Diclofenac Potassium for Oral Solution

Type of Posting	Notice of Intent to Revise
Posting Date	25-Feb-2022
Targeted Official Date	To Be Determined, Revision Bulletin
Expert Committee	Small Molecules 2

In accordance with the Rules and Procedures of the Council of Experts and the Pending Monograph Guideline, this is to provide notice that the Small Molecules 2 Expert Committee intends to revise the Diclofenac Potassium for Oral Solution monograph.

Based on the supporting data received from a manufacturer awaiting FDA approval, the Expert Committee proposes to widen the acceptance criteria for the *pH* test from 7.0–9.0 to 7.0–11.5 to accommodate drug products with wider acceptance criteria.

The proposed revision is contingent on FDA approval of a product that meets the proposed monograph specifications. The proposed revision will be published as a Revision Bulletin and an official date will be assigned to coincide as closely as possible with the FDA approval of the associated product.

See below for additional information about the proposed text.[1]

Should you have any questions, please contact Claire Chisolm, Senior Scientist II (301-230-3215 or cnc@usp.org).

[1] This text is not the official version of a *USP–NF* monograph and may not reflect the full and accurate contents of the currently official monograph. Please refer to the current edition of the *USP–NF* for official text.

USP provides this text to indicate changes that we anticipate will be made official once the product subject to this proposed revision under the Pending Monograph Program receives FDA approval. Once FDA approval is granted for the associated revision request, a Revision Bulletin will be posted that will include the changes indicated herein, as well as any changes indicated in the product's final approval, combined with the text of the monograph as effective on the date of approval. Any revisions made to a monograph under the Pending Monograph Program that are posted without prior publication for comment in the *Pharmacopeial Forum* must also meet the requirements outlined in the USP Guideline on Use of Accelerated Processes for Revisions to the *USP–NF*.

Notice of Intent to Revise
Official: To Be Determined

Diclofenac Potassium for Oral Solution

DEFINITION

Diclofenac Potassium for Oral Solution contains NLT 95.0% and NMT 105.0% of the labeled amount of diclofenac potassium ($C_{14}H_{10}Cl_2NKO_2$).

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: Dissolve 1.56 g of monobasic sodium phosphate dihydrate in 1000 mL of water. Adjust with phosphoric acid to a pH of 2.5.

Solution B: Dissolve 6.8 g of monobasic potassium phosphate and 0.88 g of sodium hydroxide in 1000 mL of water. Adjust with 1 N sodium hydroxide to a pH of 6.8.

Mobile phase: Acetonitrile and *Solution A* (40:60)

Diluent: Methanol and *Solution B* (10:90)

Standard solution: 0.2 mg/mL of USP Diclofenac Potassium RS in *Diluent*. Sonicate to dissolve, if needed.

Sample stock solution: Nominally 0.5 mg/mL of diclofenac potassium prepared as follows. Transfer a portion of finely powdered contents of NLT 5 packets of Diclofenac Potassium for Oral Solution, equivalent to 100 mg of diclofenac potassium, to a 200-mL volumetric flask. Add 140 mL of *Diluent*, and sonicate for about 10 min. Dilute with *Diluent* to volume. Centrifuge a portion of the solution. [Note—A centrifuge speed of 3500 rpm for 10 min may be suitable.]

Sample solution: Nominally 0.2 mg/mL of diclofenac potassium in *Diluent* from the *Sample stock solution*. Pass 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 × 15-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

Run time: NLT 1.4 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 potassium ($C_{14}H_{10}Cl_2NKO_2$) in the portion of Diclofenac Potassium for Oral 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 Potassium RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

- **Dissolution** ⟨711⟩

Medium: pH 6.8 phosphate buffer (19 g/L of trisodium phosphate dodecahydrate in 0.1 N hydrochloric acid, adjusted with 1 N sodium hydroxide to a pH of 6.8); 400 mL

Apparatus 2: 75 rpm

Time: 5 min

Solution A and **Chromatographic system:** Proceed as directed in the *Assay*.

Mobile phase: Acetonitrile and *Solution A* (50:50)

Standard solution: 0.125 mg/mL of USP Diclofenac Potassium RS prepared as follows. Transfer a quantity of USP Diclofenac Potassium RS to a suitable volumetric flask. Add methanol to 5% of the flask volume and sonicate to dissolve. Dilute with *Medium* to volume.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-um pore size.

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 potassium ($C_{14}H_{10}Cl_2NKO_2$) dissolved:

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

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 Potassium RS in the *Standard solution* (mg/mL)

V = volume of *Medium*, 400 mL

L = label claim of diclofenac potassium (mg/packet)

Tolerances: NLT 80% (Q) of the labeled amount of diclofenac potassium ($C_{14}H_{10}Cl_2NKO_2$) is dissolved.

- **Uniformity of Dosage Units ⟨905⟩:** Meets the requirements

IMPURITIES

- **Organic Impurities**

Solution A: Prepare as directed in the *Assay*.

Solution B: Dissolve 6.8 g of monobasic potassium phosphate in 1000 mL of water. Adjust with 1 N sodium hydroxide to a pH of 6.8.

Mobile phase: Methanol and *Solution A* (66:34)

Diluent: Methanol and *Solution B* (10:90)

Sensitivity solution: 0.5 µg/mL of USP Diclofenac Potassium RS in *Diluent*

Standard stock solution: 0.15 mg/mL of USP Diclofenac Related Compound A RS in methanol

Standard solution: 1 µg/mL of USP Diclofenac Related Compound A RS and 2.5 µg/mL of USP Diclofenac Potassium RS, prepared as follows. Transfer a volume of *Standard stock solution* and a quantity of USP Diclofenac Potassium RS to a suitable volumetric flask, and add *Diluent* to dissolve. Sonicate if needed. Dilute with *Diluent* to volume.

Sample solution: Nominally 500 µg/mL of diclofenac potassium in *Diluent*, prepared as follows. Transfer a portion of finely powdered contents of NLT 5 packets of Diclofenac Potassium for Oral Solution, equivalent to 50 mg of diclofenac potassium, to a 100-mL volumetric flask. Add 70 mL of *Diluent*, and sonicate for 10 min. Dilute with *Diluent* to volume. Pass a portion of the solution through a suitable filter of 0.45-µm pore size, and discard the first 5 mL of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; 5-µm packing L7

Flow rate: 1 mL/min

Injection volume: 25 µL

Run time: NLT 2.2 times the retention time of diclofenac

System suitability

Samples: *Sensitivity solution* and *Standard solution*

[Note—See *Table 1* for the relative retention times.]

Suitability requirements

Relative standard deviation: NMT 5.0% for diclofenac and diclofenac related compound A, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of diclofenac related compound A in the portion of Diclofenac Potassium for Oral Solution taken:

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

r_U = peak response of diclofenac related compound A from the *Sample solution*

r_S = peak response of diclofenac related compound A from the *Standard solution*

C_S = concentration of USP Diclofenac Related Compound A RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of diclofenac potassium in the *Sample solution* (µg/mL)

Calculate the percentage of any unspecified degradation product in the portion of Diclofenac Potassium for Oral Solution taken:

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

r_U = peak response of any unspecified degradation product from the *Sample solution*

r_S = peak response of diclofenac from the *Standard solution*

C_S = concentration of USP Diclofenac Potassium RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of diclofenac potassium in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Diclofenac related compound A	0.6	0.2
Diclofenac	1.0	—
Any unspecified degradation product	—	0.2
Total degradation products	—	1.0

SPECIFIC TESTS

● **Microbial Enumeration Tests** ⟨61⟩ and **Tests for Specified Microorganisms** ⟨62⟩**:** The total aerobic microbial count is NMT 10^3 cfu/g. The total combined yeasts and molds count is NMT 10^2 cfu/g. It meets the requirements of the test for absence of *Escherichia coli*.

Change to read:

● **pH** ⟨791⟩

Sample: Dissolve the contents of a unit dosage of Diclofenac Potassium for Oral Solution in 30 mL of water.

Acceptance criteria: 7.0–▲11.5▲ (TBD)

ADDITIONAL REQUIREMENTS

● **Packaging and Storage:** Store at controlled room temperature.

● **USP Reference Standards** ⟨11⟩

USP Diclofenac Potassium RS

USP Diclofenac Related Compound A RS

1-(2,6-Dichlorophenyl)indolin-2-one.

$C_{14}H_9Cl_2NO$	278.13

Page Information:

Not Applicable

Current DocID: