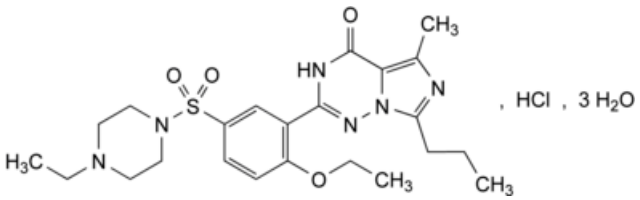
Edition: BP 2025 (Ph. Eur. 11.6 update)

Vardenafil Hydrochloride Trihydrate

General Notices

(Ph. Eur. monograph 2782)



$C_{23}H_{33}ClN_6O_4S,3H_2O$ 579.1 *330808-88-3*

Action and use

Selective inhibitor of cyclic GMP-specific phosphodiesterase type V with vasodilator action; treatment of erectile dysfunction.

Preparations

Vardenafil Orodispersible Tablets

Vardenafil Tablets

Ph Eur

DEFINITION

2-[2-Ethoxy-5-[(4-ethylpiperazin-1-yl)sulfonyl]phenyl]-5-methyl-7-propylimidazo[5,1-*f*][1,2,4]triazin-4(3*H*)-one hydrochloride trihydrate.

Content

98.0 per cent to 102.0 per cent (anhydrous substance).

CHARACTERS

Appearance

White or slightly brown or yellow powder.

Solubility

Slightly soluble in water, freely soluble in anhydrous ethanol, practically insoluble in heptane.

IDENTIFICATION

A. Infrared absorption spectrophotometry (2.2.24).

Comparison vardenafil hydrochloride CRS.

B. Water (see Tests).
C. It gives reaction (a) of chlorides (2.3.1).

TESTS

Related substances

Liquid chromatography (2.2.29). *Protect the solutions from light*.

Solvent mixture acetonitrile R, mobile phase A (20:80 *V/V*).

Test solution (a) Dissolve 50.0 mg of the substance to be examined in 20 mL of acetonitrile R and dilute to 100.0 mL with mobile phase A.

Test solution (b) Dilute 15.0 mL of test solution (a) to 50.0 mL with the solvent mixture.

Reference solution (a) Dissolve 50.0 mg of vardenafil hydrochloride CRS in 20 mL of acetonitrile R and dilute to 100.0 mL with mobile phase A. Dilute 15.0 mL of the solution to 50.0 mL with the solvent mixture.

Reference solution (b) Dilute 1.0 mL of test solution (a) to 100.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 10.0 mL with the solvent mixture.

Reference solution (c) Dissolve 5 mg of vardenafil for system suitability CRS (containing impurity A) in 2 mL of acetonitrile R and dilute to 10 mL with mobile phase A.

Column:

— *size*: *l* = 0.25 m, Ø = 3.0 mm;

— *stationary phase*: end-capped polar-embedded octadecylsilyl amorphous organosilica polymer R (5 µm);

— *temperature*: 45 °C.

Mobile phase:

— *mobile phase A*: solution containing 0.7 g/L of disodium hydrogen phosphate dihydrate R and 1.3 g/L of potassium dihydrogen phosphate R;

— *mobile phase B*: acetonitrile for chromatography R;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 2	80	20
2 - 22	80 → 25	20 → 75
22 - 27	25	75

Flow rate 0.5 mL/min.

Detection Spectrophotometer at 242 nm.

Injection 10 µL of test solution (a) and reference solutions (b) and (c).

Identification of impurities Use the chromatogram supplied with vardenafil for system suitability CRS and the chromatogram obtained with reference solution (c) to identify the peak due to impurity A.

Relative retention With reference to vardenafil (retention time = about 16 min): impurity A = about 0.8.

System suitability Reference solution (c):

— *resolution*: minimum 5.0 between the peaks due to impurity A and vardenafil.

Calculation of percentage contents:

— for each impurity, use the concentration of vardenafil hydrochloride trihydrate in reference solution (b).

Limits:

— *impurity A*: maximum 0.15 per cent;

— *unspecified impurities*: for each impurity, maximum 0.10 per cent;

— *total*: maximum 0.3 per cent;

— *reporting threshold*: 0.05 per cent.

Sulfates (*2.4.13*)

Maximum 400 ppm.

Suspend 0.5 g in 20 mL of a 5.15 g/L solution of *hydrochloric acid R* and stir for 15 min. Filter if complete dissolution is not obtained.

Water (*2.5.12*)

8.8 per cent to 10.5 per cent, determined on 60.0 mg.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Liquid chromatography (*2.2.29*) as described in the test for related substances with the following modification.

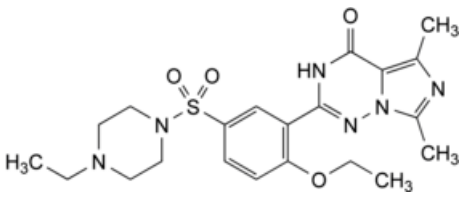
Injection 10 µL of test solution (b) and reference solution (a).

Calculate the percentage content of $C_{23}H_{33}ClN_6O_4S$ taking into account the assigned content of *vardenafil hydrochloride CRS*.

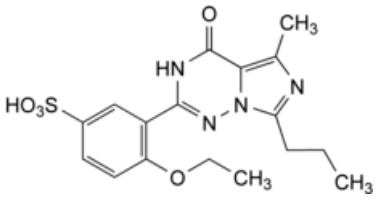
IMPURITIES

Specified impurities *A*.

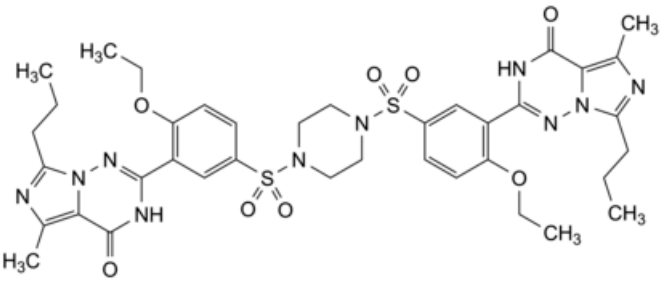
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical use (2034). It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use) *B, C.*



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-diylbis[(sulfonyl)(4-ethoxybenzene-1,3-diyl)]]bis[5-methyl-7-propylimidazo[5,1-*f*][1,2,4]triazin-4(3*H*)-one].

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