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Diclofenac Sodium Extended-Release Tablets

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click www.uspnf.com/rb-notice-diclofenac-na-ert-20241122.

DEFINITION

Diclofenac Sodium Extended-Release Tablets contain 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 diclofenac peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

• **B.** The UV (190–400 nm) spectrum of the diclofenac peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Solution A: 0.7708 g/L of ammonium acetate in water. Adjust with acetic acid to a pH of 5.3. Pass through a suitable filter of 0.2-µm pore size.

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0.00	70	30
0.50	70	30
8.50	5	95
10.00	5	95
10.01	70	30
14.00	70	30

Diluent: Acetonitrile and water (50:50)

Standard solution: 0.2 mg/mL of USP Diclofenac Sodium RS in *Diluent*

Sample solution: Nominally 0.2 mg/mL of diclofenac sodium in *Diluent* prepared as follows. Transfer a suitable portion of diclofenac sodium to a suitable volumetric flask from NLT 20 finely powdered Tablets. Add *Diluent* equivalent to 70% of the flask volume. Dissolve with the aid of sonication for 25 min at 45° and fill with *Diluent* to volume. Pass the solution through a suitable filter of 0.22-µm pore size.

[Note—Protect the *Standard solution* and *Sample solution* from light.]

Chromatographic system

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

Mode: LC

Detector: UV 280 nm. For *Identification* test *B*, use a photo-diode array detector.

Column: 10-cm × 2.0-mm; 1.9-µm packing L1

Column temperature: 35°

Flow rate: 0.3 mL/min

Injection volume: 1 µL

System suitability

Sample: *Standard solution*

[Note—See *Table 2* for relative retention times.]

Suitability requirements

Tailing factor: NMT 1.2

Relative standard deviation: NMT 2.8%

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 Tablets 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%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Test 1

Medium: 0.05 M phosphate buffer, pH 7.5; 900 mL

Apparatus 2: 50 rpm; use wire sinkers.

Times: 1, 5, 10, 16, and 24 h

Detector: UV 276 nm

Standard solution: USP Diclofenac Sodium RS in *Medium*

Analysis: Pass portions of the solution under test through a suitable filter. Dilute with *Medium*, if necessary, to a concentration similar to that of the *Standard solution*.

Tolerances: See *Table 2*.

Table 2

Time (h)	Amount Dissolved
1	15%–35%
5	45%–65%
10	65%–85%
16	75%–95%
24	NLT 80%

The percentages of the labeled amount of diclofenac sodium ($C_{14}H_{10}Cl_2NNaO_2$) dissolved at the times specified conform to *Acceptance Table 2* in ⟨711⟩.

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium, Apparatus 2, and **Analysis:** Proceed as directed for *Dissolution Test 1*.

Times: 1, 2, 4, 6, and 10 h

Tolerances: See *Table 3*.

Table 3

Time (h)	Amount Dissolved
1	NMT 28%
2	20%–40%
4	35%–60%

Time (h)	Amount Dissolved
6	50%–80%
10	NLT 65%

The percentages of the labeled amount of diclofenac sodium ($C_{14}H_{10}Cl_2NNaO_2$) dissolved at the times specified conform to *Acceptance Table 2* in ⟨711⟩.

Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

Medium and **Analysis:** Proceed as directed for *Dissolution Test 1*.

Apparatus 1: 100 rpm

Times: 2, 4, 8, and 16 h

Tolerances: See *Table 4*.

Table 4

Time (h)	Amount Dissolved
2	22%–42%
4	34%–61%
8	52%–82%
16	NLT 73%

The percentages of the labeled amount of diclofenac sodium ($C_{14}H_{10}Cl_2NNaO_2$) dissolved at the times specified conform to *Acceptance Table 2* in ⟨711⟩.

Test 4: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 4*.

Medium and **Analysis:** Proceed as directed for *Dissolution Test 1*.

Apparatus 1: 100 rpm

Times: 2, 4, 8, and 16 h

Tolerances: See *Table 5*.

Table 5

Time (h)	Amount Dissolved
2	20%–40%
4	35%–55%
8	60%–85%
16	NLT 85%

The percentages of the labeled amount of diclofenac sodium ($C_{14}H_{10}Cl_2NNaO_2$) dissolved at the times specified conform to *Acceptance Table 2* in ⟨711⟩.

▲**Test 5:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 5*.

Medium: 0.05 M phosphate buffer, pH 7.5; 900 mL, deaerated

Apparatus 2: 50 rpm; with sinkers (*Dissolution* ⟨711⟩, *Figure 2a*)

Times: 1, 2, 4, 6, and 12 h

Buffer: Dissolve 0.77 g of ammonium acetate in 1 L of water. Adjust with acetic acid to a pH of 5.3.

Mobile phase: Acetonitrile and *Buffer* (45:55)

Standard stock solution: 0.28 mg/mL of USP Diclofenac Sodium RS prepared as follows. Transfer a quantity of USP Diclofenac Sodium RS to an appropriate volumetric flask and dissolve in 5% of the flask volume of methanol. Dilute with *Medium* to volume.

Standard solution: 0.112 mg/mL of USP Diclofenac Sodium RS from the *Standard stock solution* in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding an appropriate volume of filtrate so that a consistent result can be obtained.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 35°

Flow rate: 1.2 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 concentration (C_i) of diclofenac sodium ($C_{14}H_{10}Cl_2NNaO_2$) in the sample withdrawn from the vessel at each time point (*i*):

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

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)

Calculate the percentage of the labeled amount of diclofenac sodium ($C_{14}H_{10}Cl_2NNaO_2$) dissolved at each time point (*i*):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

$$\text{Result}_3 = (\{C_3 \times [V - (2 \times V_S)]\} + [(C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

$$\text{Result}_4 = (\{C_4 \times [V - (3 \times V_S)]\} + [(C_3 + C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

$$\text{Result}_5 = (\{C_5 \times [V - (4 \times V_S)]\} + [(C_4 + C_3 + C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

C_i = concentration of diclofenac sodium in the portion of sample withdrawn at time point *i* (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

V_S = volume of the *Sample solution* withdrawn at each time point (mL)

Tolerances: See *Table 6*.

Table 6

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	1	NMT 20
2	2	20–40
3	4	35–55
4	6	50–70
5	12	NLT 80

The percentages of the labeled amount of diclofenac sodium ($C_{14}H_{10}Cl_2NNaO_2$) dissolved at the times specified conform to *Dissolution ⟨711⟩, Acceptance Table 2*.▲ (RB 1-Dec-2024)

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

IMPURITIES

Change to read:

• **Organic Impurities**

Mobile phase and **Diluent:** Proceed as directed in the *Assay*.

Standard solution: 0.001 mg/mL each of USP Diclofenac Sodium RS and USP Diclofenac Related Compound A RS in *Diluent*

Sample solution: Nominally 1.0 mg/mL of diclofenac sodium in *Diluent* prepared as follows. Transfer a suitable portion of diclofenac sodium to a suitable volumetric flask from NLT 20 finely powdered Tablets. Add *Diluent* equivalent to 70% of the flask volume. Dissolve with the aid of sonication for 25 min at 45° and fill with *Diluent* to volume. Pass the solution through a suitable filter of 0.22-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 10-cm × 2.0-mm; 1.9-µm packing L1

Column temperature: 35°

Flow rate: 0.3 mL/min

Injection volume: 1 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 5%

Signal-to-noise ratio: NLT 10

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of diclofenac related compound A in the portion of Tablets 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* (mg/mL)

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

Calculate the percentage of any other impurity in the portion of Tablets taken:

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

r_U = peak response of each individual impurity 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: See ▲*Table 7*.▲ (RB 1-Dec-2024) Disregard any impurity peak less than 0.05%.

▲Table 7▲ (RB 1-Dec-2024)

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Oxindole[a,b]	0.4	—
Diclofenac	1.0	—
Diclofenac related compound D (diclofenac bromo analog)[c,b]	1.04	—
Diclofenac related compound A	1.48	0.5

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Diclofenac alcohol analog[d,b]	1.55	—
Diclofenac benzaldehyde analog[e,b]	1.81	—
Any individual unspecified impurity	—	0.5
Total impurities[b]	—	1.5

[a] 1,3-Dihydro-2*H*-indol-2-one.

[b] Process-related impurities, not to be counted in total impurities.

[c] 2-{2-[(2-Bromo-6-chlorophenyl)amino]phenyl}acetic acid.

[d] {2-[(2,6-Dichlorophenyl)amino]phenyl}methanol.

[e] 2-[(2,6-Dichlorophenyl)amino]benzaldehyde.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature, and protect from light and moisture.
- **Labeling:** When more than one *Dissolution* test is given, the labeling states the test used only if *Test 1* is not used.
- **USP Reference Standards** ⟨11⟩

USP Diclofenac Sodium RS

USP Diclofenac Related Compound A RS

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

$C_{14}H_9Cl_2NO$ 278.13

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

Topic/Question	Contact	Expert Committee
DICLOFENAC SODIUM EXTENDED-RELEASE TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

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