Naproxen Tablets

» Naproxen Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of naproxen ($C_{14}H_{14}O_3$).

Packaging and storage—Preserve in well-closed containers.

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

Identification—Prepare a mixture of the *Standard preparation* and the *Assay preparation* (1:1), prepared as directed in the *Assay*, and chromatograph as directed in the *Assay:* the chromatogram so obtained exhibits two main peaks, corresponding to naproxen and the internal standard.

Dissolution ⟨711⟩**—**

0.1 M, pH 7.4 phosphate buffer—Dissolve 2.62 g of monobasic sodium phosphate and 11.50 g of anhydrous dibasic sodium phosphate in 1000 mL of water, and mix.

Medium: 0.1 M, pH 7.4 phosphate buffer; 900 mL.

Apparatus 2: 50 rpm.

Time: 45 minutes.

Procedure—Determine the amount of $C_{14}H_{14}O_3$ dissolved from UV absorbances at the wavelength of maximum absorbance at about 332 nm of filtered portions of the solution under test, suitably diluted with *0.1 M, pH 7.4 phosphate buffer*, in comparison with a Standard solution having a known concentration of USP Naproxen RS in the same medium.

Tolerances—Not less than 80% *(Q)* of the labeled amount of $C_{14}H_{14}O_3$ is dissolved in 45 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Assay—

Mobile phase—Prepare a suitable mixture of acetonitrile, water, and glacial acetic acid (50:49:1). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩). Increased resolution may be achieved by increasing the proportion of water in the *Mobile phase*.

Solvent mixture—Prepare a suitable mixture of acetonitrile and water (90:10).

Internal standard solution—Dilute 5 mL of butyrophenone with acetonitrile to make 100 mL. Dilute 1 mL of the resulting solution with acetonitrile to make 100 mL. Each mL of this solution contains about 0.5 µL of butyrophenone.

Standard preparation—Dissolve an accurately weighed quantity of USP Naproxen RS in *Solvent mixture* to obtain a solution having a known concentration of about 2.5 mg per mL. Transfer 1.0 mL of the resulting solution and 2.0 mL of *Internal standard solution* to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. This solution contains about 25 µg of USP Naproxen RS per mL.

Assay preparation—Weigh and finely powder not less than 20 Tablets. Transfer an accurately weighed quantity of the powder, equivalent to about 250 mg of naproxen, to a 100-mL volumetric flask. Add 10 mL of water, and sonicate for 10 minutes until the material is completely dispersed. Add about 80 mL of acetonitrile, and sonicate for an additional 5 minutes. Allow the flask to reach room temperature, dilute with acetonitrile to volume, and mix. Allow any insoluble matter to settle, then transfer 1.0 mL of the clear supernatant to a 100-mL volumetric flask, add 2.0 mL of *Internal standard solution*, dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 15-cm column that contains 5-µm packing L1. The flow rate is about 1.2 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed under *Procedure*: the column efficiency, determined from the analyte peak, is not less than 4000 theoretical plates when calculated by the formula:

$$5.545(t / W_{h/2})^2$$

the resolution between the analyte and internal standard peaks is not less than 11.5 when calculated by the formula:

$$2(t_2 - t_1) / [1.699(W_{1h/2} + W_{2h/2})]$$

and the relative standard deviation of replicate injections is not more than 1.5%.

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. The relative retention times are about 0.6 for naproxen and 1.0 for the internal standard. Calculate the quantity, in mg, of $C_{14}H_{14}O_3$ in the portion of Tablets taken by the formula:

$$10C(R_U / R_S)$$

in which C is the concentration, in µg per mL, of USP Naproxen RS in the *Standard preparation*, and R_U and R_S are the ratios of the response of the naproxen peak to the response of the internal standard peak obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Naproxen Delayed-Release Tablets

» Naproxen Delayed-Release Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of naproxen ($C_{14}H_{14}O_3$).

Packaging and storage—Preserve in well-closed containers, and store at controlled room temperature.

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

Identification—

A: *Ultraviolet Absorption* ⟨197U⟩—

Test solution—Use the solution under test as obtained in the *Buffer stage* of the *Dissolution* test.

Standard solution—Use the Standard solution prepared as directed in the *Buffer stage* of the *Dissolution* test.

B: 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*.

Dissolution, *Delayed-Release Dosage Forms, Method B* ⟨711⟩**—**

ACID STAGE—

Acid stage medium: 0.1 N hydrochloric acid; 1000 mL.

Apparatus 2: 50 rpm.

Time: 2 hours.

Procedure—Determine the amount of $C_{14}H_{14}O_3$ dissolved by employing UV absorption at the wavelength of maximum absorbance at about 332 nm on filtered portions of the solution under test, suitably diluted with *Acid stage medium,* if necessary, in comparison with a Standard solution having a known concentration of USP Naproxen RS in the same *Acid stage medium.*

Tolerances—Not more than 10% (*Q*) of the labeled amount of $C_{14}H_{14}O_3$ is dissolved in 2 hours.

BUFFER STAGE—

Buffer stage medium: 0.2 M phosphate buffer, pH 6.8; 1000 mL.

Apparatus 2: 50 rpm.

Time: 45 minutes.

Procedure—Determine the amount of $C_{14}H_{14}O_3$ dissolved by employing UV absorption at the wavelength of maximum absorbance at about 332 nm on filtered portions of the solution under test, suitably diluted with *Buffer stage medium,* if necessary, in comparison with a Standard solution having a known concentration of USP Naproxen RS in the same *Buffer stage medium.*

Tolerances—Not less than 80% *(Q)* of the labeled amount of $C_{14}H_{14}O_3$ is dissolved in 45 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

PROCEDURE FOR CONTENT UNIFORMITY—

Mobile phase, Diluent A, Diluent B, and *Chromatographic system*—Proceed as directed in the *Assay.*

Standard solution—Transfer about 12.5 mg of USP Naproxen RS, accurately weighed, to a 50-mL volumetric flask, dilute with *Diluent A* to volume, and mix well. Transfer 10 mL of this solution to a 25-mL volumetric flask, dilute with *Diluent B* to volume, and mix.

Test solution—Transfer 1 Tablet to a 200-mL volumetric flask, and add about 140 mL of *Diluent B.* Shake by mechanical means for 15 minutes, sonicate for 15 minutes, dilute with *Diluent B* to volume, and mix. Pass a portion of this solution through a filter having a porosity of 0.45-µm, pipet 2.0 mL of the filtrate for a 500-mg tablet and 2.5 mL for a 375-mg tablet into a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Assay—

Mobile phase—Prepare a filtered and degassed mixture of 1% acetic acid solution and acetonitrile (11:9).

Diluent A—Use acetonitrile and water (9:1).

Diluent B—Use acetonitrile and water (1:1).

Standard stock preparation—Transfer about 12.5 mg of USP Naproxen RS, accurately weighed, to a 25-mL volumetric flask. Dissolve in and dilute with *Diluent A* to volume, and mix.

Standard preparation—Accurately transfer 10.0 mL of the *Standard stock preparation* into a 50-mL volumetric flask, and dilute with *Mobile phase* to volume, and mix.

Assay preparation—Weigh and powder 20 Tablets. Accurately weigh an amount of the powder, equivalent to about 250 mg of naproxen, into a 100-mL volumetric flask, and add about 70 mL of *Diluent B.* Shake by mechanical means for 15 minutes, sonicate for 15 minutes, dilute with *Diluent B* to volume, and mix. Pass this solution through a filter having a porosity of 0.45-µm, transfer 2.0 mL of the filtrate into a 50-mL volumetric flask, dilute with *Mobile phase* 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 that contains 5-µm packing L1. The flow rate is about 1.0 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the tailing factor of the naproxen peak is not more than 1.5, and the relative standard deviation for replicate injections of the *Standard preparation* is not more than 2.0%.

Procedure—Separately inject equal volumes (about 50 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the naproxen peak. Calculate the quantity, in mg, of naproxen ($C_{14}H_{14}O_3$) in the portion of Tablets taken by the formula:

$$2500C(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Naproxen RS in the *Standard preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Naproxen Sodium

$C_{14}H_{13}NaO_3$ 252.24

2-Naphthaleneacetic acid, 6-methoxy-α-methyl-, sodium salt, (*S*)-.

(–)-Sodium (*S*)-6-methoxy-α-methyl-2-naphthaleneacetate [26159-34-2].

» Naproxen Sodium contains not less than 98.0 percent and not more than 102.0 percent of $C_{14}H_{13}NaO_3$, calculated on the dried basis.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩**—**
USP Naproxen Sodium RS

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 25 µg per mL.

Medium: methanol.

Absorptivities at 272 nm, calculated on the dried basis, do not differ by more than 3%.

Specific rotation ⟨781S⟩: between –15.3° and –17.0°.

Test solution: 50 mg per mL, in 0.1 N sodium hydroxide.

Loss on drying ⟨731⟩**—**Dry it in vacuum at 105° for 3 hours: it loses not more than 1.0% of its weight.

Heavy metals, *Method I* ⟨231⟩**—**Dissolve 1.0 g in 20 mL of water in a separator, add 5 mL of 1 N hydrochloric acid, and extract with successive 20-mL, 20-mL, and 10-mL portions of methylene chloride. Discard the methylene chloride extracts, and use the aqueous layer for the test: the limit is 0.002%.

Free naproxen—Dissolve about 5.0 g in 25 mL of water in a separator, and extract the solution with three 15-mL portions of chloroform. Evaporate the combined extracts on a steam bath to dryness. Dissolve the residue in 10 mL of a mixture of methanol and water (3:1) previously neutralized with 0.1 N sodium hydroxide to the phenolphthalein endpoint. Add phenolphthalein TS, and titrate with 0.10 N sodium hydroxide: not more than 2.2 mL is consumed (1.0%).

Chromatographic purity—Dissolve 100 mg in 5 mL of methanol. Dissolve a suitable quantity of USP Naproxen Sodium RS in methanol to obtain a *Standard solution* having a known concentration of about 20 mg per mL. Dilute a portion of this solution quantitatively with methanol to obtain three *Comparison solutions* having concentrations of 20, 60, and 100 µg per mL (0.1%, 0.3%, and 0.5% of the *Standard solution*), respectively. Apply separate 10-µL portions of the five solutions on the starting line to a suitable thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with a 0.25-mm layer of chromatographic silica gel mixture. Develop the chromatogram in a solvent system consisting of a mixture of toluene, tetrahydrofuran, and glacial acetic acid (30:3:1) until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the chamber, mark the solvent front, air-dry, and view under short-wavelength UV light: the R_F value of the principal spot in the chromatogram of the solution under test corresponds to that of the *Standard solution,* the intensity of any individual secondary spot does not exceed that of the 100-µg-per-mL *Comparison solution* (0.5%), and the sum of the intensities of any secondary spots, similarly compared, does not exceed 2.0%.

Assay—Dissolve about 200 mg of Naproxen Sodium, accurately weighed, in 50 mL of glacial acetic acid containing 2 drops of *p*-naphtholbenzein TS previously neutralized with 0.1 N perchloric acid if necessary. Titrate with 0.1 N perchloric acid VS. Each mL of 0.1 N perchloric acid is equivalent to 25.22 mg of $C_{14}H_{13}NaO_3$.