Diclofenac Sodium Topical Solution

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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).

Revision Bulletin
Official: April 1, 2021

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 ($C_{14}H_{10}Cl_2NNaO_2$).

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 ($C_{14}H_{10}Cl_2NNaO_2$) in the portion of Topical Solution taken:

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

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

Time (min)	Mobile Phase A (%)	Mobile Phase B (%)
0	40	60
30	40	60
48	25	75
60	25	75
62	40	60
70	40	60

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:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

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

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Diclofenac keto analog[a]	0.3	1.7	0.2
Diclofenac lactam (diclofenac related compound A)[b]	0.5	1.4	0.5
Diclofenac	1.0	—	—
Unidentified degradation product A	2.2	1.3	0.2
Any unspecified degradation product	—	1.0	0.2
Total degradation products	—	—	1.0

[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

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Not Applicable

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