Prednisolone sodium succinate for injection (Prednisoloni et natrii succinatis ad injectionem)

Description. A white powder or friable lumps; odourless.

Category. Adrenal hormone.

Labelling. The designation on the container should state the dose as the equivalent amount of prednisolone. It should also state the nature of the buffering agent. Expiry date.

Additional information. Available strengths: 20 mg, 25 mg in vials.

Requirements

The powder for injections and the reconstituted solution for injections comply with the monograph for Parenteral preparations.

Definition. Prednisolone sodium succinate powder for injections is a sterile powder of prednisolone sodium succinate prepared from prednisolone succinate with the aid of sodium hydroxide or sodium carbonate. Prednisolone sodium succinate powder for injections usually contains a suitable buffering agent. The powder is sterilized by a suitable method (see 5.8 Methods of sterilization).

The container of Prednisolone sodium succinate powder for injections contains not less than 90.0% and not more than 110.0% of the equivalent amount of prednisolone C\textsubscript{21}H\textsubscript{28}O\textsubscript{5} stated on the label.

Identity tests

- Either tests A and D or tests B, C and D may be applied.

A. Dissolve a quantity of the powder for injections equivalent to 40 mg of prednisolone in 20 mL of water, add 3 mL of hydrochloric acid (~70 g/l) TS, and extract with 25 mL of chloroform R. Filter the extract into a beaker, evaporate to dryness on a water-bath, and dry the residue at 60 °C for 1 hour. Carry out the examination as described under 1.7 Spectrophotometry in the infrared region. The infrared absorption spectrum is concordant with the spectrum obtained from prednisolone succinate RS or with a reference spectrum of prednisolone succinate.

B. Carry out the test as described under 1.14.1 Thin-layer chromatography using silica gel R4 as the coating substance and 6 volumes of 1-butanol R, 2 volumes of acetic anhydride R and 2 volumes of water as the mobile phase, prepared immediately before use. Apply separately to the plate 5 μl of each of the following two solutions. For solution (A) dissolve a quantity of the powder for injections to obtain a concentration equivalent to 2 mg of prednisolone per mL. For solution (B) dissolve 28 mg of prednisolone succinate RS in 10 mL of water. After removing the plate from the chromatographic chamber allow it to dry in air until the odour of solvent is no longer perceptible, heat to 110 °C for 10 minutes and examine the chromatogram in ultraviolet light (254 nm). The principal spot obtained with solution A corresponds in position, appearance and intensity with that obtained with solution B.

C. To a quantity of the powder for injections equivalent to 2 mg of prednisolone add 2 mL of sulfuric acid (~1760 g/l) TS and allow to stand for 2 minutes; a red colour is produced.

D. Ignite a quantity of the powder for injections equivalent to 20 mg of prednisolone and dissolve the residue in acetic acid (~60 g/l) TS. The solution yields reaction B described under 2.1 General identification tests as characteristic of sodium.

Clarity of solution. A solution containing a quantity of the powder for injections equivalent to 0.35 g of prednisolone in 10 mL of carbon-dioxide-free water R is clear. (Keep this solution for the "pH value").

Loss on drying. Dry the powder for injections at 60 °C under reduced pressure (not exceeding 0.6 kPa or 5 mm of mercury) over phosphorus pentoxide R for 3 hours; it loses not more than 20 mg/g.

pH value. pH of the solution prepared above for the test of clarity, 6.5–8.0.

Assay

Mix the contents of 10 containers and carry out the assay as described.

Dissolve a portion of the powder for injections equivalent to about 0.05 g of prednisolone, accurately weighed, in 5 mL of water and dilute with sufficient ethanol (~750 g/l) TS to produce 200 mL. Dilute 4 mL to 100 mL with ethanol (~750 g/l) TS. Transfer 20 mL of the resulting solution to a glass-stoppered 50 mL conical flask (solution A). Separately, dissolve 64 mg of prednisolone succinate RS, accurately weighed, in 100 mL of ethanol (~750 g/l) TS, add 5 mL of water and dilute with sufficient ethanol (~750 g/l) TS to produce 200 mL. Dilute 4 mL to 100 mL with ethanol (~750 g/l) TS. Transfer 20 mL of the resulting solution to a glass-stoppered 50 mL conical flask (solution B). To each flask containing solutions A and B and a third one containing 20 mL of ethanol (~750 g/l) TS to serve as a blank, add 2 mL of blue tetrazolium/ethanol TS, mix, then add 2 mL of tetrachloroammonium
hydroxide/ethanol TS, mix and allow to stand in the dark for 90 minutes.

Without delay measure the absorbance of solutions A and B against the blank using a suitable spectrophotometer at a maximum wavelength of about 525 nm.

Calculate the amount of \( C_{21}H_{28}O_5 \) in the substance being examined using the formula \( 5C(0.7827)(\frac{A_u}{A_s}) \), where \( C \) is the concentration in mg per mL of prednisolone succinate RS, 0.7827 is the ratio of the relative molecular mass of prednisolone to that of prednisolone succinate and \( A_u \) and \( A_s \) are the absorbances of solutions A and B, respectively.

**Bacterial endotoxins.** Carry out the test as described under 3.4 Test for bacterial endotoxin; contains not more than 5.8 IU of endotoxin RS per mg of prednisolone.