

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

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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 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 ($C_{21}H_{30}O_5$).

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 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 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) ▲▲^{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: ▲3.9-mm × 30-cm; 10-μm▲^{USP39} packing L1

Flow rate: 2 mL/min

Injection volume: 10 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

▲▲^{USP39}

Calculate the percentage of the labeled amount of hydrocortisone ($C_{21}H_{30}O_5$) 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 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▲^{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}

2 Neomycin

- **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 Mat-
ter 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