Neomycin Sulfate and Dexamethasone Sodium Phosphate Ophthalmic Ointment

DEFINITION

Neomycin Sulfate and Dexamethasone Sodium Phosphate Ophthalmic Ointment is a sterile ointment containing Neomycin Sulfate and Dexamethasone Sodium Phosphate. It contains the equivalent of NLT 90.0% and NMT 135.0% of the labeled amount of neomycin, and the equivalent of NLT 90.0% and NMT 110.0% of the labeled amount of dexamethasone phosphate ($C_{22}H_{30}FO_8P$).

[NOTE—Where Neomycin Sulfate and Dexamethasone Sodium Phosphate Ophthalmic Ointment is prescribed without reference to the quantity of neomycin or dexamethasone phosphate contained therein, a product containing 3.5 mg of neomycin and 0.5 mg of dexamethasone phosphate per g shall be dispensed.]

IDENTIFICATION

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

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. The pH of this solution is 9.0.
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: Transfer 5 mL of the *Solution A* to a glass-stoppered, 50-mL tube containing 5 mL of *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
Developing solvent system: Chloroform, acetone, and water (50:50:1)
Spray reagent: Dilute sulfuric acid (1 in 2)
Analysis
Samples: *Standard solution* and *Sample solution*
Apply the *Standard solution* and *Sample solution* to the 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⟩.)
Sample solution: Shake a weighed portion of Ophthalmic Ointment in a separator with about 50 mL of ether, and extract with four 20-mL portions of *Buffer B.3*. Combine the aqueous extracts, and dilute with *Buffer B.3* to a suitable volume.
Analysis: Proceed as directed in the chapter. Dilute the *Sample solution* with *Buffer B.3* to obtain a *Test Dilution* having a neomycin concentration that is nominally equivalent to the median level of the standard.
Acceptance criteria: 90.0%–135.0%

Change to read:

- **DEXAMETHASONE PHOSPHATE**

Buffer: 6.9 g/L of monobasic sodium phosphate
Mobile phase: Methanol and *Buffer* (52:48)
Diluent: Dissolve 0.29 g of dibasic sodium phosphate in 450 mL of water, and add 550 mL of alcohol.
Standard solution: 33 µg/mL of USP Dexamethasone Sodium Phosphate RS (IRA 1-May-2015) in *Diluent*. Prepare this solution freshly.
Sample solution: Nominally 30 µg/mL of dexamethasone phosphate, prepared as follows. Transfer a portion of Ophthalmic Ointment containing nominally 3 mg of dexamethasone phosphate to a suitable beaker. Add 65 mL of *Diluent*, and heat just to boiling. Pour the contents of the beaker into a separator containing 45 mL of isooctane. After shaking for 1 min, decant the lower layer into a 100-mL volumetric flask. Rinse the beaker with two 15-mL portions of *Diluent*, extracting the remaining isooctane in the separator with each portion, and decanting the lower layer from each extraction into the 100-mL volumetric flask. Dilute with *Diluent* to volume, and mix. Pass through a suitable filter.
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: 1.5 mL/min
Injection volume: 20 µL
System suitability
Sample: *Standard solution*
[NOTE—The retention time for dexamethasone phosphate is about 8.5 min.]
Suitability requirements
Relative standard deviation: NMT 1.5%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of dexamethasone phosphate ($C_{22}H_{30}FO_8P$) in the portion of Ophthalmic Ointment 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 response from the *Sample solution*
r_S = peak response 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%–110.0%

PERFORMANCE TESTS

- **MINIMUM FILL** ⟨**755**⟩**:** Meets the requirements

SPECIFIC TESTS

- **WATER DETERMINATION,** *Method I* ⟨**921**⟩
  Analysis: Use 20 mL of a mixture of toluene and methanol (7:3) in place of methanol in the titration vessel.
  Acceptance criteria: NMT 1.0%
- **STERILITY TESTS** ⟨**71**⟩**:** Meets the requirements
- **METAL PARTICLES IN OPHTHALMIC OINTMENTS** ⟨**751**⟩**:** Meets the requirements

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in collapsible ophthalmic ointment tubes.

Change to read:

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