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Nicotine Nasal Spray

General Notices

Action and use

Central nervous system stimulant; nicotine replacement therapy.

DEFINITION

Nicotine Nasal Spray is a solution of Nicotine containing suitable buffering agents in a suitable container fitted with a suitable nasal delivery system.

The nasal spray complies with the requirements stated under Nasal Preparations and with the following requirements.

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

95.0 to 105.0% of the stated amount.

Carry out all of the following procedures protected from light.

CHARACTERISTICS

Colourless or brownish solution.

IDENTIFICATION

To a volume of the nasal spray containing 20 mg of Nicotine add 5 mL of *chloroform*, dissolve with the aid of ultrasound and centrifuge for 10 minutes. Cool the mixture, add two 3-mL quantities of 0.5M *hydrochloric acid* and mix carefully. Centrifuge the mixture for 10 minutes. Transfer 5 mL of the aqueous layer to a separating funnel and add sufficient 0.5M *sodium hydroxide* to obtain a pH of 10.5, add 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

Acidity or alkalinity

pH, 6.7 to 7.3, Appendix V L.

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) Dilute a volume of the nasal spray containing 20 mg of Nicotine to 50 mL with solvent A and mix.

(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 Add 25 volumes of 1M *acetic acid* to 1000 volumes of *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 *trans*-nicotine-1′-oxide and cotinine 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 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 myosmine is not greater than 0.7 times the area of the principal peak in the chromatogram obtained with solution (2) (0.7%);

the area of any peak corresponding to *cis*-nicotine-1′-oxide is not greater than 3 times the area of the principal peak in the chromatogram obtained with solution (2) (3.0%);

the area of any peak corresponding to *trans*-nicotine-1′-oxide is not greater than 3 times the area of the principal peak in the chromatogram obtained with solution (2) (3.0%);

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 the *secondary peaks* is not greater than five times the area of the principal peak in the chromatogram obtained with solution (2) (5.0%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (3) (0.1%).

ASSAY

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

(1) To a volume of the nasal spray containing 20 mg of Nicotine add 50 mL of solvent A and mix. Dilute 1 volume of the resulting solution to 10 volumes.
(2) 0.0124% w/v of *nicotine ditartrate dihydrate BPCRS* in solvent A.
(3) 0.04% w/v of *nicotine impurity standard BPCRS* in solvent A.

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 (4), the *resolution* between *trans*-nicotine-1′-oxide and cotinine is at least 2.0.

DETERMINATION OF CONTENT

Calculate the total content of $C_{10}H_{14}N_2$ in the nasal spray 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 $C_{10}H_{14}N_2,C_8H_{12}O_{12},2H_2O$.

IMPURITIES

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