Status: Effectivity information can only be shown for content published to the website.

Update information can only be shown for content published to the website.

Rivastigmine Transdermal Patches

Details for the public consultation of this monograph are as follows:

EAG/Panel/Working Party	**Medicinal Chemicals 2**
Contact Details	helen.corns@mhra.gov.uk hannah.bowden@mhra.gov.uk
Deadline for Comment	30 September 2020
Target Publication Date (subject to change)	BP 2022
Notes	New monograph If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required.

Action and use

Cholinesterase inhibitor; treatment of dementia in Alzheimer's disease and Parkinson's disease.

DEFINITION

Rivastigmine Transdermal Patches contain Rivastigmine.

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

Content of Rivastigmine, $C_{14}H_{22}N_2O_2$

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 prepared in *methanol*.

(1) Remove the release liner from an amount of patches containing 18 mg of Rivastigmine and dissolve the contents in 50 mL of *methanol*. Mix with the aid of ultrasound for 60 minutes, allow to cool and centrifuge at 3000 rpm for 10 minutes.

(2) 0.058% w/v of *rivastigmine hydrogen tartrate BPCRS*.

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 16 cm.
(e) After removal of the plate, dry in air and examine under *ultraviolet light (254 nm)*.

MOBILE PHASE

2 volumes of *formic acid*, 5 volumes of *water*, 30 volumes of *methanol* and 70 volumes of *dichloromethane*.

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) is similar in position and size to that in the chromatogram obtained with solution (2).

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

TESTS

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions prepared in mobile phase. *Prepare the solutions immediately before use and protect from light.*

(1) Remove the release liner from one patch and dissolve the contents in sufficient *tetrahydrofuran* to produce a solution containing 0.1% w/v Rivastigmine. Mix with the aid of ultrasound for 60 minutes. Allow the solution to cool to room temperature, dilute 1 volume to 5 volumes and filter (0.45 µm PTFE filter is suitable).
(2) Dilute 1 volume of solution (1) to 100 volumes. Dilute 2 volume of this solution to 10 volumes.
(3) 0.1% w/v of *rivastigmine for system suitability EPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (XTerra RP C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.0 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 217 nm.
(f) Inject 10 µL of each solution.
(g) Allow the chromatography to proceed for 3.5 times the retention time of rivastigmine.

MOBILE PHASE

28 volumes of *acetonitrile* and 72 volumes of 10 mM*sodium-1-heptane sulfonate*, adjusted to pH 3.0 with *orthophosphoric acid*.

When the chromatograms are recorded under the prescribed conditions, the relative retention(s) with reference to rivastigmine (retention time about 7 minutes) are: impurity A, about 0.5; impurity B, about 0.7 and impurity C, about 2.5.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peak due to impurity A and impurity B is at least 7.0.

LIMITS

Identify any peak corresponding to impurity C in the chromatogram obtained with solution (1), using the chromatogram obtained with solution (3), and multiply the area of this peak by a correction factor 0.6.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity A is not greater than 1.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.3%);

the area of any peak corresponding to impurity B is not greater than 0.75 times the area of the principal peak in the chromatogram obtained with solution (2) (0.15%);

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

the sum of the areas of any *secondary peaks* is not greater than 2.5 times the principal peak in the chromatogram obtained with solution (2) (0.5%).

Disregard any peak with an area less than half the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

Uniformity of content

Comply with the requirements stated under uniformity of content, Appendix XII C3, Test C, with respect to 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 prepared in the mobile phase, protected from light.

(1) Remove the release liner from one patch and dissolve the contents in sufficient *tetrahydrofuran* to produce a solution containing 0.1% w/v Rivastigmine. Mix with the aid of ultrasound for 60 minutes. Allow the solution to cool to room temperature, dilute 1 volume to 10 volumes and filter (0.45 µm PTFE filter is suitable).
(2) 0.016% w/v of *rivastigmine hydrogen tartrate BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

DETERMINATION OF CONTENT

Calculate the content of rivastigmine, $C_{14}H_{22}N_2O_2$, in the transdermal patch from the chromatograms obtained and using the declared content of $C_{18}H_{28}N_2O_8$, in *rivastigmine hydrogen tartrate BPCRS*. Each mg of $C_{18}H_{28}N_2O_8$ is equivalent to 0.6251 mg of $C_{14}H_{22}N_2O_2$.

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 A, B and C listed under *Rivastigmine Hydrogen Tartrate*.