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

Nicotine Transdermal Patches

General Notices

Action and use

Central nervous system stimulant; nicotine replacement therapy.

DEFINITION

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

PRODUCTION

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

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

Content of nicotine, $C_{10}H_{14}N_2$

90.0 to 110.0% of the stated amount.

Carry out all of the following procedures protected from light.

IDENTIFICATION

Remove the protective liner from a patch, cut into small pieces and place a quantity of the patch containing 20 mg of Nicotine into a centrifuge tube, add 10 mL of *chloroform*, disperse with the aid of ultrasound for 30 minutes, cool and centrifuge for a further 10 minutes. Add 6 mL of 0.5M *hydrochloric acid* and centrifuge for 10 minutes. Transfer 5 mL of the aqueous layer to a separating funnel and adjust the pH to 10.5 with 0.5M *sodium hydroxide*. Extract with 3 mL of *chloroform*, shake and retain the chloroform layer. The *infrared absorption spectrum* of the solution, Appendix II A, is concordant with the *reference spectrum* of nicotine *(RS 452)*.

TESTS

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in 0.2M *potassium dihydrogen orthophosphate* adjusted to pH 2.0 with *orthophosphoric acid* (solvent A).

(1) Remove the protective liner from a whole patch and cover the exposed surface with a porous material (glass wool or tissue may be suitable). Transfer the whole patch into a separating funnel containing 50 mL of *hexane* and shake for 10 minutes. Ensure that the layers in the patch are separated and shake for a further 10 minutes. Add 20 mL of solvent A and shake for a further 10 minutes. Remove the lower aqueous layer, dilute, if necessary with solvent A to give a concentration of approximately 0.04% w/v and filter through a 0.7-µm glass filter.

(2) Dilute 1 volume of solution (1) to 100 volumes.
(3) Dilute 1 volume of solution (2) to 10 volumes.
(4) 0.04% w/v of *nicotine impurity standard BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *end-capped polar-embedded octadecylsilyl amorphous organosilica polymer* (3.5 µm) (Waters XBridge is suitable) fitted with a guard column (3 cm × 4.6 mm) packed with the same material.
(b) Use gradient 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 254 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Mobile phase A Dilute 25 volumes of 1M *acetic acid* to 1000 volumes with *water*, add 6.2 volumes of 18M *ammonia* and adjust the pH to 10 with 18M *ammonia*.

Mobile phase B *acetonitrile*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-3	100→95	0→5	linear gradient
3-32	95→60	5→40	linear gradient
32-37	60→100	40→0	linear gradient
37-45	100	0	re-equilibration

In the chromatogram obtained with solution (4):

identify the peaks due to cotinine, myosmine, *cis*-nicotine-1′-oxide and *trans*-nicotine-1′-oxide.

In the chromatogram obtained with solution (1):

identify any peak corresponding to *cis*-nicotine-1′-oxide and multiply the area of this peak by a correction factor of 1.5;

identify any peak corresponding to *trans*-nicotine-1′-oxide and multiply the area of this peak by a correction factor of 1.5.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution* between cotinine and *trans* nicotine-1′-oxide is at least 2.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to cotinine is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1.0%);

the area of any peak corresponding to myosmine is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1.0%);

the area of any peak corresponding to *cis*-nicotine-1′-oxide is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1.0%);

the area of any peak corresponding to *trans*-nicotine-1′-oxide is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1.0%);

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 any other *secondary peaks* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1.0%);

the sum of the areas of all secondary peaks is not greater than 3 times the area of the principal peak in the chromatogram obtained with solution (2) (3.0%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (3) (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 in solvent A described under Related substances test.

(1) Remove the protective liner from a whole patch and cover the exposed surface with a porous material (glass wool or tissue may be suitable). Transfer a whole patch into a separating funnel containing 50 mL of *hexane* and shake for 10 minutes. Ensure that the layers in the patch are separated and shake for a further 10 minutes. Add sufficient solvent A to produce a concentration of 0.04% w/v of nicotine and shake for a further 10 minutes. Remove the lower aqueous layer and filter through a 0.7-µm glass filter. Dilute 1 volume of the resulting solution to 10 volumes with solvent A.
(2) 0.04% w/v of *nicotine impurity standard BPCRS*.
(3) 0.0124% w/v of *nicotine ditartrate dihydrate BPCRS*.

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 *trans*-nicotine-1′-oxide and cotinine is at least 2.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{10}H_{14}N_2$ in the transdermal patch using the declared content of $C_{10}H_{14}N_2$ in *nicotine ditartrate dihydrate BPCRS*. Each mg of $C_{10}H_{14}N_2$ is equivalent to 3.074 mg of $C_{10}H_{14}N_2,C_8H_{12}O_{12},2H_2O$.

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 Nicotine.