

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.
  - C<sub>14</sub>H<sub>9</sub>Cl<sub>2</sub>NO 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 (C<sub>14</sub>H<sub>10</sub>Cl<sub>2</sub>NNaO<sub>2</sub>).

**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 C<sub>14</sub>H<sub>10</sub>Cl<sub>2</sub>NNaO<sub>2</sub> 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*

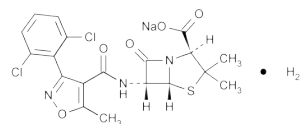
#### Acceptance criteria

**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

## Dicloxacin 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-(2α,5α,6β)]-. 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].