Ophthalmic Ointment Monographs: Tetracycline Hydrochloride 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).

Tetracycline Hydrochloride Ophthalmic Ointment

DEFINITION

Tetracycline Hydrochloride Ophthalmic Ointment contains NLT 90.0% and NMT 125.0% of the labeled amount of tetracycline hydrochloride ($C_{22}H_{24}N_2O_8 \cdot HCl$).

IDENTIFICATION

Add the following:

▲• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
▲*USP39*

ASSAY

• **PROCEDURE**

Solution A: 0.1 M ammonium oxalate
Solution B: 0.2 M dibasic ammonium phosphate
Diluent: Dimethylformamide and *Solution A* (270:680)
Mobile phase: Dimethylformamide, *Solution A*, and *Solution B* (270:680:50). Adjust, if necessary, with 3 N ammonium hydroxide or 3 N phosphoric acid to a pH of 7.6–7.7.
System suitability solution: 100 µg/mL of tetracycline hydrochloride and 25 µg/mL of USP 4-Epianhydrotetracycline Hydrochloride RS in *Diluent*
Standard stock solution: 1 mg/mL of USP Tetracycline Hydrochloride RS in methanol
Standard solution: 0.12 mg/mL of USP Tetracycline Hydrochloride RS from *Standard stock solution* in *Diluent*
Sample stock solution: Nominally 3 mg/mL of tetracycline hydrochloride prepared as follows. Transfer a portion of Ophthalmic Ointment, containing nominally 300 mg of tetracycline hydrochloride, to a glass-stoppered conical flask. Add 20 mL of cyclohexane, and shake. Add 35 mL of methanol, and sonicate for 20 min. Filter this solution into a 100-mL volumetric flask, and rinse the sides of the conical flask with 40 mL of methanol, filtering the rinsing into the volumetric flask. Dilute with methanol to volume.
Sample solution: Nominally 0.12 mg/mL of tetracycline hydrochloride in *Diluent* from *Sample stock solution*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 280 nm
Columns
Guard: 4.6-mm × 3-cm; 10-µm packing L7
Analytical: 4.6-mm × 25-cm; 5–10-µm packing L7
Flow rate: 2 mL/min
Injection volume: 20 µL
System suitability
Samples: *System suitability solution* and *Standard solution*
[NOTE—The relative retention times of 4-epianhydrotetracycline and tetracycline are 0.9 and 1.0, respectively.]
Suitability requirements
Resolution: NLT 1.2 between 4-epianhydrotetracycline and tetracycline, *System suitability solution*
Relative standard deviation: NMT 2.0%, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of tetracycline hydrochloride ($C_{22}H_{24}N_2O_8 \cdot HCl$) in the portion of Ophthalmic Ointment taken:

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

r_U = peak response of tetracycline from the *Sample solution*
r_S = peak response of tetracycline from the *Standard solution*
C_S = concentration of USP Tetracycline Hydrochloride RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of tetracycline hydrochloride in the *Sample solution* (mg/mL)
P = potency of USP Tetracycline Hydrochloride RS (µg/mg)
F = conversion factor, 0.001 mg/µg

Acceptance criteria: 90.0%–125.0%

PERFORMANCE TESTS

Delete the following:

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

SPECIFIC TESTS

Delete the following:

▲• **WATER DETERMINATION** ⟨**921**⟩**,** *Method I*
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*

• **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 Matter* and *Container Contents*.• (RB 1-Aug-2016)
▲*USP39*

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in collapsible ophthalmic ointment tubes.

Change to read:

• **USP REFERENCE STANDARDS** ⟨**11**⟩
USP 4-Epianhydrotetracycline Hydrochloride RS
▲$C_{22}H_{22}N_2O_7 \cdot HCl$ 462.88▲*USP39*
USP Tetracycline Hydrochloride RS