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

Acetylcysteine Eye Drops

General Notices

Action and use

Sulfydryl donor; mucolytic; treatment of dry eye syndrome.

DEFINITION

Acetylcysteine Eye Drops are a sterile solution of Acetylcysteine in Purified Water containing Sodium Hydroxide.

The eye drops comply with the requirements stated under Eye Preparations, and with the following requirements.

Content of acetylcysteine, $C_5H_9NO_3S$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

To a volume containing 0.8 g of Acetylcysteine add *3M hydrochloric acid* until the pH of the solution is 2.0. Add, while stirring continuously, two 200-mg portions of finely powdered *sodium chloride* followed, if necessary, by further 25-mg portions of *sodium chloride* until a precipitate begins to appear. Allow to stand for 15 minutes, filter and dry the residue at 70° at a pressure not exceeding 0.7 kPa for 2 hours. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of acetylcysteine *(RS 003)*. Examine as discs prepared using *potassium bromide*.

TESTS

Acidity

pH, 5.5 to 6.5, Appendix V L.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. With the exception of solution (3), the solutions should be prepared immediately before use.

(1) Dilute a volume of the eye drops with sufficient of the mobile phase to produce a solution containing 0.2% w/v of Acetylcysteine.
(2) 0.2% w/v of *acetylcysteine BPCRS* in the mobile phase.
(3) 0.2% w/v of *acetylcysteine BPCRS* in the mobile phase, stored at room temperature for at least 2 hours before use (generation of *N*,*N'*-diacetylcystine).
(4) Dissolve 20 mg of L-*cysteine* (impurity B) and 20 mg of L-*cystine* (impurity A) in 10 mL of 1M *hydrochloric acid*, add 40 mg of *acetylcysteine BPCRS* and immediately dilute to 100 mL with the mobile phase. Dilute 10 mL of the resulting solution to 200 mL with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 5 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (LiChrosorb RP18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 205 nm.
(f) Inject 20 µL of each solution.
(g) Inject solutions (2) and (3) and allow the chromatography to proceed for three times the retention time of acetylcysteine.

MOBILE PHASE

10 volumes of *methanol* and 90 volumes of a 0.5% w/v solution of *ammonium sulfate* containing 0.02M *sodium pentanesulfonate*. Adjust the pH of the mixture, if necessary, to pH 2.0 using 2M *hydrochloric acid*.

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to acetylcysteine (retention time about 6 minutes) are: cystine, about 0.6; cysteine, about 0.7.

SYSTEM SUITABILITY

The test is not valid unless:

in the chromatogram obtained with solution (4), the height of the trough separating the peaks corresponding to cysteine and cystine is less than one quarter of the height of the peak corresponding to cysteine;

in the chromatogram obtained with solution (3) a peak corresponding to *N,N'*-diacetyl-L-cystine appears which has a retention time of about 13 minutes. The area of this peak is greater than the area of any corresponding peak in the chromatogram obtained with solution (2).

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to *N,N'*-diacetyl-L-cystine (impurity C) is not greater than the area of the peak corresponding to acetylcysteine in the chromatogram obtained with solution (4) (1%);

the area of any peak corresponding to cysteine (impurity B) or cystine (impurity A) is not greater than the area of the corresponding peak in the chromatogram obtained with solution (4) (0.5%);

the sum of the areas of any other *secondary peaks* is not greater than the area of the peak corresponding to acetylcysteine in the chromatogram obtained with solution (4) (1%).

Disregard any peak with an area less than 0.05 times that of the peak corresponding to acetylcysteine in the chromatogram obtained with solution (4) (0.05%).

ASSAY

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

(1) Dilute a volume of the eye drops with sufficient of the mobile phase to produce a solution containing 0.2% w/v of Acetylcysteine.
(2) 0.2% w/v of *acetylcysteine BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

DETERMINATION OF CONTENT

Calculate the content of $C_5H_9NO_3S$ in the eye drops using the declared content of $C_5H_9NO_3S$ in *acetylcysteine BPCRS*.

STORAGE

Acetylcysteine Eye Drops should be protected from light and stored at a temperature of 2° to 8°.

IMPURITIES

The impurities limited by the requirements of this monograph include; L-cysteine, L-cystine and *N,N′*-diacetyl-L-cystine which correspond to impurities A, B and C of the European Pharmacopoeia monograph respectively.