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

Rotigotine Transdermal Patches

General Notices

Action and use

Dopamine agonist.

DEFINITION

Rotigotine Transdermal Patches contain Rotigotine in a suitable matrix or reservoir presentation.

The transdermal patches comply with the requirements stated under Transdermal Patches and with the following requirements.

PRODUCTION

A suitable test is carried out to demonstrate the appropriate release of rotigotine.

Content of rotigotine, $C_{19}H_{25}NOS$

90.0 to 110.0% of the stated amount.

IDENTIFICATION

A. Remove the release liner and dissolve the contents of one patch in 100 mL of 0.1M *hydrochloric acid* with the aid of ultrasound. Dilute a suitable volume of this solution with 0.1M *hydrochloric acid* to produce a solution expected to contain 0.0025% w/v of Rotigotine. The *light absorption*, Appendix II B, in the range 200 to 300 nm of the final solution obtained exhibits two maxima, at 220 nm and 272 nm.
B. In the test for Uniformity of content, the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2).

TESTS

Related substances

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

Solution A 1 volume of *methanesulfonic acid*, 200 volumes of *tert-butyl methyl ether* and 800 volumes of *propan-2-ol*.

Solution B 1 volume of *methanesulfonic acid* and 1000 volumes of *water*.

(1) To 3 whole patches, wipe the lacquer off the patches using a solution of 4% *methanolic acetic acid*, dry and dissolve with sufficient Solution A to make a solution expected to contain 0.015% w/v of Rotigotine. To 3 volumes of this solution add 7 volumes of Solution B and mix well (the solution may become turbid). Centrifuge this solution and use the supernatant liquid.

(2) Dilute 1 volume of solution (1) to 100 volumes with a solution containing 3 volumes of Solution A and 7 volumes of Solution B.
(3) To 3 volumes of a 0.015% w/v of *rotigotine impurity standard BPCRS* in solution A, add 7 volumes of solution B.
(4) To 3 volumes of a 0.0015% w/v of *rotigotine impurity B EPCRS* in solution A, add 7 volumes of solution B.
(5) Dilute 1 volume of solution (2) to 10 volumes with a solution containing 3 volumes of Solution A and 7 volumes of Solution B.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (12.5 cm × 4.6 mm) packed with *end-capped Cyanosilyl silica gel for chromatography* (5 µm) (LiChrospher 100 CN is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 220 nm.
(f) Inject 80 µL of each solution.

MOBILE PHASE

Mobile phase A 0.5 volumes of *methane sulfonic acid* and 1000 volumes of *water*.

Mobile phase B 0.5 volumes of *methane sulfonic acid* and 1000 volumes of *acetonitrile*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-2	95	5	isocratic
2-35	95→40	5→60	linear gradient
35-38	40	60	isocratic
38-39	40→95	60→5	linear gradient
39-45	95	5	re-equilibration

When the chromatograms are run under the prescribed conditions, the retention times relative to rotigotine (retention time, about 16 minutes) are: impurity B, about 0.3; impurity K, about 0.6; impurity C, about 0.7; impurity D, about 0.9.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3):

the *resolution* between the peaks due to rotigotine impurity K and impurity C is at least 2.0;

the *resolution* between the peaks due to rotigotine impurity D and rotigotine is at least 1.5.

LIMITS

Identify any peak in the chromatogram obtained with solution (1) corresponding to impurity K using the chromatogram obtained with solution (3) and multiply the area of this peak by a correction factor of 3.7. Identify any peak in the chromatogram obtained with solution (1) corresponding to impurity B using the chromatogram obtained with solution (4).

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity C is not greater than 0.6 times the area of the principal peak in the chromatogram obtained with solution (2) (0.6%);

the area of any peak corresponding to impurity B is not greater than 0.4 times the area of the principal peak in the chromatogram obtained with solution (2) (0.4%);

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

the sum of the areas of all *secondary peaks* is not greater than 1.5 times the area of the principal peak in the chromatogram obtained with solution (2) (1.5%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (5) (0.1%).

Uniformity of content

Comply with the requirements stated under uniformity of content, Appendix XII C3, Test C, with respect to the individual content of each dosage unit and using the following method of analysis.

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

Solution A 4 volumes of *propan-2-ol*, 1 volume of *tert-butyl methyl ether* and 0.005 volumes of *methanesulfonic acid*.

Solution B 1000 volumes *water* and 1 volume *methanesulfonic acid*.

(1) Remove the release liner and backing foil from 10 patches and dissolve each patch in a sufficient volume of Solution A to produce a solution expected to contain 0.045 % w/v of Rotigotine. Dilute 3 volumes of this solution to 10 volumes with Solution B and mix well (the solution may become turbid). Centrifuge this solution and use the supernatant liquid.
(2) 0.0135 % w/v of *rotigotine BPCRS* in solution B.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (7.5 cm × 4 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (4 µm) (Superspher 60 RP select B is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use a column temperature of 30°.
(e) Use a detection wavelength of 272 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

650 volumes of *water*, 350 volumes of *acetonitrile* and 0.5 volumes of *methanesulfonic acid*.

When the chromatograms are run under the prescribed conditions, the retention time of the peak due to Rotigotine is about 1.5 minutes.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2), the *symmetry factor* of the peak due to rotigotine is in the range 0.8 to 2.8.

DETERMINATION OF CONTENT

Calculate the content of $C_{19}H_{25}NOS$ in the transdermal patch using the declared content of $C_{19}H_{25}NOS$ in *rotigotine BPCRS*.

ASSAY

Use the average of the individual results determined in the test for Uniformity of content.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under *Rotigotine*.