Ophthalmic Ointment Monographs: Sulfacetamide Sodium and Prednisolone Acetate 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).

Sulfacetamide Sodium and Prednisolone Acetate Ophthalmic Ointment

DEFINITION

Sulfacetamide Sodium and Prednisolone Acetate Ophthalmic Ointment is a sterile ointment containing NLT 90.0% and NMT 110.0% of the labeled amounts of sulfacetamide sodium ($C_8H_9N_2NaO_3S \cdot H_2O$) and prednisolone acetate ($C_{23}H_{30}O_6$).

IDENTIFICATION

Change to read:

- **A.**▲ The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the tests for *Sulfacetamide Sodium* and *Prednisolone Acetate* in the *Assay*.

▲*USP39*

Add the following:

▲• **B.** The UV absorption spectra of the major peak of the *Sample solution* and that of the *Standard solution* exhibit maxima and minima at the same wavelengths, as obtained in the tests for *Sulfacetamide Sodium* and *Prednisolone Acetate* in the *Assay*.

▲*USP39*

ASSAY

Change to read:

- **SULFACETAMIDE SODIUM**

Diluent: Dilute methanol (1 in 5)

Mobile phase: Methanol, glacial acetic acid, and water (100:10:890), filtered and degassed

Standard solution: Transfer about 50 mg of USP Sulfacetamide Sodium RS to a 40-mL centrifuge tube. Add 10.0 mL of *Diluent*, insert the stopper in the tube, and mix using a vortex mixer for about 3 min to dissolve. Add 7.5 mL of heptane, insert the stopper in the tube, and mix using a vortex mixer for another 3 min. Centrifuge to effect separation of the phases. Withdraw and discard the upper heptane layer. Transfer 3.0 mL of the bottom layer to a 500-mL volumetric flask, add *Diluent* to volume, and mix.

System suitability solution: Dissolve 3 mg of sulfanilamide in 100 mL of the *Standard solution*, and mix.

Sample solution: Transfer a quantity of Ophthalmic Ointment nominally equivalent to about 100 mg of sulfacetamide sodium to a 40-mL centrifuge tube. Add 15.0 mL of heptane, insert the stopper in the tube, and mix using a vortex mixer for about 3 min to dissolve the Ophthalmic Ointment. Add 20.0 mL of *Diluent*, insert the stopper in the tube, and mix using a vortex mixer for 3 min. Centrifuge to effect separation of the phases. Withdraw and discard the upper heptane layer. Transfer 3.0 mL of the bottom layer to a 500-mL volumetric flask, dilute with *Diluent* to volume, and mix.

Chromatographic system

(See *Chromatography* ⟨621⟩*, System Suitability*.)

Mode: LC

Detector: ▲254-nm diode array▲*USP39*

Column: 4.6-mm × 25-cm; packing L1

Flow rate: 1.5 mL/min

Injection volume: 90 µL

System suitability

Samples: *Standard solution* and *System suitability solution*

Suitability requirements

Resolution: NLT 3 between the sulfacetamide and sulfanilamide peaks, ▲*System suitability solution*▲*USP39*

Column efficiency: NLT 1500 theoretical plates, ▲*Standard solution*▲*USP39*

Relative standard deviation: NMT 2.0%, ▲*Standard solution*▲*USP39*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of sulfacetamide sodium ($C_8H_9N_2NaO_3S \cdot H_2O$) 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 response of sulfacetamide sodium from the *Sample solution*

r_S = peak response of sulfacetamide sodium from the *Standard solution*

C_S = concentration of USP Sulfacetamide Sodium RS, calculated on the anhydrous basis, in the *Standard solution* (mg/mL)

C_U = nominal concentration of sulfacetamide sodium in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of sulfacetamide sodium monohydrate, 254.24

M_{r2} = molecular weight of anhydrous sulfacetamide sodium, 236.23

Acceptance criteria: 90.0%–110.0%

Change to read:

- **PREDNISOLONE ACETATE**

Diluent: Dilute methanol (9 in 10)

Mobile phase: Acetonitrile and water (400:600), filtered and degassed

Internal standard solution: 0.7 mg/mL of norethindrone in *Diluent*

Standard stock solution: 0.8 mg/mL of USP Prednisolone Acetate RS in *Diluent*

Standard solution: 0.04 mg/mL of USP Prednisolone Acetate RS prepared as follows. Transfer 5.0 mL of *Standard stock solution* to a 100-mL volumetric flask, add 5.0 mL of *Internal standard solution*, dilute with *Diluent* to volume, and mix.

Sample solution: Transfer a quantity of Ophthalmic Ointment nominally equivalent to about 4 mg of prednisolone acetate to a 50-mL centrifuge tube. Add 10.0 mL of heptane, and mix using a vortex mixer for about 2 min to dissolve the Ophthalmic Ointment. Add 5.0 mL of *Internal standard solution* and 20.0 mL of *Diluent*, and mix using a vortex mixer for 2 min. Centrifuge to effect separation of the phases. Withdraw and discard the upper heptane layer. Transfer the lower layer to a 100-mL volumetric flask. Add *Diluent* to volume, and mix.

Chromatographic system

(See *Chromatography* ⟨621⟩*, System Suitability*.)

Mode: LC
Detector: ▲254-nm diode array▲*USP39*
Column: 3.9-mm × 30-cm; packing L1
Flow rate: 1.5 mL/min
Injection volume: 40 µL
System suitability
Sample: *Standard solution*
[NOTE—The relative retention times for prednisolone acetate and norethindrone are about 1.0 and 1.5, respectively.]
Suitability requirements
Resolution: NLT 4.5 between the prednisolone and norethindrone peaks
Column efficiency: NLT 3000 theoretical plates ▲for the prednisolone peak▲*USP39*
Tailing factor: NMT 2.5 ▲for the prednisolone peak▲*USP39*
Relative standard deviation: NMT 1.5% ▲for the peak response ratio of prednisolone acetate to norethindrone▲*USP39*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of prednisolone acetate ($C_{23}H_{30}O_6$) in the portion of Ophthalmic Ointment taken:

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

R_U = peak response ratio of prednisolone acetate to the internal standard peak from the *Sample solution*
R_S = peak response ratio of prednisolone acetate to the internal standard peak from the *Standard solution*
C_S = concentration of USP Prednisolone Acetate RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of prednisolone 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

• **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 that are tamper-proof so that sterility is assured at time of first use.
• **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Prednisolone Acetate RS
USP Sulfacetamide Sodium RS