In accordance with the Rules and Procedures of the Council of Experts, the Small Molecules 2 Expert Committee has revised the Diclofenac Sodium Topical Solution monograph. The purpose for the revision is to remove the pH test from the monograph to accommodate FDA-approved drug products with different pH acceptance criteria than the one in the monograph. This product contains a limited quantity of water and the pH of this product can be formulation dependent. Please see *Topical and Transdermal Drug Products–Product Quality Tests* <3>, *pH* for additional information.

The Diclofenac Sodium Topical Solution Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Wei Yang, Scientific Liaison (301-816-8666 or wiy@usp.org).

<table>
<thead>
<tr>
<th>Type of Posting</th>
<th>Revision Bulletin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posting Date</td>
<td>26-Mar-2021</td>
</tr>
<tr>
<td>Official Date</td>
<td>1-Apr-2021</td>
</tr>
<tr>
<td>Expert Committee</td>
<td>Small Molecules 2</td>
</tr>
</tbody>
</table>
Diclofenac Sodium Topical Solution

**DEFINITION**

Diclofenac Sodium Topical Solution is a solution of Diclofenac Sodium in a suitable vehicle. It contains NLT 90.0% and NMT 110.0% of the labeled amount of diclofenac sodium (C_{14}H_{10}Cl_{2}NNaO_{2}).

**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 major peak of the Sample solution corresponds to that of the Standard solution, as obtained in the Assay.

**ASSAY**

- **Procedure**
  
  **Solution A:** Phosphoric acid and water (0.62:1000)
  **Solution B:** 1.86 g of monobasic sodium phosphate dihydrate in 1000 mL of water
  **Solution C:** Solution A and Solution B (50:50)
  **Mobile phase:** Methanol and Solution C (70:30)
  **Diluent:** Methanol and water (70:30)
  **Standard stock solution:** 0.6 mg/mL of USP Diclofenac Sodium RS prepared as follows. Transfer a quantity of USP Diclofenac Sodium RS to a suitable volumetric flask, add 20% of the flask volume of methanol, sonicate to dissolve, and dilute with Diluent to volume.
  **Standard solution:** 0.06 mg/mL of USP Diclofenac Sodium RS from Standard stock solution diluted with Diluent
  **Sample solution:** Nominally 0.06 mg/mL of diclofenac sodium prepared as follows. Transfer a quantity of Topical Solution to a suitable volumetric flask, add 20% of the flask volume of methanol, sonicate for about 10 min, and dilute with Diluent to volume. Pass a portion of the solution through a suitable filter of 0.45-µm pore size.

**Chromatographic system**

(See Chromatography (621), System Suitability.)

- **Mode:** LC
- **Detector:** UV 254 nm. For Identification B, use a diode array detector in the range of 200–400 nm.
- **Column:** 4.6-mm × 25-cm; 5-µm packing L7
- **Column temperature:** 30°
- **Flow rate:** 1 mL/min
- **Injection volume:** 10 µL
- **Run time:** NLT 2 times the retention time of diclofenac

**System suitability**

- **Sample:** Standard solution
- **Suitability requirements**
  - **Tailing factor:** NMT 2.0
  - **Relative standard deviation:** NMT 2.0%
Analysis

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of diclofenac sodium (C\textsubscript{14}H\textsubscript{10}Cl\textsubscript{2}NNaO\textsubscript{2}) in the portion of Topical Solution taken:

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

- \(r_U\) = peak response of diclofenac from the *Sample solution*
- \(r_S\) = peak response of diclofenac from the *Standard solution*
- \(C_S\) = concentration of *USP Diclofenac Sodium RS* in the *Standard solution* (mg/mL)
- \(C_U\) = nominal concentration of diclofenac sodium in the *Sample solution* (mg/mL)

**Acceptance criteria:** 90.0%–110.0%

**IMPURITIES**

- **Organic Impurities**

  **Solution A, Solution B, Solution C, and Diluent:** Prepare as directed in the *Assay*.

  **Mobile phase A:** Use Solution C.

  **Mobile phase B:** Methanol and acetonitrile (90:10)

  **Mobile phase:** See *Table 1*.

**Table 1**

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Mobile Phase A (%)</th>
<th>Mobile Phase B (%)</th>
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</thead>
<tbody>
<tr>
<td>0</td>
<td>40</td>
<td>60</td>
</tr>
<tr>
<td>30</td>
<td>40</td>
<td>60</td>
</tr>
<tr>
<td>48</td>
<td>25</td>
<td>75</td>
</tr>
<tr>
<td>60</td>
<td>25</td>
<td>75</td>
</tr>
<tr>
<td>62</td>
<td>40</td>
<td>60</td>
</tr>
<tr>
<td>70</td>
<td>40</td>
<td>60</td>
</tr>
</tbody>
</table>

**Standard stock solution:** 0.3 mg/mL of *USP Diclofenac Sodium RS* prepared as follows. Transfer a quantity of *USP Diclofenac Sodium RS* to a suitable volumetric flask, add 20% of the flask volume of methanol, sonicate to dissolve, and dilute with Diluent to volume.

**Standard solution:** 0.003 mg/mL of *USP Diclofenac Sodium RS* from *Standard stock solution* diluted with Diluent

**Sensitivity solution:** 0.3 µg/mL of *USP Diclofenac Sodium RS* in Diluent from *Standard solution*

**Sample solution:** Nominally 0.6 mg/mL of diclofenac sodium prepared as follows. Transfer a suitable quantity of the Topical Solution to a suitable volumetric flask, add 20% of the flask volume of methanol, and sonicate to disperse. Add 50% of the flask volume of Diluent, sonicate for about 15 min, and dilute with Diluent to volume. Pass a portion of the solution through a suitable filter of 0.45-µm pore size.
Chromatographic system
(See Chromatography (621), System Suitability.)

Mode: LC
Detector: UV 254 nm
Column: 4.6-mm × 25-cm; 5-µm packing L1
Column temperature: 45°
Flow rate: 1.2 mL/min
Injection volume: 20 µL

System suitability

Samples: Standard solution and Sensitivity solution

Suitability requirements

Relative standard deviation: NMT 5.0%, Standard solution
Signal-to-noise ratio: NLT 10, Sensitivity solution

Analysis

Samples: Standard solution and Sample solution

Calculate the percentage of each specified and any unspecified degradation product in the portion of Topical Solution taken:

\[
\text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_S}{C_U} \right) \times \left( \frac{1}{F} \right) \times 100
\]

\( r_U \) = peak response of each specified or unspecified degradation product from the Sample solution
\( r_S \) = peak response of diclofenac from the Standard solution
\( C_S \) = concentration of USP Diclofenac Sodium RS in the Standard solution (mg/mL)
\( C_U \) = nominal concentration of diclofenac sodium in the Sample solution (mg/mL)
\( F \) = relative response factor (see Table 2)

Acceptance criteria: See Table 2.

Table 2

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Relative Response Factor</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diclofenac keto analog(^a)</td>
<td>0.3</td>
<td>1.7</td>
<td>0.2</td>
</tr>
<tr>
<td>Diclofenac lactam (diclofenac related compound A)(^b)</td>
<td>0.5</td>
<td>1.4</td>
<td>0.5</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>1.0</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Unidentified degradation product A</td>
<td>2.2</td>
<td>1.3</td>
<td>0.2</td>
</tr>
<tr>
<td>Any unspecified degradation product</td>
<td>—</td>
<td>1.0</td>
<td>0.2</td>
</tr>
<tr>
<td>Total degradation products</td>
<td>—</td>
<td>—</td>
<td>1.0</td>
</tr>
</tbody>
</table>

\(^a\) 2-[(2,6-Dichlorophenyl)amino]phenyl-2-oxoacetic acid.
\(^b\) 1-(2,6-Dichlorophenyl)indolin-2-one.
SPECIFIC TESTS

• Microbial Enumeration Tests (61) and Tests for Specified Microorganisms (62): The total aerobic microbial count is NMT 10^2 cfu/mL, and the total combined yeasts and molds count is NMT 10 cfu/mL. It meets the requirements of the tests for absence of Staphylococcus aureus and Pseudomonas aeruginosa.

Delete the following:

▲ ph (791): 8.0–10.0 ▲ (RB 1-Apr-2021)

ADDITIONAL REQUIREMENTS

• Packaging and Storage: Store at controlled room temperature.
• USP Reference Standards (11)
  USP Diclofenac Sodium RS

Page Information:

Not Applicable

Current DocID:

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