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

Bupivacaine Injection

General Notices

This monograph does not apply to formulations where Bupivacaine Hydrochloride is encapsulated in liposomes.

Action and use

Injection for local anaesthesia.

DEFINITION

Bupivacaine Injection is a sterile solution of Bupivacaine Hydrochloride in Water for Injections.

The injection complies with the requirements stated under Parenteral Preparations and with the following requirements.

Content of anhydrous bupivacaine hydrochloride, $C_{18}H_{28}N_2O,HCl$

95.0 to 105.0% of the stated amount.

CHARACTERISTICS

A colourless or almost colourless solution.

IDENTIFICATION

To a volume of the injection containing the equivalent of 25 mg of anhydrous bupivacaine hydrochloride add 2 mL of 13.5M *ammonia*, shake and filter. Wash the precipitate with *water* and dry under vacuum at 60° for 16 hours. The *infrared absorption spectrum* of the dried residue, Appendix II A, is concordant with the *reference spectrum* of bupivacaine *(RS 034)*.

TESTS

Acidity

pH, 4.0 to 6.5, Appendix V L.

Related substances

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

(1) Dilute a volume of the injection, if necessary, to produce a solution containing the equivalent of 0.1% w/v of anhydrous bupivacaine hydrochloride.
(2) Dilute 1 volume of solution (1) to 200 volumes.
(3) 0.00002% w/v of *2,6-dimethylaniline* (impurity F).
(4) 0.002% w/v each of *bupivacaine impurity B EPCRS* and *bupivacaine impurity E EPCRS*.
(5) Dilute 1 volume of solution (2) to 5 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped ethylene-bridged octadecylsilyl silica gel* (5 µm) (X-Bridge BEH C18 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 240 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

40 volumes of 0.02M *potassium dihydrogen orthophosphate*, adjusted to pH 8.0 with *sodium hydroxide* and 60 volumes of *acetonitrile*.

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to bupivacaine (retention time about 11 minutes) are: impurity E, about 0.25; impurity B, about 0.3 and impurity F, about 0.4.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution* between the peaks due to impurity E and impurity B is at least 1.5.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity B is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the area of any peak corresponding to impurity F is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (0.02%);

the area of any other *secondary peak* is not greater than 0.4 times the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of any *secondary peaks*, excluding any peak due to impurity F, is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (1%).

Disregard any peak, excluding any peak due to impurity F, with an area less than the area of the principal peak in the chromatogram obtained with solution (5) (0.1%).

ASSAY

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

(1) Dilute a volume of the injection, if necessary, to produce a solution containing the equivalent of 0.05% w/v of anhydrous bupivacaine hydrochloride.
(2) 0.05% w/v of *bupivacaine hydrochloride BPCRS*.
(3) 0.002% w/v each of *bupivacaine impurity B EPCRS* and *bupivacaine impurity E EPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity E and impurity B is at least 1.5.

DETERMINATION OF CONTENT

Calculate the content of $C_{18}H_{28}N_2O$,HCl in the injection using the declared content of $C_{18}H_{28}N_2O$,HCl in *bupivacaine hydrochloride BPCRS*.

LABELLING

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

IMPURITIES

The impurities limited by the requirements of this monograph include impurities B, E and F listed under Bupivacaine Hydrochloride.