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Notes:	

Rotigotine Transdermal Patches

Rotigotine Preparations

Action and use

Dopamine agonist.

DEFINITION

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

PRODUCTION

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

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

Content of rotigotine, C₁₉H₂₅NOS

92.0 to 105.0% 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 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

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 2-*propanol*, 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. 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) 0.045 % w/v *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 mins.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2), the tailing factor of the peak due to Rotigotine is no more than 2.8.

DETERMINATION OF CONTENT

Calculate the content of C₁₉H₂₅NOS in the transdermal patch using the declared content of C₂₉H₄₁NOS in *rotigotine BPCRS*.

Related substances

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

Solution A 4 volumes of 2-*propanol*, 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) 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 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) 0.05% w/v of *rotigotine BPCRS* in Solution A. To 3 volumes of this solution add 7 volumes of Solution B to make a solution containing 0.015% w/v *rotigotine BPCRS*.
- (3) 0.015% w/v of *rotigotine impurity standard BPCRS*.
- (4) 0.015% w/v of each *rotigotine BPCRS* and *rotigotine impurity standard BPCRS*.
- (5) Dilute 1 volume of solution (1) to 10 volumes with *methanol*.

CHROMATOGRAPHIC CONDITIONS

- (a) Use a stainless steel column (12.5 cm × 4.6 mm) packed with *octadecylsilyl 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 10 volumes of *acetonitrile* and 90 volumes of a 0.544% w/v solution of *potassium dihydrogen orthophosphate* previously adjusted to pH 4.5 with *dilute orthophosphoric acid*.

Mobile phase B *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 of about 15.17) are: impurity B, about 0.3; impurity K, about 0.6; impurity C, about 0.7.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution factor* between the peaks due to *rotigotine* impurity B and impurity C at least 2.0.

LIMITS

In the chromatogram obtained with solution (1):

Identify any peak corresponding to impurity B, C and K using solution (3) and multiply the area of this peak by a correction factor of 0.9, 3.7 and 0.9 respectively.

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 (3) (0.4%);

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

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1%);

the sum of the areas of any *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 0.1 times the area of the principal peak in the chromatogram obtained with solution (4) (0.1%).

ASSAY

Use the average of the 10 results obtained in the test for Uniformity of content.

IMPURITIES

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