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Sildenafil Orodispersible Films

General Notices

Orodispersible Sildenafil Films

Action and use

Selective inhibitor of cyclic GMP specific phosphodiesterase (Type V) with vasodilator action; treatment of male erectile dysfunction.

DEFINITION

Sildenafil Orodispersible Films contain Sildenafil Citrate.

The films comply with the requirements stated under Oromucosal Preparations and with the following requirements.

Content of sildenafil, $C_{22}H_{30}N_6O_4S$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Shake a quantity of orodispersible films containing the equivalent of 25 mg of sildenafil with 10 mL of *methanol* and filter.
(2) 0.35% w/v of *sildenafil citrate EPCRS* in *methanol*.
(3) Equal volumes of solutions (1) and (2).

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel F_{254}* (Merck silica gel 60 F_{254} plates are suitable).
(b) Use the mobile phase as described below.
(c) Apply 10 µL of each solution.
(d) Develop the plate to 8 cm.
(e) After removal of the plate, dry in a current of warm air and examine under *ultraviolet light (254 nm)*.

MOBILE PHASE

4 volumes of *methanol* and 8 volumes of *ethyl acetate*.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) shows a single spot with the same retention and colour to solution (2).

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) corresponds in position and colour to that in the chromatogram obtained with solution (2).

B. In the Assay, the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the principal peak in the chromatogram obtained with solution (2).

TESTS

Dissolution

Comply with the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 1, rotating the basket at 100 revolutions per minute.
(b) Use 900 mL of *0.01M hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 15 minutes withdraw a sample of the medium and measure the *absorbance* of the filtered sample, suitably diluted with the dissolution medium, if necessary, to produce a solution containing the equivalent of 0.0027% w/v of sildenafil, at the maximum at 290 nm using *0.01M hydrochloric acid* in the reference cell, Appendix II B.
(2) Measure the *absorbance* of a 0.0038% w/v solution of *sildenafil citrate EPCRS* in *0.01M hydrochloric acid* at the maximum at 290 nm using *0.01M hydrochloric acid* in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of sildenafil, $C_{22}H_{30}N_6O_4S$, in the medium using the declared content of sildenafil citrate, $C_{28}H_{38}N_6O_{11}S$, in *sildenafil citrate EPCRS*. Each mg of $C_{28}H_{38}N_6O_{11}S$ is equivalent to 0.7118 mg of $C_{22}H_{30}N_6O_4S$.

LIMITS

The amount of sildenafil released is not less than 75% (Q) of the stated amount.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Disperse a quantity of orodispersible films containing the equivalent of 100 mg of sildenafil in 10 mL of *water*. Dilute to 100 mL with *acetonitrile* and filter. Dilute 1 volume of this solution to 2 volumes with the mobile phase.
(2) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase, further dilute 1 volume of this solution to 5 volumes with the same solvent.
(3) Dissolve 70 mg of *sildenafil citrate EPCRS* in 1 mL of a mixture containing 1 volume of *formic acid* and 2 volumes of *hydrogen peroxide solution (100 vol)* and allow to stand for 10 minutes. Dilute 1 volume of this solution to 250 volumes with the mobile phase (in-situ degradation of sildenafil to produce impurity B).
(4) 0.000075% w/v of *sildenafil impurity A EPCRS* in the mobile phase.
(5) Dilute 2.5 volumes of solution (2) to 10 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 3.9 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Waters Symmetry C18 is suitable).
(b) Use isocratic elution and the mobile phases described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use a column temperature of 30°.
(e) Use a detection wavelength of 290 nm.
(f) Inject 20 µL of each solution.
(g) Allow the chromatography to proceed for twice the retention time of sildenafil.

MOBILE PHASE

17 volumes of *acetonitrile*, 25 volumes of *methanol* and 58 volumes of a 0.7% v/v solution of *triethylamine* previously adjusted to pH 3.0 with *orthophosphoric acid*.

When the chromatograms are recorded under the prescribed conditions the retention time relative to sildenafil (retention time about 7 minutes) of impurity B is about 1.2.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to sildenafil and impurity B is at least 2.5.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak due to impurity A is not greater than the area of the principal peak in the chromatogram obtained with solution (4) (0.15%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of impurities is not greater than 0.50%;

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (5) (0.05%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Disperse ten films in the minimum volume of *water* possible (not exceeding 10% of the overall solvent mixture) and add sufficient *acetonitrile* to produce a solution expected to contain the equivalent of 0.1% w/v of sildenafil and filter. Dilute 1 volume of this solution to 50 volumes with mobile phase.
(2) 0.0028% w/v of *sildenafil citrate EPCRS* in the mobile phase.
(3) Dissolve 70 mg of *sildenafil citrate EPCRS* in 1 mL of a mixture containing 1 volume of *formic acid* and 2 volumes of *hydrogen peroxide solution (100 vol)* and allow to stand for 10 minutes. Dilute the resulting solution to 250 mL with the mobile phase (in-situ degradation of sildenafil to produce impurity B).

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to sildenafil and impurity B is at least 2.5.

DETERMINATION OF CONTENT

Calculate the content of sildenafil, $C_{22}H_{30}N_6O_4S$, in the orodispersible films using the declared content of sildenafil citrate, $C_{28}H_{38}N_6O_{11}S$, in *sildenafil citrate EPCRS*. Each mg of $C_{28}H_{38}N_6O_{11}S$ is equivalent to 0.7118 mg of $C_{22}H_{30}N_6O_4S$.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Sildenafil Citrate.