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

Chlorhexidine Gluconate Eye Drops

General Notices

Chlorhexidine Digluconate Eye Drops

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

Action and use

Antiseptic.

DEFINITION

Chlorhexidine Gluconate Eye Drops are a sterile solution of Chlorhexidine Gluconate in Purified Water. They are usually prepared from Chlorhexidine Gluconate Solution.

The eye drops comply with the requirements stated under Eye Preparations and with the following requirements. Where appropriate, the eye drops also comply with the requirements stated under Unlicensed Medicines.

Content of chlorhexidine gluconate, $C_{22}H_{30}Cl_2N_{10},2C_6H_{12}O_7$

95.0 to 115.0% of the stated amount.

IDENTIFICATION

A. Add 10 mL of *concentrated ammonia*, drop wise, to a volume of the eye drops containing the equivalent of 20 mg of chlorhexidine gluconate which has previously been cooled in ice. Centrifuge at 3000 rpm for 10 minutes, discard the supernatant liquid and transfer the residue to a filter which has previously been treated with *water* (Whatman GF/F paper is suitable); allow to stand until the ammonia has evaporated. Wash the residue with 10 mL of *water* and dissolve in *ethanol (70%)*. Evaporate the solvent under a stream of *nitrogen* and dry the residue at 105° for one hour. The *infrared absorption spectrum* of the dried residue, Appendix II A, is concordant with the *reference spectrum* of chlorhexidine *(RS 449)*.

B. In the Assay, the retention time of the principal peak in the chromatogram obtained with solution (1) is the same as that of the peak due to chlorhexidine in the chromatogram obtained with solution (2).

TESTS

Acidity or alkalinity

pH, 5.0 to 7.5, Appendix V L.

Related substances

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

(1) Dilute a volume of the eye drops, if necessary, to produce a solution containing the equivalent of 0.02% w/v of chlorhexidine gluconate.
(2) Dilute 1 volume of solution (1) to 100 volumes.
(3) Dilute 1 volume of solution (2) to 10 volumes.
(4) 0.001% w/v of *4-chloroaniline*.

(5) Dilute 1 volume of solution (4) and 2 volumes of a 0.0035% w/v solution of *chlorhexidine acetate BPCRS* to 20 volumes.
When the chromatograms are recorded under the prescribed conditions the retention time of chlorhexidine is about 13 minutes and the relative retention of 4-chloroaniline is about 0.3.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Phenomenex Luna C18(2) 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 254 nm.
(f) Inject 50 µL of each solution.
(g) For solution (1) allow the chromatography to proceed for 6 times the retention time of chlorhexidine.

Equilibrate the column with mobile phase for at least 1 hour.

MOBILE PHASE

120 volumes of *glacial acetic acid*, 270 volumes of *water* and 730 volumes of *methanol* containing 0.2% w/v of *sodium octanesulfonate*.

SYSTEM SUITABILITY

Use the chromatogram obtained with solution (4) to identify the peak due to 4-chloroaniline.

The test is not valid unless, in the chromatogram obtained with solution (5), the *resolution* between the two principal peaks is at least 23.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak due to 4-chloroaniline is not greater that the area of the principal peak in the chromatogram obtained with solution (2) (1%);

the area of any *secondary peak* is not greater than 1.5 times the area of the principal peak in the chromatogram obtained with solution (2) (1.5%);

the area of not more than one *secondary peak* is greater than the area of the principal peak in the chromatogram obtained with solution (2) (1%);

the sum of the areas of all the *secondary peaks* is not greater than 3.5 times the area of the principal peak in the chromatogram obtained with solution (2) (3.5%).

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.

(1) Dilute a volume of the eye drops, if necessary, with sufficient *water* to produce a solution containing the equivalent of 0.02% w/v of chlorhexidine gluconate.
(2) 0.014% w/v of *chlorhexidine acetate BPCRS* in *water*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (10 µm) (Partisil 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 *perchloric acid*, 35 volumes of *methanol* and 64 volumes of *water*.

DETERMINATION OF CONTENT

Calculate the content of $C_{22}H_{30}Cl_2N_{10},2C_6H_{12}O_7$ in the eye drops using the declared content of $C_{22}H_{30}Cl_2N_{10}$ in *chlorhexidine acetate BPCRS*. Each mg of $C_{22}H_{30}Cl_2N_{10}$ is equivalent to 1.776 mg of $C_{22}H_{30}Cl_2N_{10},2C_6H_{12}O_7$.

STORAGE

Chlorhexidine Gluconate Eye Drops should be protected from light.

LABELLING

The quantity of active ingredient is stated in terms of the equivalent amount of chlorhexidine gluconate.