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

Lidocaine and Adrenaline Injection / Lidocaine and Epinephrine Injection

General Notices

Action and use

Local anaesthetic + class I antiarrhythmic; adrenoceptor agonist.

DEFINITION

Lidocaine and Adrenaline Injection is a sterile solution of Lidocaine Hydrochloride Monohydrate and Adrenaline Acid Tartrate in Water for Injections.

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

Content of lidocaine hydrochloride monohydrate, $C_{14}H_{22}N_2O,HCl,H_2O$

95.0 to 105.0% of the stated amount.

Content of adrenaline, $C_9H_{13}NO_3$

87.5 to 112.5% of the stated amount.

CHARACTERISTICS

A colourless solution.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions in *water*.
(1) Dilute a quantity of the injection, if necessary, to produce a solution containing 0.2% w/v of Lidocaine Hydrochloride Monohydrate.
(2) 0.2% w/v of *lidocaine hydrochloride BPCRS*.
(3) 0.2% w/v of each of *lidocaine hydrochloride BPCRS* and *bupivacaine hydrochloride BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a silica gel precoated plate (Merck silica gel 60G plates are suitable).
(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, dry it in a current of cold air, heat at 110° for 1 hour, place the hot plate in a tank of chlorine gas prepared by the addition of *hydrochloric acid* to a 5% w/v solution of *potassium permanganate* contained in a beaker placed in the tank and allow to stand for 2 minutes. Dry the plate in a current of cold air until an area of the plate below the line of application gives at most a very faint blue colour with a 0.5% w/v solution of *potassium iodide* in *starch mucilage*; avoid prolonged exposure to cold air. Spray the plate with a 0.5% w/v solution of *potassium iodide* in *starch mucilage*.

MOBILE PHASE

5 volumes of *methanol* and 95 volumes of *dichloromethane*.

SYSTEM SUITABILITY

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

CONFIRMATION

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

B. In the Assay for adrenaline, the chromatogram obtained with solution (1) shows a peak with the same retention time as the principal peak in the chromatogram obtained with solution (2).

Acidity

pH, 3.0 to 4.5, Appendix V L.

ASSAY

For lidocaine hydrochloride monohydrate

Make a quantity containing 0.1 g of Lidocaine Hydrochloride Monohydrate alkaline with 2M *sodium hydroxide* and extract with three 20-mL quantities of *chloroform*, washing each extract with the same 10 mL of *water*. Filter the washed extracts through a filter paper moistened with *chloroform* and wash the filter with 10 mL of *chloroform*. Add the washings to the filtrate and carry out Method I for *non-aqueous titration*, Appendix VIII A, using *0.02M perchloric acid VS* as titrant and *crystal violet solution* as indicator. Each mL of *0.02M perchloric acid VS* is equivalent to 5.776 mg of $C_{14}H_{22}N_2O,HCl,H_2O$.

For adrenaline

Prepare a solution by adding 8.0 g of *tetramethylammonium hydrogen sulfate*, 2.2 g of *sodium heptanesulfonate* and 2 mL of 0.1M *disodium edetate* to a mixture of 900 mL of *water* and 100 mL of *methanol*, adjust the pH to 3.5 using 1M *sodium hydroxide* and filter through glass microfibre paper under reduced pressure (solution A).

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

(1) Dilute the injection with solution A, if necessary, to contain 0.0005% w/v of adrenaline and dilute 5 mL of the resulting solution to 10 mL with solution A.
(2) Dilute 5 mL of a 0.001% w/v solution of *adrenaline acid tartrate BPCRS* to 10 mL with solution A.
(3) Mix 5 mL of solution (2) with 5 mL of a 0.001% w/v solution of *noradrenaline acid tartrate* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 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 2 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 205 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

A solution prepared by adding 4.0 g of *tetramethylammonium hydrogen sulfate*, 1.1 g of *sodium heptanesulfonate* and 2 mL of 0.1M *disodium edetate* to a mixture of 950 mL of *water* and 50 mL of *methanol* and adjusting the pH to 3.5 with 1M *sodium hydroxide*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the two principal peaks is at least 2.0.

DETERMINATION OF CONTENT

Calculate the content of $C_9H_{13}NO_3$ in the injection using the declared content of $C_9H_{13}NO_3$ in *adrenaline acid tartrate BPCRS*.

STORAGE

Lidocaine and Adrenaline Injection should be protected from light.

LABELLING

The quantity of Adrenaline Acid Tartrate is stated in terms of the equivalent amount of adrenaline (epinephrine).