Assay—Dissolve about 0.5 g of Flurbiprofen, accurately weighed, in 100 mL of alcohol, previously neutralized with 0.1 N sodium hydroxide VS to the phenolphthalein endpoint, add phenolphthalein TS, and titrate with 0.1 N sodium hydroxide VS to the first appearance of a faint pink color that persists for not less than 30 seconds. Each mL of 0.1 N sodium hydroxide is equivalent to 24.43 mg of $C_{15}H_{13}FO_2$.

Flurbiprofen Tablets

» Flurbiprofen Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of flurbiprofen ($C_{15}H_{13}FO_2$).

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩**—**
USP Flurbiprofen RS

Identification—

A: Place a number of Tablets, equivalent to about 100 mg of flurbiprofen, in a flask, add 10 mL of 0.1 N hydrochloric acid, and sonicate until the Tablets disintegrate. Extract with two 15-mL portions of ether, combining the ether extracts in a flask containing about 1 g of anhydrous sodium sulfate. Decant the ether, and evaporate to dryness: the IR absorption spectrum of a mineral oil dispersion of the residue so obtained exhibits maxima only at the same wavelengths as that of a similar preparation of USP Flurbiprofen RS.

B: The retention time of the flurbiprofen peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

Dissolution ⟨711⟩**—**

pH 7.2 Phosphate buffer—Dissolve 245 g of monobasic potassium phosphate and 50 g of sodium hydroxide in water to make 2000 mL of solution. Dilute 333 mL of this stock solution to 6000 mL with water. If necessary, adjust with 5 N sodium hydroxide or with phosphoric acid to a pH of 7.20 ± 0.05.

Medium: pH 7.2 phosphate buffer; 900 mL.

Apparatus 2: 50 rpm.

Time: 45 minutes.

Procedure—Determine the amount of $C_{15}H_{13}FO_2$ dissolved from UV absorbances at the wavelength of maximum absorbance at about 247 nm on filtered portions of the solution under test, suitably diluted with *Dissolution Medium*, in comparison with a Standard solution having a known concentration of USP Flurbiprofen RS in the same *Medium*.

Tolerances—Not less than 75% *(Q)* of the labeled amount of $C_{15}H_{13}FO_2$ is dissolved in 45 minutes.

Uniformity of dosage units ⟨905⟩**:** meet the requirements, the following procedure being used where the test for *Content Uniformity* is required.

Procedure for content uniformity—Proceed as directed in the *Assay*, except in preparing the *Assay preparation* to use 1 Tablet and to use 10.0 mL of *Internal standard solution* for each 25 mg of flurbiprofen in the Tablet, based on the labeled amount.

Assay—

Mobile phase—Dissolve 1.4 g of monobasic sodium phosphate in 570 mL of water, add 430 mL of acetonitrile, and adjust with phosphoric acid to a pH of 3.0. Filter and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Internal standard solution—Dissolve acetophenone in *Mobile phase* to obtain a solution having a concentration of about 0.8 µL per mL.

Standard preparation—Accurately weigh about 30 mg of USP Flurbiprofen RS. Add 10.0 mL of *Internal standard solution*, and swirl to dissolve. This stock solution contains about 3 mg of USP Flurbiprofen RS per mL. Dilute a portion of this stock solution with 20 volumes of *Mobile phase*, and mix.

Assay preparation—Place 3 Tablets in a stoppered container. Based on the labeled amount, in mg, of flurbiprofen in each Tablet, add 25.0 mL of *Internal standard solution* for each 75 mg of flurbiprofen in the 3 Tablets. Shake by mechanical means for about 15 minutes, and centrifuge. Dilute a portion of this solution with 20 volumes of *Mobile phase*, and mix.

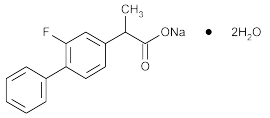
Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4-mm × 25-cm column containing packing L7. The flow rate is about 2 mL per minute. Chromatograph the *Standard preparation*, and record the responses as directed for *Procedure:* the relative retention times are about 0.4 for acetophenone and 1.0 for flurbiprofen; the resolution, *R,* between the acetophenone and flurbiprofen is not less than 8; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of flurbiprofen ($C_{15}H_{13}FO_2$) in the portion of Tablets taken by the formula:

$$(WV / 10)(R_U / R_S)$$

in which W is the quantity, in mg, of USP Flurbiprofen RS used to prepare the *Standard preparation; V* is the volume, in mL, of *Internal standard solution* used to prepare the *Assay preparation;* and R_U and R_S are the ratios of the flurbiprofen peak response to the acetophenone peak response obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Flurbiprofen Sodium



$C_{15}H_{12}FNaO_2 \cdot 2H_2O$ 302.27
[1,1′-Biphenyl]-4-acetic acid, 2-fluoro-α-methyl, sodium salt dihydrate, (±)-.
Sodium (±)-2-(2-fluoro-4-biphenylyl)propionate dihydrate.
Anhydrous 266.25

» Flurbiprofen Sodium contains not less than 97.0 percent and not more than 103.0 percent of $C_{15}H_{12}FNaO_2 \cdot 2H_2O$.

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩**—**
USP Flurbiprofen RS
USP Flurbiprofen Sodium RS
USP Flurbiprofen Related Compound A RS
2-(4-Biphenylyl)propionic acid.
$C_{15}H_{14}O_2$ 226.28

Identification—

A: *Infrared Absorption* ⟨197M⟩—

Test specimen: previously dried.

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 10 µg per mL.

Medium: pH 6.0 buffer consisting of 2.42 g of monobasic sodium phosphate and 0.66 g of dibasic sodium phosphate dissolved in water to make 1000 mL.

Absorptivities at 246 nm, calculated on the dried basis, do not differ by more than 3.0%.

C: The residue obtained by igniting it meets the requirements of the tests for *Sodium* ⟨191⟩.

Specific rotation ⟨781S⟩: between –0.45° and +0.45°.

Test solution: 50 mg per mL, in methanol.

Loss on drying ⟨731⟩—Dry about 0.3 g of it in vacuum at a pressure not exceeding 1 mm of mercury over phosphorus pentoxide in a suitable drying tube at 60° for 18 hours: it loses not less than 11.3% and not more than 12.5% of its weight.

Heavy metals, *Method II* ⟨231⟩: 0.001%.

Limit of flurbiprofen related compound A—

Diluent, *Mobile phase*, and *System suitability preparation*—Proceed as directed in the *Assay.*

Standard solution—Use *Standard flurbiprofen related compound A preparation*, prepared as directed in the *Assay.*

Test solution—Use the *Assay preparation*.

Chromatographic system—Proceed as directed in the *Assay*, except to chromatograph the *Standard solution* instead of the *Standard preparation.*

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the percentage of flurbiprofen related compound A in the portion of Flurbiprofen Sodium taken by the formula:

$$200(C/W)(r_U / r_S)$$

in which *C* is the concentration, in µg per mL, of USP Flurbiprofen Related Compound A RS in the *Standard solution; W* is the weight, in mg, of the portion of Flurbiprofen Sodium taken to prepare the *Test solution;* and r_U and r_S are the peak areas for flurbiprofen related compound A obtained from the *Test solution* and the *Standard solution*, respectively: not more than 1.5% is found.

Assay—

Diluent—Mix 500 mL of methanol and 250 mL of water.

Mobile phase—Prepare a filtered and degassed mixture of acetonitrile, water, and glacial acetic acid (50:49:1). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard flurbiprofen related compound A preparation—Dissolve an accurately weighed quantity of USP Flurbiprofen Related Compound A RS in methanol to obtain a stock solution having a known concentration of about 150 µg per mL. Transfer 1.0 mL of this solution to a 200-mL volumetric flask, dilute with *Diluent* to volume, and mix.

Standard preparation—Dissolve an accurately weighed quantity of USP Flurbiprofen RS in methanol to obtain a stock solution having a known concentration of about 1 mg per mL. Transfer 5.0 mL of this solution to a 100-mL volumetric flask, dilute with *Diluent* to volume, and mix.

System suitability preparation—Transfer 5 mL of the stock solution used to prepare the *Standard preparation* and 2 mL of the stock solution used to prepare the *Standard flurbiprofen related compound A preparation* to a 100-mL volumetric flask, dilute with *Diluent* to volume, and mix.

Assay preparation—Transfer about 100 mg of Flurbiprofen Sodium, accurately weighed, to a 100-mL volumetric flask, dissolve in and dilute with methanol to volume, and mix. Transfer 5.0 mL of this solution to a second 100-mL volumetric flask, dilute with *Diluent* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.0-mm × 25-cm column that contains 10-µm packing L7. The flow rate is about 2 mL per minute. Chromatograph the *System suitability preparation*, and record the peak responses as directed for *Procedure:* the resolution, *R,* between flurbiprofen related compound A and flurbiprofen is not less than 1.0. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the tailing factor is not more than 2.5; and the relative standard deviation for replicate injections is not more than 1.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the percentage of $C_{15}H_{12}FNaO_2 \cdot 2H_2O$ in the portion of Flurbiprofen Sodium taken by the formula:

$$200(302.27/244.27)(C/W)(r_U / r_S)$$

in which 302.27 and 244.27 are the molecular weights of flurbiprofen sodium dihydrate and anhydrous flurbiprofen, respectively; *C* is the concentration, in µg per mL, of USP Flurbiprofen RS in the *Standard preparation; W* is the weight, in mg, of the portion of Flurbiprofen Sodium taken to prepare the *Assay preparation;* and r_U and r_S are the flurbiprofen peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Flurbiprofen Sodium Ophthalmic Solution

» Flurbiprofen Sodium Ophthalmic Solution contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of flurbiprofen sodium ($C_{15}H_{12}FNaO_2 \cdot 2H_2O$).

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—
USP Flurbiprofen RS
USP Flurbiprofen Related Compound A RS
2-(4-Biphenylyl)propionic acid.
$C_{15}H_{14}O_2$ 226.28

Identification—The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation*, as obtained in the *Assay*.

pH ⟨791⟩: between 6.0 and 7.0.

Antimicrobial effectiveness ⟨51⟩: meets the requirements.

Sterility ⟨71⟩—It meets the requirements when tested as directed for *Membrane Filtration* under *Test for Sterility of the Product to be Examined.*

Assay—

Diluent, Mobile phase, Standard flurbiprofen related compound A preparation, Standard preparation, and *System suitability preparation*—Proceed as directed in the *Assay* under *Flurbiprofen Sodium*.

Assay preparation—Use the undiluted Ophthalmic Solution.

Chromatographic system—Proceed as directed in the *Assay* under *Flurbiprofen Sodium*, using a 4.0-mm × 5-cm guard column that contains 5-µm packing L1.

Procedure—Separately inject equal volumes (about 15 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and meas-