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
- Chlorotetracycline 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 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 Zinc, and Hydrocortisone Ophthalmic Ointment

DEFINITION
Neomycin and Polymyxin B Sulfates, Bacitracin Zinc, and Hydrocortisone Ophthalmic Ointment is a sterile ointment containing Neomycin Sulfate, Polymyxin B Sulfate, Bacitracin Zinc, and Hydrocortisone. It 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 (C21H30O5).

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

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 nominal 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 25-mL portions of 0.01 N hydrochloric acid. Combine the acid extracts, and dilute with 0.01 N hydrochloric acid to a suitable volume.
  Analysis: Proceed as directed in the chapter. Dilute the Sample solution with Buffer B.1 to obtain a Test Dilution having a concentration that is nominally equivalent to the median level of the standard (1.0 bacitracin Unit/mL). If the Sample solution has a concentration of less than 100 bacitracin Units/mL, add hydrochloric acid to each Test Dilution of the standard to obtain the same concentration of hydrochloric acid as in the Test Dilution of the sample.
  Acceptance criteria: 90.0%–140.0%

Change to read:
- HYDROCORTISONE
  Mobile phase: Methanol, glacial acetic acid, and water (500:1:500) \(\text{USP39}\)
  Diluent: Methanol and water (1:1)
  Standard solution: 0.15 mg/mL of USP Hydrocortisone RS in Diluent
  Sample solution: Transfer 1.5 g of Ophthalmic Ointment to a separator. Add 3 mL of \(n\)-hexane, and warm gently on a steam bath with mild agitation until dissolved. Add 7 mL of \(n\)-hexane, mix by swirling, and extract with four 15-mL portions of Diluent. Collect the extracts in a 100-mL volumetric flask, dilute with Diluent to volume, and mix. Filter the solution, rejecting the first 10 mL of the filtrate.
  Chromatographic system
  (See Chromatography (621), System Suitability.)
  Mode: LC
  Detector: UV 254 nm
  Column: \(\text{\textregistered}\) 3.9-mm \(\times\) 30-cm; \(10-\mu\text{m}\) \(\text{USP39}\) packing L1
  Flow rate: 2 mL/min
  Injection volume: 10 \(\mu\text{L}\)
  System suitability
  Samples: Standard solution
  Suitability requirements
  Relative standard deviation: NMT 2.0%
  Analysis
  Samples: Standard solution and Sample solution
  \(\text{USP39}\)
  Calculate the percentage of the labeled amount of hydrocortisone (C21H30O5) in the portion of Ophthalmic Ointment taken:

\[
\text{Result} = \left(\frac{r_0}{r_s}\right) \times \left(\frac{C_s}{C_U}\right) \times 100
\]

\(r_0\) = peak response from the Sample solution
\(r_s\) = peak response from the Standard solution
\(C_s\) = concentration of USP Hydrocortisone RS in the Standard solution (mg/mL)
\(C_U\) = nominal concentration of hydrocortisone in the Sample solution (mg/mL)
  Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Delete the following:
- **MINIMUM FILL (755):** Meets the requirements \(\text{USP39}\)

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% \(\text{USP39}\)

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• **STERILITY TESTS (71):** Meets the requirements

Delete the following:

**METAL PARTICLES IN OPHTHALMIC OINTMENTS (751):**
Meets the requirements

▲ **METAL PARTICLES IN OPHTHALMIC OINTMENTS (751):**
Meets the requirements

▲ **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 RS
  - USP Neomycin Sulfate RS
  - USP Polymyxin B Sulfate RS

▲