoxy-3-(5-methyl-4-oxo-7-propyl-3,4-dihydroimidazo [5,1-*f*][1,2,4]triazin-2-yl)benzenesulfonic acid.

[c] 2,2'-[(Piperazine-1,4-disulfonyl)bis(6-ethoxy-3,1-phenylene)]bis[5-methyl-7-propylimidazo[5,1-*f*][1,2,4]-triazin-4(3*H*)-one.

SPECIFIC TESTS

• **Water Determination,** *Method I*⟨921⟩**:** 8.8%–10.5%

ADDITIONAL REQUIREMENTS

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

• **USP Reference Standards** ⟨11⟩

USP Vardenafil Hydrochloride RS

USP Vardenafil System Suitability RS

This mixture contains Vardenafil Hydrochloride and approximately 1% of 7-methyl vardenafil (2-{2-ethoxy-5-[(4-ethylpiperazin-1-yl)sulfonyl]phenyl}-5,7-dimethylimidazo[5,1-*f*][1,2,4]triazin-4(3*H*)-one).

$C_{21}H_{28}N_6O_4S$ 460.55

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

Topic/Question	Contact	Expert Committee
VARDENAFIL HYDROCHLORIDE	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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