Ophthalmic Ointment Monographs: Neomycin and Polymyxin B Sulfates, Bacitracin, and Hydrocortisone Acetate Ophthalmic Ointment

Type of Posting	Revision Bulletin
Posting Date	29–Jul–2016
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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 and Polymyxin B Sulfates, Bacitracin, and Hydrocortisone Acetate Ophthalmic Ointment

DEFINITION

Neomycin and Polymyxin B Sulfates, Bacitracin, and Hydrocortisone Acetate Ophthalmic Ointment contains the equivalent of NLT 90.0% and NMT 140.0% of the labeled amounts of neomycin, polymyxin B, and bacitracin, and NLT 90.0% and NMT 110.0% of the labeled amount of hydrocortisone acetate in a suitable ointment base.

IDENTIFICATION

- **A. THIN-LAYER CHROMATOGRAPHIC IDENTIFICATION TEST ⟨201BNP⟩:** Meets the requirements
- **B.** The retention time of the hydrocortisone acetate peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay* for *Hydrocortisone Acetate.*

ASSAY

- **NEOMYCIN**

  (See *Antibiotics—Microbial Assays* ⟨81⟩.)
  Sample solution: Shake a portion of Ophthalmic Ointment in a separator with 50 mL of ether. 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%–140.0%
- **POLYMYXIN B**

  (See *Antibiotics—Microbial Assays* ⟨81⟩.)
  Sample solution: Shake a portion of Ophthalmic Ointment with 50 mL of ether in a separator. Extract with four 25-mL portions of *Buffer B.6*. Combine the aqueous extracts, and dilute with *Buffer B.6* to a suitable volume.
  Analysis: Proceed as directed in the chapter. Dilute the *Sample solution* with *Buffer B.6* to obtain a *Test Dilution* having a concentration that is nominally equivalent to the median level of the standard (10 polymyxin B units/mL). Add to each *Test Dilution* of the standard a quantity of USP Neomycin Sulfate RS, dissolved in *Buffer B.6*, to obtain the same concentration of neomycin as in the *Test Dilution* of the sample.
  Acceptance criteria: 90.0%–140.0%
- **BACITRACIN**

  (See *Antibiotics—Microbial Assays* ⟨81⟩.)
  Sample solution: Shake a portion of Ophthalmic Ointment with 50 mL of ether in a separator. Extract with four 20-mL portions of *Buffer B.1*. Combine the buffer extracts, and dilute with *Buffer B.1* to a suitable volume.
  Analysis: Proceed as directed in the chapter. Add sufficient 0.01 N hydrochloric acid to a portion of the *Sample solution* so that the amount of hydrochloric acid in the *Test Dilution* is the same as in the median level of the standard. Dilute with *Buffer B.1* to obtain a *Test Dilution* having a bacitracin concentration that is nominally equivalent to the median level of the standard.
  Acceptance criteria: 90.0%–140.0%

Change to read:

- **HYDROCORTISONE ACETATE**

  Mobile phase: Butyl chloride, water-saturated butyl chloride, tetrahydrofuran, methanol, and glacial acetic acid (475:475:70:35:30)
  Standard solution: 0.10 mg/mL of USP Hydrocortisone Acetate RS in water-saturated chloroform
  Sample solution: Nominally 0.10 mg/mL of hydrocortisone acetate from Ophthalmic Ointment prepared as follows. Transfer a portion of Ophthalmic Ointment containing nominally 2.5 mg of hydrocortisone acetate to a closable container. Add 25.0 mL of water-saturated chloroform and about 10 glass beads. Securely close the container, and shake vigorously for approximately 15 min. Centrifuge, and use the clear, lower chloroform layer.
  Chromatographic system
  (See *Chromatography* ⟨621⟩*, System Suitability*.)
  Mode: LC
  Detector: UV 254 nm
  Column: ▲3.9-mm × 30-cm; 10-µm▲*USP39* packing L3
  System suitability
  Sample: *Standard solution*
  Suitability requirements
  Relative standard deviation: NMT 2.0%
  Analysis
  Samples: *Standard solution* and *Sample solution*
  Calculate the percentage of the labeled amount of hydrocortisone acetate ($C_{23}H_{32}O_6$) in the portion of Ophthalmic Ointment taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

  r_U = peak response from the *Sample solution*
  r_S = peak response from the *Standard solution*
  C_S = concentration of USP Hydrocortisone Acetate RS in the *Standard solution* (mg/mL)
  C_U = nominal concentration of hydrocortisone 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

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 0.5%
▲*USP39*

Change to read:

- **STERILITY TESTS ⟨71⟩:** ▲Meets the requirements▲*USP39*

Delete the following:

▲• **METAL PARTICLES IN OPHTHALMIC OINTMENTS** ⟨**751**⟩**:** It 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.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Bacitracin Zinc RS
  USP Hydrocortisone Acetate RS
  USP Neomycin Sulfate RS
  USP Polymyxin B Sulfate RS