Water for injections (Aqua pro injectione)

2020-01

Description. A clear and colourless liquid; odourless.

Category. Solvent.

Labelling. The designation on the container should indicate that water for injections is non-sterile.

Storage. Water for injections should be kept in a well-closed container.

Additional information. *CAUTION*: Water for injections is not sterile. It is not a final dosage form, but an intermediate product in the manufacture of parenteral preparations, either for bulk injectable solutions or for "Sterile water for injections".

Requirements

Definition. Water for injections is pyrogen-free. It contains no added substance.

Manufacture. Water for injections is obtained from drinking water[1] or Purified water by distillation in an apparatus of which the parts in contact with the liquid are of neutral glass, quartz, or suitable metal and fitted with an effective device to prevent entrainment of droplets. The first portion of the distillate obtained when the apparatus begins to function is discarded. The distillate is collected and stored in conditions designed to prevent growth of microorganisms and to avoid any other contamination.

[1] WHO Guidelines for drinking-water quality (WHO, Geneva, 2017, web link: https://www.who.int/water_sanitation_health/publications/drinking-water-quality-guidelines-4-including-1st-addendum/en/)

Other technologies proven to be equal or superior to distillation, and meeting the pharmacopoeial requirements, can be used. Details on specific points to be conserved are outlined in the guidance on *Production of water for injection by means other than distillation* (WHO Expert Committee on Specifications for Pharmaceutical Preparations: fifty-fourth report, WHO Technical Report Series, No. 1025, 2020, Annex 3).

Heavy metals. Use 40 mL, adjust the pH with acetic acid (~60 g/l) PbTS, and proceed as described under 2.2.3 Limit test for heavy metals, procedure 1; determine the heavy metals content according to Method A, allowing to stand for 10 minutes; the colour is not darker than that of 40 mL of the same untreated Water for injections, the pH of which has been similarly adjusted.

Ammonia. Transfer 50 mL to a comparison tube, add 2 mL of alkaline potassio-mercuric iodide TS, and observe down the vertical axis of the tube in diffused light against a white background; the colour produced is not more intense than that of 50 mL of ammonia-free water R with the addition of 2 mL of dilute ammonium chloride TS.

Calcium and magnesium. To 100 mL add 2 mL of ammonium chloride buffer, pH 10.0, TS, 50 mg of mordant black 11 R, and 0.5 mL of disodium edetate (0.01 mol/l) VS; a pure blue colour is produced.

Carbon dioxide. To 25 mL add 25 mL of calcium hydroxide TS; it remains clear.

Chlorides. To 10 mL add 1 mL of silver nitrate (40 g/l) TS and allow to stand for 5 minutes; it remains clear and colourless.

Nitrates. Carefully superimpose 5 mL on 5 mL of diphenylamine/sulfuric acid TS, ensuring that the liquids do not mix; no blue colour appears at the interface of the two liquids.

Sulfates. To 10 mL add 1 mL of barium chloride (50 g/l) TS and allow to stand for 5 minutes; it remains clear and colourless.

Oxidizable matter. To 100 mL add 10 mL of sulfuric acid (~100 g/l) TS and 0.2 mL of potassium permanganate (0.02 mol/l) VS and boil for 3 minutes; the colour is not completely destroyed.

Non-volatile residue. Boil 500 mL on a hot plate or over a flame until the volume is reduced to about 50 mL, then evaporate on a water-bath to dryness. Dry the residue for 1 hour at 105 °C; not more than 5 mg (0.01 mg/mL).

Acidity or alkalinity. To 10 mL add 2 drops of methyl red/ethanol TS; no red colour appears. To a further 10 mL portion add 5 drops of bromothymol blue/ethanol TS; no blue colour develops.

Bacterial endotoxins. Carry out the test as described under 3.4 Test for bacterial endotoxins; contains not more than 0.25 IU of endotoxin RS per mL.