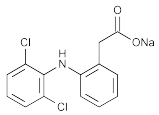
centage of the labeled amount of diclofenac potassium ($C_{14}H_{10}Cl_2KNO_2$) in the portion of the Tablets taken by the formula:

$$100(C_S / C_U)(r_U / r_S)$$

in which C_S is the concentration, in mg per mL, of diclofenac potassium in the *Standard preparation;* C_U is the concentration, in mg per mL, of diclofenac potassium in the *Assay preparation,* based on the label claim; and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Diclofenac Sodium



$C_{14}H_{10}Cl_2NNaO_2$ 318.13
Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, monosodium salt.
Sodium [*o*-(2,6-dichloroanilino)phenyl]acetate [15307-79-6].

» Diclofenac Sodium contains not less than 99.0 percent and not more than 101.0 percent of $C_{14}H_{10}Cl_2NNaO_2$, calculated on the dried basis.

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.
$C_{14}H_9Cl_2NO$ 278.14

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: The retention time of the diclofenac peak in the chromatogram of the *Test solution* corresponds to that of the *Resolution solution* as obtained in the test for *Chromatographic purity*.

C: The residue obtained by igniting it responds to the flame test for *Sodium* ⟨191⟩.

Color of solution—A 1 in 20 solution of it in methanol is colorless to faintly yellow, and the absorbance of the solution, determined in a 1-cm cell at 440 nm, is not more than 0.050, methanol being used as the blank.

Clarity of solution—The solution prepared as directed under *Color of solution* is not significantly less clear than an equal volume of methanol contained in a similar vessel and examined similarly.

pH ⟨791⟩: between 7.0 and 8.5, in a solution (1 in 100).

Loss on drying ⟨731⟩—Dry it at 105° to 110° for 3 hours: it loses not more than 0.5% of its weight.

Delete the following:

•**Heavy metals,** *Method II* ⟨231⟩—To prepare the *Test Preparation*, use a 100-mL borosilicate glass beaker or a quartz crucible. If the residue is not completely white after the ignition at 500° to 600°, add enough hydrogen peroxide to dissolve it, heat gently until dry, and ignite for 1 hour. Repeat the hydrogen peroxide treatment and ignition until the residue is completely white. Proceed as directed in *Test Preparation*, beginning with "Cool, add 4 mL of 6 N hydrochloric acid." The limit is 0.001%.• (Official 1-Dec-2015)

Chromatographic purity—

pH 2.5 Phosphate buffer—Mix equal volumes of 0.01 M phosphoric acid and 0.01 M monobasic sodium phosphate. If necessary, adjust with additional portions of the appropriate component to a pH of 2.5 ± 0.2.

Mobile phase—Prepare a filtered and degassed mixture of methanol and *pH 2.5 Phosphate buffer* (700:300). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩). [NOTE—Increasing the proportion of buffer increases resolution.]

Diluent—Prepare a mixture of methanol and water (70:30).

Standard solution—Prepare a solution of USP Diclofenac Related Compound A RS in methanol having a known concentration of about 0.75 mg per mL. Quantitatively dilute an accurately measured volume of this stock solution with *Diluent* to obtain a solution having a known concentration of about 1.5 µg per mL.

Resolution solution—Prepare a solution in *Diluent* containing 20 µg of diethyl phthalate, 7.5 µg of USP Diclofenac Related Compound A RS, and 0.75 mg of USP Diclofenac Sodium RS per mL.

Test solution—Transfer about 75 mg of Diclofenac Sodium, accurately weighed, to a 100-mL volumetric flask, dissolve in and dilute with *Diluent* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 25-cm column containing packing L7 (end-capped). The flow rate is about 1 mL per minute. Chromatograph the *Resolution solution,* and record the peak responses as directed for *Procedure:* the relative retention times are about 0.5 for diethyl phthalate, 0.6 for diclofenac related compound A, and 1.0 for diclofenac; and the resolution, *R,* between diethyl phthalate and diclofenac related compound A is not less than 2.2, and that between diclofenac related compound A and diclofenac is not less than 6.5. Chromatograph the *Standard solution*, and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 5%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the peak responses over a period of 2.5 times the retention time of diclofenac. Calculate the percentage of diclofenac related compound A in the portion of Diclofenac Sodium taken by the formula:

$$10(C / W)(r_U / r_S)$$

in which C is the concentration, in µg per mL, of USP Diclofenac Related Compound A RS in the *Standard solution;* W is the quantity, in mg, of Diclofenac Sodium taken to prepare the *Test solution;* and r_U and r_S are the diclofenac related compound A peak responses obtained from the *Test solution* and the *Standard solution,* respectively: not more than 0.2% is found. Calculate the percentage of each other impurity in the portion of Diclofenac Sodium taken by the formula:

$$10(C / W)(r_i / r_S)$$

in which r_i is the response of an individual impurity peak obtained from the *Test solution,* and the other terms are as defined above: not more than 0.2% of any individual impurity is found. The sum of all of the impurities found is not more than 0.5%.

Assay—Dissolve about 450 mg of Diclofenac Sodium, accurately weighed, in 25 mL of glacial acetic acid, and titrate with 0.1 N perchloric acid VS, determining the endpoint potentiometrically. Perform a blank determination, and

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make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 31.81 mg of $C_{14}H_{10}Cl_2NNaO_2$.

Diclofenac Sodium Delayed-Release Tablets

DEFINITION

Diclofenac Sodium Delayed-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. IDENTIFICATION TESTS—GENERAL,** *Sodium* ⟨**191**⟩**:** It meets the requirements of the flame test.

ASSAY

- **PROCEDURE**

Solution A: Mix equal volumes of 0.01 M phosphoric acid and 0.01 M monobasic sodium phosphate. If necessary, adjust with additional portions of the appropriate component to a pH of 2.5 ± 0.2.

Mobile phase: Methanol and *Solution A* (7:3)

[NOTE—Increasing the proportion of buffer increases resolution.]

Diluent: Methanol and water (7:3)

System suitability 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*

Standard solution: 0.75 mg/mL of USP Diclofenac Sodium RS in *Diluent*

Sample solution: Transfer 20 Tablets to a volumetric flask of such capacity that when filled to volume, a concentration of 0.75 mg/mL of diclofenac sodium is obtained. Add *Diluent* to about 70% of the capacity of the flask, and shake by mechanical means for NLT 30 min to disintegrate the Tablets. Cool to room temperature, and dilute with *Diluent* to volume. Pass a portion of the solution through a filter of 0.5-µm or finer pore size, and use the filtrate as the *Sample solution*.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; packing L7 (end-capped)

Flow rate: 1 mL/min

Injection size: 10 µL

System suitability

Samples: *System suitability solution* and *Standard 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; NLT 6.5 between the diclofenac related compound A and diclofenac peaks, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{14}H_{10}Cl_2NNaO_2$ in the portion of Tablets taken:

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

r_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**⟩**:** Proceed as directed for *Procedure*, *Apparatus 1 and Apparatus 2*, *Delayed-Release Dosage Forms*, *Method B* to determine the amount of $C_{14}H_{10}Cl_2NNaO_2$ dissolved.

Acid stage

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm, paddles constructed of (or coated with) polytef being used

Time: 2 h

Detector: UV maxima at about 276 nm

Standard solution: Transfer 68 mg of USP Diclofenac Sodium RS to a 100-mL volumetric flask, add 10.0 mL of 0.1 N sodium hydroxide, and dilute with water to volume. Transfer 2.0 mL of this solution to a second 100-mL volumetric flask, dilute with a mixture of 0.1 N hydrochloric acid and 5 N sodium hydroxide (900:20) to volume, and mix. This *Standard solution* contains 13.6 µg/mL of USP Diclofenac Sodium RS.

Sample solution: At the end of 2 h, remove each Tablet, or the major portion thereof if the Tablet is not intact, from the individual vessels, and subject them to the test under *Buffer stage*. To the 0.1 N hydrochloric acid remaining in each vessel, add 20.0 mL of 5 N sodium hydroxide, and stir for 5 min.

Buffer stage

Medium: pH 6.8 phosphate buffer; 900 mL

Apparatus 2: 50 rpm

Time: 45 min

Detector: UV maxima at about 276 nm

Solution A: 76 mg/mL of tribasic sodium phosphate

pH 6.8 phosphate buffer: *Solution A* and 0.1 N hydrochloric acid (1:3), adjusted with 2 N hydrochloric acid or 2 N sodium hydroxide to a pH of 6.8 ± 0.05, if necessary

Standard solution: Transfer 68 mg of USP Diclofenac Sodium RS to a 100-mL volumetric flask. Add 10.0 mL of 0.1 N sodium hydroxide, dilute with water to volume, and mix. Transfer 3.0 mL of this solution to a 100-mL volumetric flask, dilute with *Buffer stage Medium* to volume, and mix. The final concentration is about 0.0204 mg/mL of diclofenac sodium.

Sample solution: Sample per *Dissolution* ⟨711⟩. Dilute with *Medium* to a concentration similar to that of the *Standard solution*.

Tolerances: NLT 75% (Q) of the labeled amount of $C_{14}H_{10}Cl_2NNaO_2$ is dissolved.

- **UNIFORMITY OF DOSAGE UNITS** ⟨**905**⟩**:** Meet the requirements

IMPURITIES

Organic Impurities

- **PROCEDURE**

Solution A, Mobile phase, Diluent, System suitability solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

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

Standard solution: 4 µg/mL of USP Diclofenac Related Compound A RS from the *Standard stock solution* in *Diluent*

Analysis: Measure the peak responses over a period of 40 min.

USP Monographs

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