BRIEFING

Oxiconazole Nitrate Lotion. Because there is no existing *USP* monograph for this drug product, a new monograph, based on validated methods of analysis, is being proposed. The liquid chromatographic procedure in the *Assay* and test for *Organic Impurities* is based on analyses performed with the Phenomenex Gemini C6-Phenyl brand of column with L11 packing. The typical retention time for the oxiconazole peak is about 15 min.

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Comment deadline: May 31, 2017

Add the following:

■**Oxiconazole Nitrate Lotion**

DEFINITION

Oxiconazole Nitrate Lotion contains an amount of oxiconazole nitrate ($C_{18}H_{13}Cl_4N_3O \cdot HNO_3$) equivalent to NLT 95.0% and NMT 110.0% of the labeled amount of oxiconazole ($C_{18}H_{13}Cl_4N_3O$).

IDENTIFICATION

- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B.** The UV spectrum of the *Sample solution* exhibits maxima and minima at the same wavelengths as those of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

Buffer: 1.26 g/L of ammonium formate in water. Adjust with formic acid to a pH of 4.0.

Solution A: Acetonitrile and *Buffer* (27:73)

Solution B: Acetonitrile and *Buffer* (50:50)

Mobile phase: See *Table 1*. [Note—This is effectively a two-stage isocratic run with gradient shifts between each isocratic stage. If the ethylparaben peak is not fully eluted during the first isocratic stage on a level baseline, add 1 min to each time interval from the 5 min time point onwards.]

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
5	100	0
7	0	100
26	0	100
28	100	0
36	100	0

Internal standard solution: 0.4 mg/mL of USP Ethylparaben RS in *Solution B*. Sonicate, if necessary, to dissolve.

Standard stock solution: 0.58 mg/mL of USP Oxiconazole Nitrate RS in *Solution B*. Sonicate, if necessary, to dissolve.

Standard solution: 0.046 mg/mL of USP Oxiconazole Nitrate RS and 0.02 mg/mL of USP Ethylparaben RS from *Standard stock solution* and *Internal standard solution*, respectively, in *Solution B*

Sensitivity solution: 0.023 µg/mL of USP Oxiconazole Nitrate RS and 0.01 µg/mL of USP Ethylparaben RS from *Standard solution* in *Solution B*

Sample solution: Nominally 0.04 mg/mL of oxiconazole in *Solution B* prepared as follows. Transfer about 0.4 g of Lotion into a 100-mL volumetric flask. Add 5.0 mL of *Internal standard solution* and about 50 mL of *Solution B*. Heat the solution in a 60° water bath for about 10 min and vortex for 1 min. Cool the mixture in an ice-water bath for at least 10 min. Repeat the heating and cooling step two more times. Add a few milliliters of *Solution B* along the walls of the volumetric flask. Allow the solution to cool to room temperature for NLT 60 min. Dilute with *Solution B* to volume and pass through a suitable filter of 0.2-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 220 nm. For *Identification B*, use a diode array detector in the range of 200–350 nm.

Column: 3.0-mm × 10-cm; 3-µm packing L11

Column temperature: 30°

Flow rate: 0.6 mL/min

Injection volume: 25 µL

System suitability

Samples: *Standard solution* and *Sensitivity solution*

[Note—The relative retention times for ethylparaben and oxiconazole nitrate are 0.4 and 1.0 respectively, *Standard solution*.]

Suitability requirements

Tailing factor: NMT 2.0 for the oxiconazole peak, *Standard solution*

Relative standard deviation: NMT 2.0% for the peak response ratio of oxiconazole to ethylparaben, *Standard solution*

Signal-to-noise ratio: NLT 5 for the oxiconazole peak, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of oxiconazole ($C_{18}H_{13}Cl_4N_3O$) in the portion of Lotion taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

R_U = peak response ratio of oxiconazole to ethylparaben from the *Sample solution*

R_S = peak response ratio of oxiconazole to ethylparaben from the *Standard solution*

C_S = concentration of USP Oxiconazole Nitrate RS in the *Standard solution* (mg/mL)

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

M_{r1} = molecular weight of oxiconazole, 429.13

M_{r2} = molecular weight of oxiconazole nitrate, 492.14

Acceptance criteria: 95.0%–110.0%

IMPURITIES

- **Organic Impurities**

Buffer, Solution A, Solution B, Internal standard solution, Standard stock solution, Standard solution, Sensitivity solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Analysis

Sample: *Sample solution*

Calculate the percentage of each individual impurity in the portion of Lotion taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response of any individual impurity from the *Sample solution*

r_T = sum of the peak responses of all the peaks from the *Sample solution*

Acceptance criteria: See *Table 2*. Disregard any impurity peak less than 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Oxiconazole related compound B[a,b]	0.13	—
Oxiconazole related compound A (oxiconazole-*E*-isomer)[c]	0.91	2.0
Oxiconazole	1.0	—
Total impurities[d]	—	1.0

a (*Z*)-1-(2,4-Dichlorophenyl)-2-(1*H*-imidazol-1-yl)ethanone oxime.

b This is a process impurity which is controlled in the drug substance and is included in the table for identification only.

c 2′,4′-Dichloro-2-imidazol-1-ylacetophenone (*E*)-[*O*-(2,4-dichlorobenzyl)oxime].

d Total impurities excludes oxiconazole related compound A.

PERFORMANCE TESTS

- **Minimum Fill** ⟨755⟩**:** Meets the requirements

SPECIFIC TESTS

- **Microbial Enumeration Tests** ⟨61⟩ and **Tests for Specified Microorganisms** ⟨62⟩**:** The total aerobic microbial count is NMT 10^2 cfu/g, and the total combined molds and yeasts count is NMT 10^2 cfu/g. It also meets the requirement for absence of *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*.
- **pH** ⟨791⟩

Sample: 4 g of Lotion in 36 mL of water. Cover with parafilm and mix this sample on a stir plate with a magnetic stir bar for at least 5 min or until the sample is homogeneous.

Acceptance criteria: 2.5–4.0

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers, and store at room temperature.
- **USP Reference Standards** ⟨11⟩

  USP Ethylparaben RS
  USP Oxiconazole Nitrate RS

■1S (*USP41*)

Auxiliary Information - Please check for your question in the FAQs before contacting USP.