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Hydrocortisone Sodium Phosphate Injection

» Hydrocortisone Sodium Phosphate Injection is a sterile, buffered solution of Hydrocortisone Sodium Phosphate in Water for Injection. It contains the equivalent of not less than 90.0 percent and not more than 115.0 percent of the labeled amount of hydrocortisone ($C_{21}H_{30}O_5$).

Packaging and storage—Preserve in single-dose or multiple-dose containers, preferably of Type I glass.

USP Reference standards ⟨11⟩—

USP Hydrocortisone RS

USP Hydrocortisone Phosphate Triethylamine RS $C_{21}H_{31}O_8P \cdot C_6H_{15}N$ 543.64

Identification—

Change to read:

A: ▲*Spectroscopic Identification Tests* ⟨197⟩*, Ultraviolet-Visible Spectroscopy: 197U*▲ (CN 1-May-2020) —

Solution: 20 µg per mL, USP Hydrocortisone Phosphate Triethylamine RS being used to prepare the Standard solution.

Medium: water.

B: Place 5 mL of the *Assay preparation*, obtained as directed in the *Assay*, in a glass-stoppered, 50-mL tube, and add 5 mL of a solution prepared by dissolving 50 mg of alkaline phosphatase enzyme in 50 mL of *pH 9 buffer with magnesium* prepared as directed in the *Assay* under *Hydrocortisone Sodium Phosphate*. Allow to stand at room temperature for 2 hours, with occasional mixing, and extract with 25 mL of methylene chloride. Evaporate 15 mL of the methylene chloride extract on a steam bath to dryness, and dissolve the residue in 0.5 mL of methylene chloride. Apply 5 µL of this solution and 5 µL of a solution of USP Hydrocortisone RS in methylene chloride containing 300 µg per mL to a thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with a 0.25-mm layer of chromatographic silica gel mixture. Allow the spots to dry, and develop the chromatogram in a tank completely lined with filter paper, using a solvent system consisting of a mixture of 50 parts of chloroform, 50 parts of acetone, and 1 part of water, until the solvent front has moved about three-fourths of the length of the plate. Remove the plate, mark the solvent front, and dry. Spray the plate with dilute sulfuric acid (1 in 2), and heat at 105° until brown or black spots appear: the R_F value of the principal spot obtained from the solution under test corresponds to that obtained from the Standard solution.

Bacterial Endotoxins Test ⟨85⟩ —It contains not more than 1.25 USP Endotoxin Units per mg of hydrocortisone.

pH ⟨791⟩: between 7.5 and 8.5.

Particulate Matter in Injections ⟨788⟩: meets the requirements for small-volume injections.

Other requirements—It meets the requirements under *Injections and Implanted Drug Products* ⟨1⟩.

Assay—

Phenylhydrazine hydrochloride solution—Dissolve 65 mg of phenylhydrazine hydrochloride in 100 mL of dilute sulfuric acid (3 in 5), add 50 mL of isopropyl alcohol, and mix. Prepare this solution fresh daily.

Standard preparation—Dissolve a suitable quantity of USP Hydrocortisone Phosphate Triethylamine RS, accurately weighed, in water, and dilute quantitatively and stepwise with water to obtain a solution having a known concentration of about 110 µg per mL.

Assay preparation—Pipet a volume of Injection, equivalent to about 100 mg of hydrocortisone sodium phosphate, into a 100-mL volumetric flask, and dilute with water to volume. Pipet 10 mL of this solution into a separator, wash the solution with two 25-mL portions of methylene chloride, and discard the washings. Transfer the aqueous layer to a 100-mL volumetric flask, dilute with water to volume, and mix.

Procedure—Pipet 2 mL each of the *Standard preparation* and the *Assay preparation* into separate glass-stoppered, 50-mL conical flasks. To each flask, and to a similar flask containing 2.0 mL of water to provide a blank, add 10.0 mL of *Phenylhydrazine hydrochloride solution*, and mix. Place the flasks in a water bath maintained at a temperature of 60° for 2 hours, then cool the solutions to room temperature. Concomitantly determine the absorbances of the solutions from the *Assay preparation* and the *Standard preparation* at the wavelength of maximum absorbance at about 410 nm, with a suitable spectrophotometer, using the blank to set the instrument. Calculate the quantity, in mg, of $C_{21}H_{30}O_5$ in each mL of the Injection taken by the formula:

$$0.667(C/V)(A_U/A_S)$$

in which 0.667 is the ratio of the molecular weight of hydrocortisone to that of hydrocortisone phosphate triethylamine; *C* is the concentration, in µg per mL, of USP Hydrocortisone Phosphate Triethylamine RS in the *Standard preparation*; *V* is the volume, in mL, of Injection taken; and A_U and A_S are the absorbances of the solutions from the *Assay preparation* and the *Standard preparation*, respectively.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
HYDROCORTISONE SODIUM PHOSPHATE INJECTION	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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