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

Adrenaline and Cocaine Intranasal Solution / Epinephrine and Cocaine Intranasal Solution

General Notices

NOTE: *This monograph has been developed to cover unlicensed formulations.*

Action and use

Adrenoceptor agonist + local anaesthetic.

DEFINITION

Adrenaline and Cocaine Intranasal Solution contains Adrenaline Acid Tartrate and Cocaine Hydrochloride in a suitable vehicle.

The intranasal solution complies with the requirements stated under Nasal Preparations and with the following requirements. Where appropriate, the intranasal solution also complies with the requirements stated under Unlicensed Medicines.

Content of adrenaline, $C_9H_{13}NO_3$

95.0 to 105.0% of the stated amount.

Content of cocaine hydrochloride, $C_{17}H_{21}NO_4$,HCl

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. In the Assay for adrenaline, the principal peak in the chromatogram obtained with solution (1) has the same retention time as that in the chromatogram obtained with solution (2).
B. In the Assay for cocaine hydrochloride, the principal peak in the chromatogram obtained with solution (1) has the same retention time as that in the chromatogram obtained with solution (2).
C. To 10 ml of the intranasal solution add 2 mL of a 10% w/v solution of *disodium hydrogen orthophosphate* and sufficient *iodinated potassium iodide solution* to produce a brown colour and remove excess iodine by adding 0.1M *sodium thiosulfate* drop wise. A red colour is produced.
D. Yields reaction A characteristic of *chlorides*, Appendix VI.

TESTS

Acidity

pH, 2.0 to 4.0, Appendix V L.

Related substances (for cocaine hydrochloride)

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

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(1) Dilute a volume of the intranasal solution with sufficient mobile phase to produce a solution containing 0.04% w/v of Cocaine Hydrochloride.
(2) 0.0008% w/v of *benzoylecgonine hydrate* in the mobile phase.
(3) 0.0008% w/v of *benzoic acid* in the mobile phase.
(4) 0.0008% w/v of each of *benzoylecgonine hydrate* and *benzoic acid* in solution (1).

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (10 µm) (Partisil 10 ODS is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 240 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

1 volume of 9M *perchloric acid*, 35 volumes of *methanol* and 64 volumes of *water*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution* between the peaks corresponding to benzoylecgonine and benzoic acid is at least 2.0.

LIMITS

In the chromatogram obtained with solution (1):

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

the area of any peak corresponding to benzoic acid is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (2%).

The total impurity content is not greater than 2%.

ASSAY

For adrenaline

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

(1) Dilute a suitable volume of the intranasal solution with sufficient mobile phase to produce a solution containing the equivalent of 0.011% w/v of adrenaline.
(2) 0.02% w/v of *adrenaline acid tartrate BPCRS* in the mobile phase.
(3) 0.02% w/v of *adrenaline acid tartrate BPCRS* and 0.02% w/v of *noradrenaline acid tartrate* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Nucleosil C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 205 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Dissolve 4.0 g of *tetramethylammonium hydrogen sulfate*, 1.1 g of *sodium heptanesulfonate* and 2 mL of 0.1M *disodium edetate* in a mixture of 950 mL of *water* and 50 mL of *methanol* and adjust the pH to 3.5 with 1M *sodium hydroxide*.

SYSTEM SUITABILITY

The assay is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the two principal peaks is at least 2.0.

DETERMINATION OF CONTENT

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Calculate the content of $C_9H_{13}NO_3$ in the intranasal solution from the chromatograms obtained and using the declared content of $C_9H_{13}NO_3$ in *adrenaline acid tartrate BPCRS*.

For cocaine hydrochloride

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

(1) Dilute a volume of the intranasal solution containing 40 mg of Cocaine Hydrochloride with sufficient *water* to produce 100 mL.
(2) 0.04% w/v of *cocaine hydrochloride BPCRS* in *water*.
(3) 0.0008% w/v of each of *benzoylecgonine hydrate* and *benzoic acid* in solution (1).

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (10 µm) (Partisil 10 ODS is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 240 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

1 volume of 9M *perchloric acid*, 35 volumes of *methanol* and 64 volumes of *water*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks corresponding to benzoylecgonine and benzoic acid is at least 2.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{17}H_{21}NO_4$,HCl in the intranasal solution from the chromatograms obtained and using the declared content of $C_{17}H_{21}NO_4$,HCl in *cocaine hydrochloride BPCRS*.

STORAGE

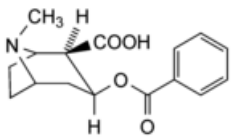
Adrenaline and Cocaine Intranasal Solution should be protected from light.

LABELLING

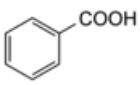
The quantity of adrenaline acid tartrate is stated in terms of the equivalent amount of adrenaline (epinephrine).

IMPURITIES

The impurities limited by the requirements of this monograph include:



1. Benzoylecgonine,



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2. Benzoic acid.