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

Betamethasone Injection

General Notices

Action and use

Glucocorticoid.

DEFINITION

Betamethasone Injection is a sterile solution of Betamethasone Sodium Phosphate in Water for Injections.

The injection complies with the requirements stated under Parenteral Preparations and with the following requirements.

Content of betamethasone, $C_{22}H_{29}FO_5$

92.5 to 107.5% of the stated amount.

IDENTIFICATION

A. To a volume of the injection containing the equivalent of 4 mg of betamethasone add 1 mL of *water* and sufficient *absolute ethanol* to produce 40 mL. Place 2 mL of the solution in a stoppered tube, add 10 mL of *phenylhydrazine-sulfuric acid solution*, mix, warm in a water bath at 60° for 20 minutes and cool immediately. The *absorbance* of the resulting solution at the maximum at 450 nm is not more than 0.1, Appendix II B.
B. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Dilute the injection, if necessary, with sufficient *water* to produce a solution containing the equivalent of 2 mg of betamethasone per mL.
(2) 0.25% w/v solution of *betamethasone sodium phosphate BPCRS* in *water*.
(3) A mixture of equal volumes of solutions (1) and (2).
(4) A mixture of equal volumes of solution (1) and a 0.25% w/v solution of *prednisolone sodium phosphate BPCRS* in *water*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel GF_{254}*.
(b) Use the mobile phase as described below and prepare immediately before use.
(c) Apply 5 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, allow it to 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*.

CONFIRMATION

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

the chromatogram obtained with solution (4) shows two principal spots with almost identical Rf values.

Secondary spots due to excipients may also be observed in the chromatograms obtained with solutions (1), (3) and (4).

C. Evaporate a volume containing the equivalent of 2 mg of betamethasone to dryness on a water bath, dissolve the residue in 2 mL of *sulfuric acid* and allow to stand for 2 minutes. No red colour is produced.

TESTS

Alkalinity

pH, 8.0 to 9.0, Appendix V L.

Colour

The injection, diluted if necessary with *water* to contain the equivalent of 2 mg of betamethasone per mL, is not more intensely coloured than *reference solution* BY_4, Appendix IV B, Method I.

Related substances

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

(1) Dilute the injection with mobile phase, if necessary, to give a solution containing the equivalent of 0.10% w/v of betamethasone.
(2) Dilute 1 volume of solution (1) to 50 volumes with mobile phase.
(3) 0.0060% w/v each of *betamethasone sodium phosphate BPCRS* and *betamethasone* in mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 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. 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 protected from light.

(1) Dilute a volume of the injection containing the equivalent of 8 mg of betamethasone to 50 mL with *methanol (50%)*.
(2) Dilute 5 mL of a 0.045% w/v solution of *betamethasone sodium phosphate BPCRS* in *water* (solution A) to 10 mL with *methanol*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 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.

MOBILE PHASE

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

DETERMINATION OF CONTENT

Calculate the content of $C_{22}H_{29}FO_5$ in the injection, determining the exact strength of $C_{22}H_{29}FO_5$ in solution (2) as follows.
Dilute 3 mL of solution A to 50 mL with *water* and measure the *absorbance*, Appendix II B, of the resulting solution at the maximum at 241 nm, taking 391 as the value of A(1%, 1 cm) for betamethasone.

STORAGE

Betamethasone Injection should be stored at a temperature not exceeding 30° and protected from light.

LABELLING

The quantity of active ingredient is stated in terms of the equivalent amount of betamethasone in a suitable dose-volume.