



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

Betamethasone and Clioquinol Cream

[General Notices](#)

Action and use

Glucocorticoid.

DEFINITION

Betamethasone and Clioquinol Cream contains Betamethasone Valerate and Clioquinol, the latter in [very fine powder](#), in a suitable basis.

The cream complies with the requirements stated under Topical Semi-solid Preparations and with the following requirements.

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

90.0 to 110.0% of the stated amount.

Content of clioquinol, C_9H_5ClINO

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) Disperse a quantity of the preparation being examined containing the equivalent of 0.5 mg of betamethasone in 20 mL of [methanol](#) (80%) by heating on a water bath until the methanol begins to boil. Shake vigorously, cool in ice and centrifuge. Transfer 10 mL of the supernatant liquid to a separating funnel, add 3 mL of [water](#) and 5 mL of [chloroform](#), shake vigorously, allow the layers to separate and evaporate the chloroform layer to dryness in a current of [nitrogen](#) with gentle heating. Dissolve the residue in 1 mL of [chloroform](#).
- (2) 0.03% w/v of [betamethasone valerate BPCRS](#) in [chloroform](#).

CHROMATOGRAPHIC CONDITIONS

- (a) Use as the coating [silica gel G](#).
- (b) Use the mobile phase as described below.
- (c) Apply 10 μ L of each solution.
- (d) Develop the plate to 15 cm.
- (e) After removal of the plate, allow it to dry in air, heat at 105° for 5 minutes and spray while hot with [alkaline tetrazolium blue solution](#).

MOBILE PHASE

5 volumes of [absolute ethanol](#), 10 volumes of [acetone](#) and 100 volumes of [chloroform](#).

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) corresponds in position and colour to that in the chromatogram obtained with solution (2).

B. In the Assay for betamethasone the chromatogram obtained with solution (1) shows a peak with the same retention time as the peak due to betamethasone valerate in the chromatogram obtained with solution (3).

C. In the Assay for clioquinol the chromatogram obtained with solution (1) shows a peak with the same retention time as the peak due to clioquinol in the chromatogram obtained with solution (2).

ASSAY

For betamethasone

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

(1) Shake a quantity of the cream containing the equivalent of 2 mg of betamethasone with 100 mL of hot hexane for 2 minutes, cool, extract the mixture with 20 mL of ethanol (96%) and filter the lower, ethanolic layer through absorbent cotton previously washed with ethanol (75%). Repeat the extraction of the hexane mixture with two 10-mL quantities of ethanol (75%), filtering each extract in turn through the absorbent cotton and dilute the combined filtrates to 50 mL with ethanol (75%).

(2) Prepared in the same manner as solution (1) but add 5 mL of a 0.072% w/v solution of beclometasone dipropionate BPCRS (internal standard) in ethanol (80%) before diluting to 50 mL.

(3) Mix 2 volumes of a solution containing 0.024% w/v of betamethasone valerate BPCRS and 0.0012% w/v of betamethasone 21-valerate BPCRS in ethanol (80%) with 1 volume of a 0.072% w/v solution of the internal standard in ethanol (80%) and dilute to 10 volumes with the same solvent.

CHROMATOGRAPHIC CONDITIONS

- Use a stainless steel column (10 cm × 5 mm) packed with octadecylsilyl silica gel for chromatography (5 µm) (Spherisorb ODS 1 is suitable).
- Use isocratic elution and the mobile phase described below.
- Use a flow rate of 2 mL per minute.
- Use a column temperature of 60°.
- Use a detection wavelength of 238 nm.
- Inject 20 µL of each solution.

MOBILE PHASE

42 volumes of absolute ethanol and 58 volumes of water.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the resolution factor between the peaks due to betamethasone valerate (retention time about 5 minutes) and betamethasone 21-valerate (retention time about 7 minutes) is more than 1.0, if necessary adjust the mixture of absolute ethanol and water in the mobile phase.

DETERMINATION OF CONTENT

Calculate the content of $C_{22}H_{29}FO_5$ in the cream using the declared content of $C_{22}H_{29}FO_5$ in betamethasone valerate BPCRS.

For clioquinol

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

(1) Add 80 mL of a hot 80% v/v solution of 2-methoxyethanol to a quantity of the cream containing 30 mg of Clioquinol and heat on a water bath for 5 minutes, swirling vigorously. Cool to room temperature, dilute to 100 mL with the same solvent, mix and filter. To 5 mL of the filtrate add 1 mL of a solution containing 1% w/v of nickel(II) chloride hexahydrate and dilute to 50 mL with the mobile phase.

(2) Mix 5 mL of a solution containing 0.024% w/v of clioquinol BPCRS in an 80% v/v solution of 2-methoxyethanol and 1 mL of a solution containing 1% w/v of nickel(II) chloride hexahydrate in water and dilute to 50 mL with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

- (a) Use a stainless steel column (25 cm × 4.6 mm) packed with [phenyl silica gel for chromatography](#) (5 µm) (Spherisorb Phenyl is suitable).
- (b) Use isocratic elution and the mobile phase described below.
- (c) Use a flow rate of 1.5 mL per minute.
- (d) Use an ambient column temperature.
- (e) Use a detection wavelength of 273 nm.
- (f) Inject 20 µL of each solution.

MOBILE PHASE

0.024% w/v of *nickel(II) chloride hexahydrate* in a mixture of 2 volumes of [methanol](#), 3 volumes of [acetonitrile](#) and 5 volumes of [water](#).

DETERMINATION OF CONTENT

Calculate the content of C₉H₅ClINO in the cream using the declared content of C₉H₅ClINO in [clioquinol BPCRS](#).

STORAGE

Betamethasone and Clioquinol Cream should be protected from light.

LABELLING

The quantity of active ingredient with respect to Betamethasone Valerate is stated in terms of the equivalent amount of betamethasone.