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

Cefalexin Oral Suspension

General Notices

Action and use

Cephalosporin antibacterial.

DEFINITION

Cefalexin Oral Suspension is a suspension of Cefalexin Monohydrate in a suitable flavoured vehicle. It is prepared by dispersing the dry ingredients in the specified volume of Water just before issue for use.

The dry ingredients comply with the requirements for Powders and Granules for Oral Solutions and Oral Suspensions stated under Oral Liquids.

Content of anhydrous cefalexin, $C_{16}H_{17}N_3O_4S$

When freshly constituted, not more than 120.0% of the stated amount. When stored at the temperature and for the period stated on the label during which the Oral Suspension may be expected to be satisfactory for use, not less than 80.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Shake a quantity of the oral suspension containing the equivalent of 0.2 g of anhydrous cefalexin with 70 mL of *methanol*, filter, evaporate to dryness and dissolve the residue in sufficient 0.5M *hydrochloric acid* to produce 50 mL.
(2) 0.4% w/v of *cefalexin BPCRS* in a mixture of equal volumes of *methanol* and 0.067M *mixed phosphate buffer pH 7.0*.
(3) 0.4% w/v of each of *cefalexin BPCRS* and *cefradine BPCRS* in a mixture of equal volumes of *methanol* and 0.067M *mixed phosphate buffer pH 7.0*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silanised silica gel HF_{254}*.
(b) Use the mobile phase as described below.
(c) Apply 1 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, allow it to dry and examine under *ultraviolet light (254 nm)*.

MOBILE PHASE

15 volumes of *acetone* and 85 volumes of a 15.4% w/v solution of *ammonium acetate*, previously adjusted to pH 6.2 with 5 M *acetic acid*.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) shows two clearly separated spots.

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) is similar in position and size to that in the chromatogram obtained with solution (2).

B. In the Assay, the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2).

TESTS

Related substances

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

(1) Shake a quantity of the oral suspension containing 0.1g of anhydrous cefalexin with 50 mL of *water* for 30 minutes, dilute to 100 mL using mobile phase A and filter.
(2) Mix 1 volume of a solution containing 0.1% w/v *7-aminodesacetoxycephalosporanic acid BPCRS* (impurity B) in solution A, with 1 volume of a solution containing 0.1% w/v *D-phenylglycine* (impurity A) in mobile phase A. Dilute to 100 volumes.
(3) 0.001% w/v each of *dimethylformamide* and *dimethylacetamide*.
(4) Mix 1 volume of solution (1) with 1 volume of a solution containing 0.1% w/v *cefotaxime sodium EPCRS* in mobile phase A and dilute to 100 volumes.
(5) Dilute 1 volume of solution (2) to 10 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) packed with *spherical octadecylsilyl silica gel for chromatography* (5 µm) (ACE 5 C18 is suitable).
(b) Use gradient 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 220 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Mobile phase A phosphate buffer solution pH 5.0.

Mobile phase B *methanol R2*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-1	98	2	isocratic
1-20	98→70	2→30	linear gradient
20-23	70	30	isocratic
23-24	70→98	30→2	linear gradient
24-30	98	2	re-equilibration

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to cefalexin (retention time about 12 minutes) are: impurity A, about 0.10; impurity B, about 0.13; cefotaxime, about 1.1.

SYSTEM SUITABILITY

The test is not valid unless:

in the chromatogram obtained with solution (2), the *resolution* between the peaks due to impurity A and impurity B is at least 2.0 and;

in the chromatogram obtained with solution (4), the *resolution* between the peaks due to cefalexin and cefotaxime is at least 1.5.

LIMITS

Identify any peak due to dimethylformamide and dimethylacetamide in the chromatogram obtained with solution (1) using the chromatogram obtained with solution (3).

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity B is not greater than the area of the peak due to impurity B in the chromatogram obtained with solution (2) (1%);

the area of any other *secondary peak* is not greater than the area of the peak due to impurity A in the chromatogram obtained with solution (2) (1%);

the sum of the areas of any *secondary peaks* is not greater than 3 times the area of the peak due to impurity A in the chromatogram obtained with solution (2) (3%).

Disregard any peaks due to dimethylformamide and dimethylacetamide and any peaks with an area less than the area of the peak due to impurity A in the chromatogram obtained with solution (5) (0.1%).

ASSAY

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

(1) Shake a weighed quantity of the oral suspension containing the equivalent of 0.25 g of anhydrous cefalexin with 100 mL of *water* for 30 minutes. Add sufficient *water* to produce 500 mL and filter.
(2) 0.05% w/v of *cefalexin BPCRS*.
(3) 0.01% w/v of each of *cefalexin BPCRS* and *cefradine BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Nucleosil C18 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 254 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

2 volumes of *methanol*, 5 volumes of *acetonitrile*, 10 volumes of a 1.36% w/v solution of *potassium dihydrogen orthophosphate* and 83 volumes of *water*.

SYSTEM SUITABILITY

The Assay is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks corresponding to cefalexin and cefradine is at least 4.0.

Inject solution (2) six times. The Assay is not valid unless the relative standard deviation of the area of the principal peak is at most 1.0%.

DETERMINATION OF CONTENT

Determine the *weight per mL* of the oral suspension, Appendix V G, and calculate the content of $C_{16}H_{17}N_3O_4S$, weight in volume, using the declared content of $C_{16}H_{17}N_3O_4S$ in *cefalexin BPCRS*.

Repeat the procedure using a portion of the oral suspension that has been stored at the temperature and for the period stated on the label during which it may be expected to be satisfactory for use.

STORAGE

The Oral Suspension should be stored at the temperature and used within the period stated on the label.

LABELLING

The quantity of active ingredient is stated in terms of the equivalent amount of anhydrous cefalexin.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Cefalexin Monohydrate.