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.

(CHM1: S. Shivaprasad.)
Correspondence Number—C156779

Comment deadline: May 31, 2017

Add the following:

Oxiconazole Nitrate Lotion

DEFINITION

Oxiconazole Nitrate Lotion contains an amount of oxiconazole nitrate (C₁₈H₁₃Cl₄N₃O·HNO₃) equivalent to NLT 95.0% and NMT 110.0% of the labeled amount of oxiconazole (C₁₈H₁₃Cl₄N₃O).

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>
<thead>
<tr>
<th>Time (min)</th>
<th>Solution A (%)</th>
<th>Solution B (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>26</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>28</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>36</td>
<td>100</td>
<td>0</td>
</tr>
</tbody>
</table>

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_{4}N_{3}O) in the portion of Lotion taken:

\[
\text{Result} = \left( \frac{R_U}{R_S} \right) \times \left( \frac{C_S}{C_U} \right) \times \left( \frac{M_{r1}}{M_{r2}} \right) \times 100
\]

\( R_U \) = 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)
\[ M_{r1} = \text{molecular weight of oxiconazole, 429.13} \]
\[ M_{r2} = \text{molecular weight of oxiconazole nitrate, 492.14} \]

**Acceptance criteria:** 95.0%–110.0%

### IMPURITIES

- **Organic Impurities**


**Analysis**

**Sample:** *Sample solution*

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

\[
\text{Result} = \left( \frac{r_U}{r_T} \right) \times 100
\]

- \( r_U \) = 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>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxiconazole related compound B (^{a,b})</td>
<td>0.13</td>
<td>—</td>
</tr>
<tr>
<td>Oxiconazole related compound A (oxiconazole-(E)-isomer) (^c)</td>
<td>0.91</td>
<td>2.0</td>
</tr>
<tr>
<td>Oxiconazole</td>
<td>1.0</td>
<td>—</td>
</tr>
<tr>
<td>Total impurities (^d)</td>
<td>—</td>
<td>1.0</td>
</tr>
</tbody>
</table>

\(^a\) (Z)-1-\((2,4\text{-Dichlorophenyl})-2-(\text{1H-imidazol-1-yl})\text{ethanone oxime.}\)
\(^b\) This is a process impurity which is controlled in the drug substance and is included in the table for identification only.
\(^c\) \(2',4'\text{-Dichloro-2-imidazol-1-ylacetophenone (E)-[O-(2,4-dichlorobenzyl)oxime].}\)
\(^d\) 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 10² cfu/g, and the total combined molds and yeasts count is NMT 10² 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

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