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

Betamethasone Eye Drops

General Notices

Action and use

Glucocorticoid.

DEFINITION

Betamethasone Eye Drops are a sterile solution of Betamethasone Sodium Phosphate in Purified Water.

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

Content of betamethasone sodium phosphate, $C_{22}H_{28}FNa_2O_8P$

90.0 to 110.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Use the eye drops, diluted if necessary with *water*, to contain 0.1% w/v of Betamethasone Sodium Phosphate.
(2) 0.1% w/v of *betamethasone sodium phosphate BPCRS*.
(3) A mixture of equal volumes of solutions (1) and (2).
(4) A mixture of equal volumes of solution (2) and a 0.1% w/v solution of *prednisolone sodium phosphate BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel GF_{254}*.
(b) Use the mobile phase as described below.
(c) Apply 10 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry in air, heat at 110° for 10 minutes and examine under *ultraviolet light (254 nm)*.

MOBILE PHASE

20 volumes of *acetic anhydride*, 20 volumes of *water* and 60 volumes of *butan-1-ol*, prepared immediately before use.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (4) shows two principal spots with almost identical Rf values.

CONFIRMATION

The chromatograms obtained with solutions (1), (2) and (3) show single principal spots with similar Rf values.

B. In the Assay, the chromatogram obtained with solution (2) shows a peak with the same retention time as the peak due to betamethasone sodium phosphate in the chromatogram obtained with solution (1).

C. To a volume containing 0.2 mg of Betamethasone Sodium Phosphate, add slowly 1 mL of *sulfuric acid* and allow to stand for 2 minutes. A brownish yellow colour but no red colour or yellowish green fluorescence is produced.

TESTS

Acidity or alkalinity

pH, 7.0 to 8.5, Appendix V L.

Related substances

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

(1) Dilute the eye drops if necessary to give a solution containing 0.10% w/v of Betamethasone Sodium Phosphate.
(2) Dilute 1 volume of solution (1) to 50 volumes with *water*.
(3) 0.0060% w/v each of *betamethasone sodium phosphate BPCRS* and *betamethasone*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (20 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (10 µm) (Spherisorb ODS 1 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use a column temperature of 60°.
(e) Use a detection wavelength of 241 nm.
(f) Inject 20 µL of each solution.
(g) For solutions (1) and (2) record the chromatogram for three times the retention time of the principal peak.

MOBILE PHASE

40 volumes of *methanol* and 60 volumes of *citro-phosphate buffer pH 5.0*.

SYSTEM SUITABILITY

The test is not valid unless in the chromatogram obtained with solution (3) the *resolution factor* between the peaks due to betamethasone sodium phosphate and betamethasone is at least 3.5.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to betamethasone is not greater than 1.3 times the area of the principal peak in the chromatogram obtained with solution (2) (2.6%);

the area of any other *secondary peak* is not greater than 1.5 times the area of the principal peak in the chromatogram obtained with solution (2) (3%);

the sum of the areas of all the *secondary peaks* is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (2) (5%).

Disregard any peak the area of which is less than 0.05 times the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

ASSAY

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

(1) Mix a quantity of the eye drops containing 5 mg of Betamethasone Sodium Phosphate with 10 mL of *methanol* and dilute to 25 mL with *water*.

(2) A mixture of 5 mL of a 0.1% w/v solution of *betamethasone sodium phosphate BPCRS* in *water* (solution A) and 10 mL of a 0.06% w/v solution of *hydrocortisone* (internal standard) in *methanol* and sufficient *water* to produce 25 mL.
(3) Prepare in the same manner as solution (1) but using 10 mL of the internal standard solution in place of the methanol.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (20 cm × 5 mm) packed with *octadecylsilyl silica gel for chromatography* (10 µm) (Spherisorb ODS 1 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use a column temperature of 60°.
(e) Use a detection wavelength of 241 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

45 volumes of *methanol* and 55 volumes of *citro-phosphate buffer pH 5.0*.

DETERMINATION OF CONTENT

Calculate the content of $C_{22}H_{28}FNa_2O_8P$ in solution A by measuring the *absorbance*, Appendix II B, of an aliquot diluted with *water* to contain 0.002% w/v of Betamethasone Sodium Phosphate at the maximum at 241 nm and taking 297 as the value of A(1%, 1 cm) at the maximum at 241 nm. Calculate the content of $C_{22}H_{28}FNa_2O_8P$ in the eye drops using peak areas.

STORAGE

Betamethasone Eye Drops should be protected from light.