Neomycin Sulfate and Dexamethasone Sodium Phosphate Ophthalmic Solution

DEFINITION

Neomycin Sulfate and Dexamethasone Sodium Phosphate Ophthalmic Solution is a sterile, aqueous solution of Neomycin Sulfate and Dexamethasone Sodium Phosphate. It contains the equivalent of NLT 90.0% and NMT 130.0% of the labeled amount of neomycin, and the equivalent of NLT 90.0% and NMT 115.0% of the labeled amount of dexamethasone phosphate ($C_{22}H_{30}FO_8P$). It may contain one or more suitable buffers, dispersants, and preservatives.

[NOTE—Where Neomycin Sulfate and Dexamethasone Sodium Phosphate Ophthalmic Solution is prescribed, without reference to the amount of neomycin or dexamethasone phosphate contained therein, a product containing 3.5 mg/mL of neomycin and 1.0 mg/mL of dexamethasone phosphate shall be dispensed.]

IDENTIFICATION

- **A. THIN-LAYER CHROMATOGRAPHIC IDENTIFICATION TEST ⟨201BNP⟩:** Meets the requirements for neomycin

Delete the following:

- **B. THIN-LAYER CHROMATOGRAPHY**

Buffer: 3.1 g/L of boric acid, 203 mg/L of magnesium chloride and 860 mg/L of sodium hydroxide in water
Solution A: 1 mg/mL of alkaline phosphatase enzyme in *Buffer*
Standard solution: 300 µg/mL of USP Dexamethasone RS in methylene chloride
Sample stock solution: Use the *Sample solution* prepared as directed in the *Assay* for *Dexamethasone Phosphate*.
Sample solution: Add 5 mL of Solution A to a glass stoppered 50-mL tube containing 5 mL of the Sample stock solution, incubate at 37° for 45 min, then add 25 mL of methylene chloride, and shake for 2 min. Evaporate 15 mL of the methylene chloride extract on a steam bath to dryness, and dissolve the residue in 1 mL of methylene chloride.
Chromatographic system
(See *Chromatography* ⟨621⟩, *Thin-Layer Chromatography*.)
Adsorbent: 0.25-mm layer of chromatographic silica gel
Application volume: 5 µL
Spray reagent: Dilute sulfuric acid (1 in 2)
Developing solvent system: Chloroform, acetone, and water (50:50:1)
Analysis
Samples: *Sample solution* and *Standard solution*
Apply the *Standard solution* and the *Sample solution* to the thin-layer chromatographic plate and allow the spots to dry. Develop the chromatogram using the *Developing solvent system* in a tank completely lined with filter paper, until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the developing tank, mark the solvent front, and allow the spots to dry. Spray the plate with *Spray reagent*, and heat at 105° until brown or black spots appear.
Acceptance criteria: The R_F value of the principal spot from the *Sample solution* corresponds to that from the *Standard solution*. (IRA 1-May-2015)

Add the following:

- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay* for *Dexamethasone Phosphate*. (IRA 1-May-2015)

ASSAY

- **NEOMYCIN**

(See *Antibiotics—Microbial Assays* ⟨81⟩.)
Analysis: Dilute an aliquot of Ophthalmic Solution with *Buffer B.3* to obtain a *Test Dilution* with a neomycin concentration that is nominally equivalent to the median level of the standard (1.0 µg/mL).
Acceptance criteria: 90.0%–130.0%

Change to read:

- **DEXAMETHASONE PHOSPHATE**

Solution A: 0.29 g/L of dibasic sodium phosphate
Solution B: 13.80 g/L of monobasic sodium phosphate
Mobile phase: Acetonitrile and *Solution B* (31:69)
Standard solution: 27 µg/mL of USP Dexamethasone Sodium Phosphate RS (IRA 1-May-2015) in *Solution A*. Pass through a filter of 1-µm or finer pore size.
Sample solution: Nominally 25 µg/mL of dexamethasone phosphate from Ophthalmic Solution in *Solution A* prepared as follows. Slowly dilute a portion of Ophthalmic Solution with *Solution A* to volume, mix, and pass through a suitable filter of 1-µm or finer pore size.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 254 nm
Column: 3.9-mm × 30-cm; 10-µm (IRA 1-May-2015) packing L1
Flow rate: 1.3 mL/min
Injection volume: 50 µL
System suitability
Sample: *Standard solution*
[NOTE—The retention time for dexamethasone phosphate is about 8.5 min.]
Suitability requirements (IRA 1-May-2015)
Relative standard deviation: NMT 2.0%
Analysis
Samples: *Sample solution* and *Standard solution*
Calculate the percentage of the labeled amount of dexamethasone phosphate ($C_{22}H_{30}FO_8P$) in each mL of the Ophthalmic Solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100 \quad \text{(IRA 1-May-2015)}$$

r_U = peak area from the *Sample solution*
r_S = peak area from the *Standard solution*
C_S = concentration of USP Dexamethasone Sodium Phosphate RS (IRA 1-May-2015) in the *Standard solution* (µg/mL)

C_U = nominal concentration of dexamethasone phosphate in the *Sample solution* (µg/mL)
M_{r1} = molecular weight of dexamethasone phosphate, 472.44
M_{r2} = molecular weight of dexamethasone sodium phosphate, 516.40 • (IRA 1-May-2015)

Acceptance criteria: 90.0%–115.0%

SPECIFIC TESTS

- **STERILITY TESTS ⟨71⟩:** Meets the requirements
- **pH ⟨791⟩:** 6.0–8.0

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers, and avoid exposure to excessive heat.

Change to read:

- **USP REFERENCE STANDARDS ⟨11⟩**
  • USP Dexamethasone Sodium Phosphate RS • (IRA 1-May-2015)
  USP Neomycin Sulfate RS