Ophthalmic Ointment Monographs: Gentamicin and Prednisolone Acetate 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).

Gentamicin and Prednisolone Acetate Ophthalmic Ointment

DEFINITION

Gentamicin and Prednisolone Acetate Ophthalmic Ointment contains the equivalent of NLT 90.0% and NMT 120.0% of the labeled amount of gentamicin, and NLT 90.0% and NMT 110.0% of the labeled amount of prednisolone acetate ($C_{23}H_{30}O_6$).

IDENTIFICATION

Change to read:

- **A. THIN-LAYER CHROMATOGRAPHY**

  Standard solution: 1 mg/mL of USP Gentamicin Sulfate RS in water

  Sample solution: Nominally 1 mg/mL of gentamicin from Ophthalmic Ointment prepared as follows. Shake a quantity of Ophthalmic Ointment, containing nominally 5 mg of gentamicin, with a mixture of 200 mL of chloroform and 5 mL of water. Allow to separate, and filter the aqueous layer.

  Chromatographic system

  (See *Chromatography* ⟨621⟩*, Thin-Layer Chromatography*.)

  Adsorbent: 0.25-mm layer of chromatographic silica gel ▲▲*USP39*

  Application volume: 20 µL

  Developing solvent system: Mix chloroform, methanol, and ammonium hydroxide (20:13:10), allow to separate, and use the lower layer.

  Analysis

  Samples: *Standard solution* and *Sample solution*

  Apply the *Standard solution* and *Sample solution* to the plate. Place the plate in a chromatographic chamber, and develop the chromatogram in the *Developing solvent system* until the solvent front has moved three-fourths of the length of the plate. Remove the plate from the chamber, air-dry, and expose the plate to vapors of iodine in a detection jar containing iodine crystals.

  Acceptance criteria: The intensities and R_F values of the three principal spots from the *Sample solution* correspond to those from the *Standard solution*.

- **B.** The retention time of the prednisolone acetate peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay* for *Prednisolone Acetate*.

ASSAY

- **GENTAMICIN**

  (See *Antibiotics—Microbial Assays* ⟨81⟩.)

  Sample solution: Shake a portion of Ophthalmic Ointment containing nominally 1 mg of gentamicin with about 50 mL of ether in a separator, and extract with four 20-mL portions of *Buffer B.3* (see the chapter). Combine the buffer extracts, and dilute with *Buffer B.3* to a suitable volume to obtain a *Test Dilution* having a gentamicin concentration that is nominally equivalent to the median level of the standard.

  Analysis: Proceed as directed in the chapter.

  Acceptance criteria: 90.0%–120.0%

Change to read:

- **PREDNISOLONE ACETATE**

  Mobile phase: Acetonitrile and water (40:60) ▲▲*USP39*

  Internal standard solution: 2.7 mg/mL of fluorometholone acetate in methanol

  Standard stock solution: 0.38 mg/mL of USP Prednisolone Acetate RS in methanol

  Standard solution: 0.06 mg/mL of USP Prednisolone Acetate RS in methanol prepared as follows. Transfer 8.0 mL of *Standard stock solution* to a 50-mL volumetric flask, add 25 mL of *n*-hexane, and shake. Add 2.0 mL of *Internal standard solution,* dilute with methanol to volume, and shake vigorously for 30 s. Allow the layers to separate, remove the upper *n*-hexane layer by aspiration, and discard the aspirate. Dilute the solution in the volumetric flask with methanol to volume. Centrifuge a portion of this solution, and use the clear supernatant.

  Sample solution: Nominally 0.06 mg/mL of prednisolone acetate from Ophthalmic Ointment in methanol prepared as follows. Transfer a portion of Ophthalmic Ointment, containing nominally 3 mg of prednisolone acetate, to a 50-mL volumetric flask, add 25 mL of *n*-hexane, and shake. Add 2.0 mL of *Internal standard solution*, dilute with methanol to volume, and shake vigorously for 30 s. Allow the layers to separate, remove the upper *n*-hexane layer by aspiration, and discard the aspirate. Dilute the solution in the volumetric flask with methanol to volume. Centrifuge a portion of this solution, and use the clear supernatant.

  Chromatographic system

  (See *Chromatography* ⟨621⟩*, System Suitability*.)

  Mode: LC

  Detector: UV 254 nm

  Column: 3.9-mm × ▲30-cm; 10-µm▲*USP39* packing L1

  Flow rate: 2 mL/min

  Injection volume: 30 µL

  System suitability

  Sample: *Standard solution*

  Suitability requirements

  Resolution: NLT 2.0 between the prednisolone acetate and fluorometholone acetate peaks

  Tailing factor: NMT 1.5 ▲▲*USP39*

  Relative standard deviation: NMT 2.0%

  Analysis

  Samples: *Standard solution* and *Sample solution*

  Calculate the percentage of the labeled amount of prednisolone acetate ($C_{23}H_{30}O_6$) in the portion of Ophthalmic Ointment taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

  R_U = peak area response ratio of prednisolone acetate to fluorometholone acetate from the *Sample solution*

  R_S = peak area response ratio of prednisolone acetate to fluorometholone acetate from the *Standard solution*

  C_S = concentration of USP Prednisolone Acetate RS in the *Standard solution* (mg/mL)

  C_U = nominal concentration of prednisolone acetate in the *Sample solution* (mg/mL)

  Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Delete the following:

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

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

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*

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

Change to read:

• **PACKAGING AND STORAGE:** ▲Preserve in collapsible ophthalmic ointment tubes. Store at controlled room temperature.▲*USP39*
• **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Gentamicin Sulfate RS
USP Prednisolone Acetate RS