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Diclofenac Potassium for Oral Solution

DEFINITION

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click *www.uspnf.com/rb-diclofenac-na-for-os-20220429*.

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▲ (RB 31-Mar-2022)

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

Topic/Question	Contact	Expert Committee
DICLOFENAC POTASSIUM FOR ORAL SOLUTION	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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