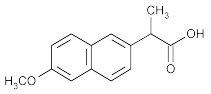
Naproxen



$C_{14}H_{14}O_3$ 230.26
2-Naphthaleneacetic acid, 6-methoxy-α-methyl-, (*S*)-.
(+)-(*S*)-6-Methoxy-α-methyl-2-naphthaleneacetic acid [22204-53-1].

» Naproxen contains not less than 98.5 percent and not more than 101.5 percent of $C_{14}H_{14}O_3$, calculated on the dried basis.

Packaging and storage—Preserve in tight containers.

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

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 25 µg per mL.

Medium: methanol.

Absorptivities at 271 nm, calculated on the dried basis, do not differ by more than 3%.

Specific rotation ⟨781S⟩**:** between +83.0° and +89.5°.

Test solution: 10 mg per mL, in methyl isobutyl ketone.

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

Heavy metals, *Method II* ⟨231⟩**:** 0.002%.

Chromatographic purity—Dissolve 100 mg of Naproxen in methanol, and dilute with methanol to 5.0 mL to obtain the *Test solution.* Dissolve a suitable quantity of USP Naproxen 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 and stepwise 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 to the starting line of 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 *Test solution* corresponds to that of the *Standard solution,* and any other spot obtained from the *Test solution* does not exceed, in size or intensity, the principal spot obtained from 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 500 mg of Naproxen, accurately weighed, in a mixture of 75 mL of methanol and 25 mL of water that has been previously neutralized to the phenolphthalein endpoint with 0.1 N sodium hydroxide. Dissolve by gentle warming, if necessary, add phenolphthalein TS, and titrate with 0.1 N sodium hydroxide VS. Each mL of 0.1 N sodium hydroxide is equivalent to 23.03 mg of $C_{14}H_{14}O_3$.

Naproxen Oral Suspension

» Naproxen Oral Suspension contains 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 tight, light-resistant containers. Store at room temperature.

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 thus obtained exhibits two main peaks corresponding to naproxen and the internal standard.

Uniformity of dosage units ⟨905⟩**—**

FOR ORAL SUSPENSION PACKAGED IN SINGLE-UNIT CONTAINERS: meets the requirements.

Deliverable volume ⟨698⟩**—**

FOR ORAL SUSPENSION PACKAGED IN MULTIPLE-UNIT CONTAINERS: meets the requirements.

pH ⟨791⟩**:** between 2.2 and 3.7.

Assay—

Mobile phase—Prepare a mixture of 500 mL of methanol, 500 mL of water, and 2.46 g of anhydrous sodium acetate, and mix until dissolved. Adjust with glacial acetic acid to a pH of 5.8. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Internal standard solution—Prepare a solution of ethylparaben in methanol containing about 1.1 mg per mL.

Standard preparation—Transfer about 62.5 mg of USP Naproxen RS, accurately weighed, to a 50-mL volumetric flask, add about 30 mL of methanol, and sonicate to dissolve. Add 5.0 mL of *Internal standard solution,* dilute with methanol to volume, and mix. Transfer 2.0 mL of this solution to a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. This solution contains about 50 µg of USP Naproxen RS and 4.4 µg of ethylparaben per mL.

Assay preparation—Transfer an accurately measured volume of Oral Suspension, previously well-mixed and free from air bubbles, equivalent to about 125 mg of naproxen, to a 100-mL volumetric flask, using a "to contain" pipet. Rinse the pipet several times with methanol, and add the rinsings to the volumetric flask. Add 10.0 mL of *Internal standard solution*, dilute with methanol to volume, and mix. Transfer 2.0 mL of this solution to a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. Filter, if necessary, to obtain a clear solution.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 2 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the relative retention times are about 0.6 for ethylparaben and 1.0 for naproxen; the resolution, *R,* between ethylparaben and naproxen is not less than 3.0; the tailing factor for the naproxen peak is not more than 2.0; and the relative standard deviation for replicate injections is not more than 1.5%.

Procedure—Separately inject equal volumes (about 35 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 naproxen ($C_{14}H_{14}O_3$) in each mL of the Oral Suspension taken by the formula:

$$2.5(C / V)(R_U / R_S)$$

in which C is the concentration, in µg per mL, of USP Naproxen RS in the *Standard preparation; V* is the volume, in mL, of Oral Suspension taken to prepare the *Assay preparation;* and R_U and R_S are the ratios of the response of the naproxen peak to the response of the ethylparaben peak obtained from the *Assay preparation* and the *Standard preparation,* respectively.