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

Hydrocortisone Sodium Succinate Injection

General Notices

Action and use

Corticosteroid.

DEFINITION

Hydrocortisone Sodium Succinate Injection is a sterile solution of Hydrocortisone Sodium Succinate in Water for Injections. It is prepared by dissolving Hydrocortisone Sodium Succinate for Injection in the requisite amount of Water for Injections immediately before use.

The injection complies with the requirements stated under Parenteral Preparations.

STORAGE

Hydrocortisone Sodium Succinate Injection deteriorates on storage and should be used immediately after preparation.

HYDROCORTISONE SODIUM SUCCINATE FOR INJECTION

DEFINITION

Hydrocortisone Sodium Succinate for Injection is a sterile material prepared from Hydrocortisone Hydrogen Succinate with the aid of a suitable alkali. It may contain excipients. It is supplied in a sealed container.

The contents of the sealed container comply with the requirements for Powders for Injections or Infusions stated under Parenteral Preparations and with the following requirements.

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

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. The *infrared absorption spectrum*, Appendix II A, is concordant with the *reference spectrum* of hydrocortisone sodium succinate *(RS 180)*.
B. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions in 1 volume of *methanol* and 9 volumes of *dichloromethane*.
(1) 0.1% w/v solution of the contents of the sealed container.
(2) 0.1% w/v of *hydrocortisone hydrogen succinate BPCRS*.
(3) 0.1% w/v each of *hydrocortisone hydrogen succinate BPCRS* and *methylprednisolone hydrogen succinate EPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel GF_{254}*.
(b) Use the mobile phase as described below.
(c) Apply 5 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, allow to dry in air and examine in daylight and under *ultraviolet light (365 nm)*.

MOBILE PHASE

1 volume of *anhydrous formic acid*, 10 volumes of *absolute ethanol* and 150 volumes of *dichloromethane*.

SYSTEM SUITABILITY

The test is not valid unless, by each method of visualisation, the chromatogram obtained with solution (3) shows two spots which may not be completely separated.

CONFIRMATION

By each method of visualisation, the principal spot in the chromatogram obtained with solution (1) corresponds in position to that in the chromatogram obtained with solution (2).

TESTS

Acidity or alkalinity

pH of a solution containing the equivalent of 5% w/v of hydrocortisone, 6.5 to 8.0, Appendix V L.

Related substances

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

(1) Dissolve a sufficient quantity of the contents of the sealed container in a mixture of equal volumes of *acetonitrile* and *water* to produce a solution containing the equivalent of 0.25% w/v of hydrocortisone.
(2) Dilute 2 volumes of solution (1) to 100 volumes with a mixture of equal volumes of *acetonitrile* and *water*.
(3) Dilute 1 volume of a 0.035% w/v solution of *hydrocortisone BPCRS* in *acetonitrile* to 2 volumes with *water*.
(4) Dilute a solution containing 0.04% w/v each of *hydrocortisone hydrogen succinate BPCRS* and *dexamethasone BPCRS* in *acetonitrile* with an equal volume of *water*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Hypersil ODS 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 20 µL of each solution.
(g) For solution (1) allow the chromatography to proceed for twice the retention time of the principal peak.

MOBILE PHASE

330 volumes of *acetonitrile*, 600 volumes of *water* and 1 volume of *orthophosphoric acid* which is allowed to equilibrate and then diluted to 1000 volumes with *water*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution factor* between the peaks corresponding to dexamethasone and hydrocortisone hydrogen succinate is at least 5.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to hydrocortisone is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (7%);

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

Uniformity of content

The content of hydrocortisone in each of 10 individual containers as determined in the Assay is not less than 92.5% and not more than 107.5% of the content of hydrocortisone stated on the label, except that in one container the weight may be not less than 85.0% and not more than 115.0% of the stated content.

ASSAY

Dissolve the contents of a sealed container in sufficient *water* to produce a solution containing the equivalent of 0.001% w/v of hydrocortisone. Measure the *absorbance* of the resulting solution at the maximum at 248 nm, Appendix II B, and calculate the content of $C_{21}H_{30}O_5$ taking 449 as the value of A(1%, 1 cm) at the maximum at 248 nm. Repeat the procedure with a further nine sealed containers and calculate the average content of $C_{21}H_{30}O_5$ per container from the ten individual results thus obtained.

LABELLING

The label of the sealed container states the quantity of hydrocortisone sodium succinate contained in it in terms of the equivalent amount of hydrocortisone.