Quinine dihydrochloride injection (Quinini dihydrochloridi injectio)

2015-01

Description. Quinine dihydrochloride injection is an almost colourless to light yellow solution.

Category. Antimalarial drug.

Storage. Quinine dihydrochloride injection should be protected from light.

Labelling. The designation on the container should state that the solution must be diluted to a strength not exceeding 30 mg per mL before administration.

Additional information. Care must be taken to ensure slow intravenous administration.

Strength in the current WHO Model list of essential medicines (EML): 300 mg/mL.

Requirements

Complies with the monograph for *Parenteral preparations*.

Definition. Quinine dihydrochloride injection is usually a concentrated, sterile solution of quinine dihydrochloride in water for injections. The solution is sterilized by "Heating in an autoclave" or any other suitable method (see *5.8 Methods of sterilization*).

Quinine dihydrochloride injection contains not less than 95.0% and not more than 105.0% of the amount of $C_{20}H_{24}N_2O_2,2HCl$ stated on the label.

Identity tests

A. Dilute a volume of the injection to a concentration of 0.5 mg of Quinine dihydrochloride per mL. To 10 mL of this solution add 0.05 mL of sulfuric acid (~100 g/L) TS; a strong blue fluorescence is produced. (Keep the solution for test B.)

B. To the solution prepared for test A add 0.15 mL of bromine TS1 and 1 mL of ammonia (~100 g/L) TS; an emerald-green colour is produced.

C. The injection yields reaction A described under *2.1 General identification tests* as characteristic of chlorides.

pH value. pH of the injection, 1.5–3.0.

Related cinchona alkaloids. Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography using silica gel R1 as the coating substance and a mixture of 10 volumes of chloroform R, 8 volumes of acetone R and 2.5 volumes of diethylamine R as the mobile phase. Apply separately to the plate 5 µL of each of the following four solutions. For solution (A) dilute a volume of the injection with ethanol (~750 g/L) TS to obtain a concentration equivalent to 10 mg of Quinine dihydrochloride per mL. For solution (B) dissolve 12.5 mg of quinine R in 50 mL of ethanol (~750 g/L) TS. For solution (C) dissolve 12.5 mg of cinchonidine R in 50 mL of ethanol (~750 g/L) TS. For solution (D) mix 1 mL of solution B with 1 mL of solution C. After removing the plate from the chromatographic chamber allow it to dry in a current of air for 15 minutes and repeat the development. Heat the plate at 105 °C for 30 minutes, allow to cool, spray with potassium iodoplatinate TS and examine the chromatogram in daylight.

Any spot obtained with solution A, other than the principal spot, is not more intense than that obtained with solution B or solution C. If any spot is obtained with solution A immediately below the principal spot it is disregarded. The test is valid only if the chromatogram obtained with solution D shows two distinctly separated spots.

Limit of dihydroquinine. Dilute an accurately measured volume of the injection equivalent to 0.2 g of Quinine dihydrochloride with water to 20 mL. Add 0.5 g of potassium bromide R, 15 mL of hydrochloric acid (~70 g/L) TS and 0.1 mL of methyl red/ethanol TS. Titrate with potassium bromate (0.0167 mol/L) VS until a yellow colour is produced. Add 0.5 g of potassium iodide R in 200 mL of water, stopper the flask and allow to stand in the dark for 5 minutes. Titrate the iodine liberated by excess potassium bromate in the solution with sodium thiosulfate (0.1 mol/L) VS, adding 2 mL of starch TS when the solution has reached a light yellow colour. Repeat the procedure without the injection solution being examined and make any necessary corrections.

Each mL of potassium bromate (0.0167 mol/L) VS is equivalent to 19.87 mg of $C_{20}H_{24}N_2O_2,2HCl$. Express the results of both the above determination and the assay in percentages. The difference between the two is not more than 10%.

Assay. Transfer an accurately measured volume of the injection equivalent to about 0.5 g of Quinine dihydrochloride to a separator and add 20 mL of water and 5 mL of sodium hydroxide (~200 g/L) TS. Extract with successive quantities, each of 10 mL, of chloroform R until complete extraction of the alkaloid is effected. Wash each extract with the same two quantities, each of 5 mL, of water. Evaporate the combined chloroform layer, dissolve the residue in 50 mL of acetic anhydride R, add 10 mL of glacial acetic acid R and titrate with perchloric acid (0.1 mol/L) VS as described under *2.6 Non-aqueous titration*, method A.

Each mL of perchloric acid (0.1 mol/L) VS is equivalent to 19.87 mg of $C_{20}H_{24}N_2O_2,2HCl$.

Bacterial endotoxins. Carry out the test as described under *3.4 Test for bacterial endotoxins*; contains less than 1.0 IU of endotoxin per mg Quinine dihydrochloride.