

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.

Naloxone Nasal Spray

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

EAG/Panel/Working Party	Medicinal Chemicals 3
Contact Details	michael.whaley@mhra.gov.uk maryna.dmitriieva@mhra.gov.uk sophie.cherrington@mhra.gov.uk bpcom@mhra.gov.uk
Deadline for Comment	31 st December 2026
Target Publication Date (subject to change)	BP 2028
Notes	New monograph If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required.

Action and use

Opioid receptor antagonist.

DEFINITION

Nasal Spray is a solution of [Naloxone Hydrochloride](#) in a suitable vehicle in a suitable metered-dose container.

The nasal spray complies with the requirements stated under [Nasal Preparations](#) and with the following requirements.

Content of naloxone hydrochloride, C₁₉H₂₁NO₄, HCl

95.0 to 105.0% of the stated amount.

IDENTIFICATION

In the Assay, record the UV spectrum of the principal peak in the chromatograms obtained with solutions (1) and (2) with a diode array detector in the range of 200 to 400 nm.

The UV spectrum of the principal peak in the chromatogram obtained with solution (1) is concordant with that of the peak in the chromatogram obtained with solution (2);

the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2).

TESTS

Related substances

Carry out the method for [liquid chromatography](#), [Appendix III D](#), using the following solutions protected from light.

Solution A 10 volumes of [methanol](#) and 90 volumes of 0.002M [sulfuric acid](#).

- (1) Dilute a volume of the nasal spray to produce a solution containing 0.04% w/v of Naloxone Hydrochloride with a mixture of 2 volumes 0.001% w/v of [ethylenediaminetetraacetic acid](#) and 98 volumes of solution A.
- (2) Dilute 1 volume of solution (1) to 200 volumes in [methanol](#) (30%).
- (3) 0.0001% w/v of [naloxone impurity D EPCRS](#) and 0.04% w/v of [naloxone hydrochloride BPCRS](#) in [methanol](#) (30%).
- (4) Dilute 1 volume of solution (2) to 5 volumes in [methanol](#) (30%).

CHROMATOGRAPHIC CONDITIONS

- (a) Use a stainless steel column (10 cm × 3.0 mm) packed with [base-deactivated end-capped octadecylsilyl silica gel for chromatography](#) (3 µm) (Hypersil BDS C18 is suitable).
- (b) Use gradient elution and the mobile phase described below.
- (c) Use a flow rate of 0.9 mL per minute.
- (d) Use a column temperature of 30°.
- (e) Use a detection wavelength of 210 nm.
- (f) Inject 20 µL of each solution.

MOBILE PHASE

Mobile phase A 1.25 volumes of 10% v/v of [sulfuric acid](#), 140 volumes of [acetonitrile](#) and 860 volumes of a solution containing 0.355% w/v of [sodium sulfate](#) and 0.375% w/v of [sodium dodecyl sulfate](#).

Mobile phase B 1 volume of 10% v/v of [sulfuric acid](#), 430 volumes of [acetonitrile](#) and 570 volumes of a solution containing 0.495% w/v of [sodium sulfate](#) and 0.490% w/v of [sodium dodecyl sulfate](#).

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-12	90.5	9.5	isocratic
12-26	90.5→67	9.5→33	linear gradient
26-36	67→10	33→90	linear gradient
36-49	10	90	isocratic
49-50	10→90.5	90→9.5	linear gradient

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
50-60	90.5	9.5	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless:

in the chromatogram obtained with solution (3), the [resolution](#) between the peaks due to impurity D and naloxone is at least 1.5.

in the chromatogram obtained with solution (4), the [signal-to-noise ratio](#) of the peak due to naloxone is at least 25.

CALCULATION OF IMPURITIES

For each impurity, use the concentration of naloxone hydrochloride in solution (2).

For the reporting threshold, use the concentration of naloxone hydrochloride in solution (4).

Naloxone hydrochloride retention time: about 21 minutes.

Relative retentions: impurity D, about 0.95; impurity E, about 1.9.

Correction factors; impurity D, multiply by 0.8, impurity E, multiply by 2.3.

LIMITS

- unspecified impurities: for each impurity, not more than 0.5%;
- total impurities: not more than 2.0%;
- reporting threshold: 0.1%.

ASSAY

Carry out the method for [liquid chromatography](#), [Appendix III D](#), using the following solutions protected from light.

Solution A: 30 volumes of [methanol](#) and 70 volumes of [water](#)

(1) Dilute a volume of the nasal spray to produce a solution containing 0.002% w/v of Naloxone Hydrochloride in solution A.

(2) 0.002% w/v of [naloxone hydrochloride BPCRS](#) in solution A.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (12.5 cm × 4.0 mm) packed with [base-deactivated end-capped octadecylsilyl silica gel for chromatography](#) (5 µm) (Phenomenex LiChrospher 60) 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 a column temperature of 60°.
- (e) Use a detection wavelength of 230nm.
- (f) Inject 20 µL of each solution.

MOBILE PHASE

15 volumes of [methanol](#) mixed with 85 volumes of buffer solution containing 0.657% of w/v of [potassium chloride](#), adjusted to pH 2.0 with [hydrochloric acid](#).

When the chromatograms are recorded under the prescribed conditions, the retention time of Naloxone Hydrochloride is about 2.3 minutes.

DETERMINATION OF CONTENT

Calculate the content of $C_{19}H_{21}NO_4 \cdot HCl$, in the nasal spray from chromatograms obtained and using the declared content of $C_{19}H_{21}NO_4 \cdot HCl$ in [naloxone hydrochloride BPCRS](#).

LABELLING

The quantity of active ingredient is stated in terms of the equivalent amount of naloxone hydrochloride.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities listed under [Naloxone hydrochloride](#) and

 1. [1S,5R,13R,17S)-4-Allyl-10,17-dihydroxy-12-oxa-4-azapentacyclo[9.6.1.0~1,13~.0~5,17~.0~7,18~]octadeca-7(18),8,10-trien-14-one 4-oxide (Naloxone N-Oxide)]

1. [1S,5R,13R,17S)-4-Allyl-10,17-dihydroxy-12-oxa-4-azapentacyclo[9.6.1.0~1,13~.0~5,17~.0~7,18~]octadeca-7(18),8,10-trien-14-one 4-oxide (Naloxone N-Oxide)]