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

Hydrocortisone Sodium Phosphate Oral Solution

General Notices

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

Action and use

Corticosteroid.

DEFINITION

Hydrocortisone Sodium Phosphate Oral Solution is a solution containing Hydrocortisone Sodium Phosphate in a suitable flavoured vehicle.

The oral solution complies with the requirements stated under Oral Liquids and with the following requirements. Where appropriate, the oral solution also complies with the requirements stated under Unlicensed Medicines.

Content of hydrocortisone, $C_{21}H_{30}O_5$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Dilute a volume of the oral solution containing the equivalent of 0.25 g of hydrocortisone to 100 mL with *water*.
(2) 0.34% w/v of *hydrocortisone sodium phosphate BPCRS* in *methanol* .
(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 *betamethasone sodium phosphate BPCRS* in *methanol*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel G*.
(b) Use the mobile phase described below.
(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 until the solvent has evaporated, spray with *ethanolic sulfuric acid (20%)*, heat at 120° for 10 minutes and examine under *ultraviolet light (365 nm)*.

MOBILE PHASE

A freshly prepared mixture of 20 volumes of *acetic anhydride*, 20 volumes of *water* and 60 volumes of *butan-1-ol*.

SYSTEM SUITABILITY

The test is not valid unless the principal spot in the chromatogram obtained with solution (3) appears as a single compact spot and the chromatogram obtained with solution (4) exhibits two principal spots with almost identical Rf values.

CONFIRMATION

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

B. Evaporate 0.1 mL to dryness on a water bath and dissolve the residue in 2 mL of *sulfuric acid*. A yellowish green fluorescence is produced immediately (distinction from betamethasone sodium phosphate, dexamethasone sodium phosphate and prednisolone sodium phosphate).

TESTS

Alkalinity

pH, 7.5 to 8.5, Appendix V L.

Related substances

Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.

(1) Dilute a suitable volume of the oral solution with *water* to contain the equivalent of 0.75% w/v of hydrocortisone.
(2) 1.0% w/v of *hydrocortisone sodium phosphate BPCRS* in *methanol*.
(3) Equal volumes of solutions (1) and (2).
(4) 0.020% w/v of *hydrocortisone BPCRS* in *methanol*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel* GF_{254}.
(b) Use the mobile phase described below.
(c) Apply 2 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, allow it to dry in air for 5 minutes and examine under *ultraviolet light (254 nm)*.

MOBILE PHASE

1.2 volumes of *water*, 8 volumes of *methanol*, 15 volumes of *ether* and 77 volumes of *dichloromethane*.

SYSTEM SUITABILITY

The test is not valid unless the principal spot in the chromatogram obtained with solution (3) appears as a single compact spot.

LIMITS

Any *secondary spot* in the chromatogram obtained with solution (1) is not more intense than the spot in the chromatogram obtained with solution (4) (3%).

ASSAY

Dilute a volume of the oral solution containing the equivalent of 20 mg of hydrocortisone to 100 mL with *water*. To 5 mL add 15 mL of *water*, 2.5 g of *sodium chloride* and 0.5 mL of *hydrochloric acid* and extract with three 25-mL quantities of *chloroform*. Wash each chloroform layer with the same 1 mL quantity of 0.1M *hydrochloric acid*, add the washings to the aqueous solution and discard the chloroform. Extract the aqueous solution with two 10-mL quantities of *tributyl orthophosphate*, discard the aqueous phase and extract the combined tributyl phosphate solutions with two 25-mL quantities of a solution containing 10% w/v of *sodium chloride* and 1% w/v of *anhydrous disodium hydrogen orthophosphate*. Filter the extracts successively through absorbent cotton and wash the filter with 10 mL of the chloride–phosphate solution. Dilute the combined filtrates to 100 mL with the chloride–phosphate solution and measure the *absorbance* of the resulting solution at the maximum at 248 nm, Appendix II B, using in the reference cell a solution prepared in the same manner but using 20 mL of a solution containing 2.5 g of *sodium chloride* and 0.5 mL of *hydrochloric acid* and beginning at the words ‘Extract the aqueous solution …’. Calculate the content of hydrocortisone sodium phosphate as $C_{21}H_{30}O_5$ taking 447 as the value of A (1%, 1 cm) at the maximum at 248 nm.

STORAGE

Hydrocortisone Sodium Phosphate Oral Solution should be protected from light. The oral solution should not be allowed to freeze.

LABELLING

The strength is stated in terms of the equivalent amount of hydrocortisone in a suitable dose-volume.