Ophthalmic Ointment Monographs: Atropine Sulfate 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).

Atropine Sulfate Ophthalmic Ointment

DEFINITION

Atropine Sulfate Ophthalmic Ointment is Atropine Sulfate in a suitable ophthalmic ointment base. It contains NLT 90.0% and NMT 110.0% of the labeled amount of atropine sulfate monohydrate [$(C_{17}H_{23}NO_3)_2 \cdot H_2SO_4 \cdot H_2O$]. It is sterile.

IDENTIFICATION

Change to read:

- **A. IDENTIFICATION—ORGANIC NITROGENOUS BASES ⟨181⟩**▲
  Standard solution: Proceed as directed in the chapter.
  ▲*USP39*
  Sample solution: Transfer a portion of Ophthalmic Ointment, equivalent to 50 mg of atropine sulfate, to a suitable separator, and dissolve in 25 mL of ether. Add 25 mL of 0.01 N hydrochloric acid, shake vigorously, allow the layers to separate, and discard the organic phase. Heat the aqueous phase gently on a steam bath while passing nitrogen through the solution to expel any residual ether.
  ▲
  Instrumental conditions and **Analysis:** Proceed as directed in the chapter.
  ▲*USP39*
  Acceptance criteria: Meets the requirements
- **B. IDENTIFICATION TESTS—GENERAL,** *Sulfate* **⟨191⟩**
  Sample solution: Transfer 5 g of Ophthalmic Ointment to a separator, dissolve in 50 mL of ether, and extract with 20 mL of water.
  Acceptance criteria: Meets the requirements

ASSAY

- **PROCEDURE**
  Buffer: 34.8 g of dibasic potassium phosphate in 900 mL of water. Adjust to a pH of 9.0 by the addition of 3 M hydrochloric acid or 1 M sodium hydroxide, as necessary.
  Internal standard solution: 0.5 mg/mL of homatropine hydrobromide in water. Prepare fresh daily.
  Standard stock solution: 0.1 mg/mL of USP Atropine Sulfate RS in water
  Standard solution: 0.5 mg/mL of atropine sulfate prepared as follows. Pipet 10 mL of *Standard stock solution* into a separator, add 2.0 mL of *Internal standard solution* and 5.0 mL of *Buffer*, and adjust the solution in the separator with 1 M sodium hydroxide to a pH of 9.0. Extract with two 10-mL portions of methylene chloride, filter the methylene chloride extracts through 1 g of anhydrous sodium sulfate supported by a small cotton plug in a funnel into a 50-mL beaker, and evaporate to near-dryness under a stream of nitrogen. Dissolve the residue in 2.0 mL of methylene chloride. Prepare fresh daily.
  Sample solution: Nominally 0.5 mg/mL of atropine sulfate prepared as follows. Transfer Ophthalmic Ointment, equivalent to 10 mg of atropine sulfate, to a separator containing 50 mL of ether. Shake to dissolve, extract with three 25-mL portions of 0.1 M sulfuric acid, collect the acid extracts in a 100-mL volumetric flask, and dilute with 0.1 M sulfuric acid to volume. Pipet 10 mL of this solution and treat as follows. Add 2.0 mL of *Internal standard solution* and 5.0 mL of *Buffer*, and adjust the solution in the separator with 1 M sodium hydroxide to a pH of 9.0. Extract with two 10-mL portions of methylene chloride, filter the methylene chloride extracts through 1 g of anhydrous sodium sulfate supported by a small cotton plug in a funnel into a 50-mL beaker, and evaporate to near-dryness under a stream of nitrogen. Dissolve the residue in 2.0 mL of methylene chloride.
  Chromatographic system
  (See *Chromatography* ⟨621⟩*, System Suitability*.)
  Mode: GC
  Detector: Flame ionization
  Column: 2-mm × 1.8-m glass; packed with a 3% phase G3 on support S1AB
  Temperatures
  Column: 225°
  Injection port: 250°
  Detector: 250°
  Flow rate: 25 mL/min
  Carrier gas: Nitrogen
  Injection volume: 1 µL
  System suitability
  Sample: *Standard solution*
  Suitability requirements
  Resolution: NLT 4.0
  Tailing factor: NMT 2.0
  Relative standard deviation: NMT 2.0%
  Analysis
  Samples: *Standard solution* and *Sample solution*
  Calculate the percentage of the labeled amount of atropine sulfate monohydrate [$(C_{17}H_{23}NO_3)_2 \cdot H_2SO_4 \cdot H_2O$] in the portion of Ophthalmic Ointment taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

  R_U = peak area ratio of atropine to homatropine from the *Sample solution*
  R_S = peak area ratio of atropine to homatropine from the *Standard solution*
  C_S = concentration of USP Atropine Sulfate RS in the *Standard solution* (mg/mL)
  C_U = nominal concentration of the *Sample solution* (mg/mL)
  M_{r1} = molecular weight of atropine sulfate monohydrate, 694.85
  M_{r2} = molecular weight of anhydrous atropine sulfate, 676.83
  Acceptance criteria: 90.0%–110.0%

SPECIFIC TESTS

- **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*• (RB 1-Aug-2016) in *Ophthalmic Products—Quality Tests* ⟨771⟩, •*Drug Product Quality, Universal Tests, Particulate and Foreign Matter.*• (RB 1-Aug-2016)
▲*USP39*

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in collapsible ophthalmic ointment tubes.
- **USP REFERENCE STANDARDS ⟨11⟩**
  USP Atropine Sulfate RS