

Calculate the percentage of diclofenac related compound A in relation to the quantity of diclofenac sodium 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 each impurity other than diethyl phthalate, if present, in relation to the diclofenac sodium in the portion of Tablets taken:

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

- r_U = peak response for each impurity 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)

Acceptance criteria

- Individual impurities:** NMT 0.5% of diclofenac related compound A; NMT 1.0% of any other individual impurity
- Total impurities:** NMT 1.5%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers.
- **USP REFERENCE STANDARDS** <11>
 - USP Diclofenac Sodium RS
 - USP Diclofenac Related Compound A RS
 - N-(2,6-Dichlorophenyl)indolin-2-one.
 - C₁₄H₉Cl₂NO 278.14

Diclofenac Sodium Extended-Release Tablets

DEFINITION

Diclofenac Sodium Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of diclofenac sodium (C₁₄H₁₀Cl₂NNaO₂).

IDENTIFICATION

- **A.** The retention time of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B. THIN-LAYER CHROMATOGRAPHIC IDENTIFICATION TEST** <201>
 - Standard solution:** 2.0 mg/mL of USP Diclofenac Sodium RS in methanol. [NOTE—Shake by mechanical means for 10 min before makeup to final volume.]
 - Sample solution:** Equivalent to 2.0 mg/mL of diclofenac sodium from a portion of the powder (NLT 10 Tablets) in methanol. [NOTE—Sonicate for 10 min, and shake by mechanical means for 10 min before makeup to final volume. Centrifuge this solution, and use the clear supernatant.]
 - Developing solvent system:** Methanol, toluene, and glacial acetic acid (8:12:0.1)

ASSAY

• **PROCEDURE**

[NOTE—Protect the *Standard solution*, *System suitability solution*, and *Sample solution* from light.]
Diluent: Methanol and water (7:3)
Buffer: 0.01 M phosphoric acid and 0.01 M monobasic sodium phosphate. Adjust with appropriate component to a pH of 2.5.
Mobile phase: Methanol and *Buffer* (7:3)
Standard solution: 0.5 mg/mL of USP Diclofenac Sodium RS in *Diluent*
Resolution solution: 20 µg/mL of diethyl phthalate, 7.5 µg/mL of USP Diclofenac Related Compound A RS, and 0.75 mg/mL of USP Diclofenac Sodium RS in *Diluent*
Sample solution: Powder NLT 20 Tablets, and transfer a weighed portion of the powder, equivalent to 100 mg of diclofenac sodium, to a 200-mL volumetric flask, and add 150 mL of *Diluent*. Heat on a steam bath for 3–5 min, and sonicate for 20 min. Cool to room temperature, and dilute with *Diluent* to volume. Place the flask in an ice bath for 45 min, shaking occasionally to precipitate out any undissolved waxy material. Pass a portion of the chilled solution through a filter of 0.45-µm or finer pore size. Allow the filtrate to reach room temperature before using.

Chromatographic system

(See *Chromatography* <621>, *System Suitability*.)

- Mode:** LC
- Detector:** UV 254 nm
- Column:** 4.6-mm × 25-cm; packing L7
- Flow rate:** 1 mL/min
- Injection size:** 10 µL

System suitability

Samples: *Standard solution* and *Resolution solution*
 [NOTE—The relative retention times for diethyl phthalate, diclofenac related compound A, and diclofenac are 0.5, 0.6, and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.2 between the diethyl phthalate and diclofenac related compound A peaks, and NLT 3.8 between the diclofenac related compound A and diclofenac peaks, *Resolution solution*
Relative standard deviation: NMT 2.0% for diclofenac, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*
 Calculate the percentage of C₁₄H₁₀Cl₂NNaO₂ 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

• **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*

Tolerances: The percentages of the labeled amount of $C_{14}H_{10}Cl_2NNaO_2$ dissolved at the times specified conform to *Acceptance Table 2*.

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

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

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

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

Tolerances: The percentages of the labeled amount of $C_{14}H_{10}Cl_2NNaO_2$ dissolved at the times specified conform to *Acceptance Table 2*.

Time (h)	Amount Dissolved
1	NMT 28%
2	20%–40%
4	35%–60%
6	50%–80%
10	NLT 65%

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: The percentages of the labeled amount of $C_{14}H_{10}Cl_2NNaO_2$ dissolved at the times specified conform to *Acceptance Table 2*.

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

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 *Test 1*.

Apparatus 1: 100 rpm

Times: 2, 4, 8, and 16 h

Tolerances: The percentages of the labeled amount of $C_{14}H_{10}Cl_2NNaO_2$ dissolved at the times specified conform to *Acceptance Table 2*.

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

- **UNIFORMITY OF DOSAGE UNITS (905):** Meet the requirements

IMPURITIES

Organic Impurities

PROCEDURE

Diluent, Buffer, Mobile phase, Resolution solution, Sample solution, Chromatographic system, and Sys-

Standard stock solution: 0.8 mg/mL of USP Diclofenac Related Compound A RS in *Diluent*

Standard solution: 4 µg/mL of USP Diclofenac Related Compound A RS, made by diluting a measured volume of *Standard stock solution* with *Diluent*

System suitability solution: 0.5 mg/mL of USP Diclofenac Sodium RS in *Diluent*

System suitability

Samples: *Resolution solution* and *System suitability solution*

[NOTE—The relative retention times for diethyl phthalate, diclofenac related compound A, and diclofenac are 0.5, 0.6, and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.2 between the diethyl phthalate and diclofenac related compound A peaks; and NLT 3.8 between the diclofenac related compound A and the diclofenac peaks, *Resolution solution*

Standard deviation: NMT 2.0% for the diclofenac peak, *System suitability solution*

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of each impurity in the portion of Tablets taken:

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

r_U = peak response for any impurity from the *Sample solution*

r_S = peak response for USP Diclofenac Related Compound A RS from the *Standard solution*

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

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

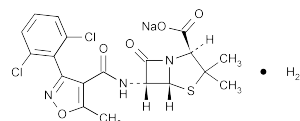
Acceptance criteria

Total impurities: NMT 1.5%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers. Store at controlled room temperature, and protect from light.
- **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
N-(2,6-Dichlorophenyl)indolin-2-one.
 $C_{14}H_9Cl_2NO$ 278.14

Dicloxacillin Sodium



$C_{19}H_{16}Cl_2N_3NaO_5S \cdot H_2O$ 510.32

4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[3-(2,6-dichlorophenyl)-5-methyl-

4-isoxazolyl]carbonyl]amino]-3,3-dimethyl-7-oxo-, monosodium salt, monohydrate, [2S-(2 α ,5 α ,6 β)]-

Monosodium (2S,5R,6R)-6-[3-(2,6-dichlorophenyl)-5-methyl-4-isoxazolecarboxamido]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate monohydrate [13412-64-1].

Anhydrous 492.32 [343-55-5].