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

Flucloxacillin Infusion

General Notices

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

Action and use

Penicillin antibacterial.

DEFINITION

Flucloxacillin Infusion is a sterile solution containing Flucloxacillin Sodium Monohydrate and a suitable buffer. It is supplied as a ready-to-use solution.

The infusion complies with the requirements stated under Parenteral Preparations and with the following requirements. Where appropriate, the infusion also complies with the requirements stated under Unlicensed Medicines.

Content of flucloxacillin, $C_{19}H_{17}ClFN_3O_5S$

90.0 to 105.0% of the stated amount.

CHARACTERS

A clear, colourless solution.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Dilute a volume of the infusion with sufficient *phosphate buffer pH 7.0* to produce a solution containing the equivalent of 0.25% w/v of flucloxacillin.
(2) 0.25% w/v of *flucloxacillin sodium BPCRS* in *phosphate buffer pH 7.0*.
(3) 0.25% w/v of each of *cloxacillin sodium BPCRS*, *dicloxacillin sodium BPCRS* and *flucloxacillin sodium BPCRS* in *phosphate buffer pH 7.0*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a *TLC silica gel silanised plate* (Merck silanised silica gel 60 plates are suitable).
(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 in air, expose to iodine vapour until the spots appear and examine in daylight.

MOBILE PHASE

30 volumes of *acetone* and 70 volumes of a 15.4% w/v solution of *ammonium acetate* adjusted to pH 5.0 with *glacial acetic acid* .

SYSTEM SUITABILITY

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

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) is similar in position, colour 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 principal peak in the chromatogram obtained with solution (2).

TESTS

Acidity or alkalinity

pH, 5.5 to 7.5, Appendix V L.

Related substances

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

(1) Dilute a volume of the infusion with sufficient of the mobile phase to produce a solution containing the equivalent of 0.1% w/v of flucloxacillin.
(2) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase.
(3) Dilute 1 volume of solution (2) to 10 volumes with the mobile phase.
(4) 0.01% w/v of each of *cloxacillin sodium BPCRS* and *flucloxacillin sodium BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Hypersil 5 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 225 nm.
(f) Inject 20 µL of each solution.
(g) For solution (1), allow the chromatography to proceed for six times the retention time of the principal peak.

MOBILE PHASE

25 volumes of *acetonitrile* and 75 volumes of a 0.27% w/v solution of *potassium dihydrogen orthophosphate* adjusted to pH 5.0 with 2M *sodium hydroxide*.

When the chromatograms are recorded under the prescribed conditions, the retention time of flucloxacillin is about 12 minutes and the relative retention of cloxacillin is about 0.8.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution* between the peaks due to cloxacillin and flucloxacillin is at least 2.5.

LIMITS

In the chromatogram obtained with solution (1):

the area of any *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1%);

the sum of the areas of any *secondary peaks* is not greater than five times the area of the principal peak in the chromatogram obtained with solution (2) (5%).

Disregard any peak with an area less than half the area of the principal peak in the chromatogram obtained with solution (3) (0.05%).

Bacterial endotoxins

Dilute the infusion with *water BET* to contain the equivalent of 9 mg of flucloxacillin per mL (solution A). The endotoxin limit concentration of solution A is 3.5 IU per mL, Appendix XIV C.

ASSAY

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

(1) Dilute a volume of the infusion with sufficient of the mobile phase to produce a solution containing the equivalent of 0.1% w/v of flucloxacillin; dilute 1 volume of the resulting solution to 10 volumes with the mobile phase.
(2) 0.011% w/v of *flucloxacillin sodium BPCRS* in the mobile phase.
(3) 0.01% w/v of each of *cloxacillin sodium BPCRS* and *flucloxacillin sodium BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The Assay is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to cloxacillin and flucloxacillin is at least 2.5.

DETERMINATION OF CONTENT

Calculate the content of $C_{19}H_{17}ClFN_3O_5S$ in the infusion using the declared content of $C_{19}H_{16}ClFN_3NaO_5S$ in *flucloxacillin sodium BPCRS*. Each mg of $C_{19}H_{16}ClFN_3NaO_5S$ is equivalent to 0.9538 mg of $C_{19}H_{17}ClFN_3O_5S$.

STORAGE

Flucloxacillin Infusion should be stored at a temperature of 2° to 8°.

LABELLING

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