Ophthalmic Ointment Monographs: Neomycin Sulfate and Dexamethasone Sodium Phosphate Ophthalmic Ointment

Type of Posting	Revision Bulletin
Posting Date	29–Jul–2016
Official Date	01–Aug–2016
Expert Committee	Chemical Medicines Monographs 1 to 6
Reason for Revision	Compliance

In accordance with the Rules and Procedures of the 2015-2020 Council of Experts, the Chemical Medicines Expert Committees 1 to 6 has revised the monographs listed below. The purpose of the revision is to replace the requirement to comply with the entire content of the USP general chapter *Ophthalmic Products—Quality Tests* <771> with a requirement to comply only with the subsection for *Particulate and Foreign Matter* in *Ophthalmic Products—Quality Tests* <771>, and with the section for *Container Content* for those monographs where the requirement for Minimum Fill was deleted.

- Atropine Sulfate Ophthalmic Ointment
- Bacitracin Ophthalmic Ointment
- Bacitracin Zinc and Polymyxin B Sulfate Ophthalmic Ointment
- Bland Lubricating Ophthalmic Ointment
- Chloramphenicol and Polymyxin B Sulfate Ophthalmic Ointment
- Chloramphenicol Ophthalmic Ointment
- Chlortetracycline Hydrochloride Ophthalmic Ointment
- Ciprofloxacin Ophthalmic Ointment
- Dexamethasone Sodium Phosphate Ophthalmic Ointment
- Erythromycin Ophthalmic Ointment
- Gentamicin and Prednisolone Acetate Ophthalmic Ointment
- Gentamicin Sulfate Ophthalmic Ointment
- Hydrocortisone Acetate Ophthalmic Ointment
- Idoxuridine Ophthalmic Ointment
- Neomycin and Polymyxin B Sulfates, Bacitracin Zinc, and Hydrocortisone Acetate Ophthalmic Ointment
- Neomycin and Polymyxin B Sulfates and Bacitracin Ophthalmic Ointment
- Neomycin and Polymyxin B Sulfates and Bacitracin Zinc Ophthalmic Ointment
- Neomycin and Polymyxin B Sulfates and Dexamethasone Ophthalmic Ointment
- Neomycin and Polymyxin B Sulfates Ophthalmic Ointment
- Neomycin and Polymyxin B Sulfates, Bacitracin Zinc, and Hydrocortisone Ophthalmic Ointment
- Neomycin and Polymyxin B Sulfates, Bacitracin, and Hydrocortisone Acetate Ophthalmic Ointment
- Neomycin Sulfate and Dexamethasone Sodium Phosphate Ophthalmic Ointment
- Neomycin Sulfate Ophthalmic Ointment
- Oxytetracycline Hydrochloride and Polymyxin B Sulfate Ophthalmic Ointment
- Sodium Chloride Ophthalmic Ointment
- Sulfacetamide Sodium and Prednisolone Acetate Ophthalmic Ointment
- Sulfacetamide Sodium Ophthalmic Ointment
- Tetracycline Hydrochloride Ophthalmic Ointment
- Tobramycin and Dexamethasone Ophthalmic Ointment
- Tobramycin Ophthalmic Ointment

The Revision Bulletins for the monographs listed above supersede the currently official version of these monographs. The Revision Bulletin will be incorporated in the First Supplement to USP 40–NF 35.

Should you have any questions, please contact Margareth R. C. Marques, M.Sc., Ph.D. (301-816-8106 or mrm@usp.org).

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 *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:

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

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

Delete the following:

▲• **MINIMUM FILL** ⟨**755**⟩**:** Meets the requirements ▲*USP39*

SPECIFIC TESTS

Delete the following:

▲• **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%
▲*USP39*

• **STERILITY TESTS** ⟨**71**⟩**:** Meets the requirements

Delete the following:

▲• **METAL PARTICLES IN OPHTHALMIC OINTMENTS** ⟨**751**⟩**:** Meets the requirements▲*USP39*

Change to read:

▲• **OTHER REQUIREMENTS:** It meets the requirements •for *Particulate and Foreign Matter* and *Container Contents*• (RB 1-Aug-2016) in *Ophthalmic Products—Quality Tests* ⟨771⟩, •*Drug Product Quality, Universal Tests, Particulate and Foreign Matter* and *Container Contents*.• (RB 1-Aug-2016)
▲*USP39*

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