Naproxen Sodium Tablets

DEFINITION

Naproxen Sodium Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of naproxen sodium ($C_{14}H_{13}NaO_3$).

IDENTIFICATION

- **A. IDENTIFICATION TESTS—GENERAL ⟨191⟩,** *Chemical Identification Tests, Sodium*
  Sample: Transfer an amount nominally equivalent to about 250 mg of naproxen sodium from finely powdered Tablets to a centrifuge tube. Add 12 mL of water and 1 mL of hydrochloric acid. A dense white precipitate is formed. Centrifuge the mixture. Use the clear supernatant for the test.
  Acceptance criteria: Meets the requirements
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **C.** The UV absorption spectra of the major peak of the *Sample solution* and that of the *Standard solution* exhibit maxima and minima at the same wavelengths, as obtained in the *Assay*.

ASSAY

Change to read:

- **PROCEDURE**
  Mobile phase: Acetonitrile, water, and glacial acetic acid (450:540:10)
  Standard solution: 0.1 mg/mL of USP Naproxen Sodium RS in *Mobile phase*
  Sample stock solution: Nominally 1.0 mg/mL of naproxen sodium from Tablets prepared as follows. Transfer an appropriate amount of naproxen sodium from NLT 20 Tablets, finely powdered, to a suitable volumetric flask. Add 15% of the volume of water and sonicate for 5 min. Add 50% of the volume of *Mobile phase* and sonicate for an additional 30 min, shaking intermittently. Allow the solution to cool to room temperature and then dilute with *Mobile phase* to volume. Centrifuge or pass a portion of this solution through a suitable filter. (IRA 1-May-2018)
  Sample solution: Nominally equivalent to 0.1 mg/mL of naproxen sodium in *Mobile phase* from *Sample stock solution*
  Chromatographic system
  (See *Chromatography* ⟨621⟩, *System Suitability*.)
  Mode: LC
  Detector: UV 254 nm, diode array
  Column: 4.6-mm × 15-cm; 5-µm packing L7
  Flow rate: 1.2 mL/min
  Injection volume: 20 µL
  Run time: NLT 2 times the retention time of naproxen
  System suitability
  Sample: *Standard solution*
  Suitability requirements
  Tailing factor: NMT 2.0
  Relative standard deviation: NMT 2.0%
  Analysis
  Samples: *Standard solution* and *Sample solution*
  Calculate the percentage of the labeled amount of naproxen sodium ($C_{14}H_{13}NaO_3$) in the portion of Tablets taken:

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

r_U = peak response of naproxen from the *Sample solution*
r_S = peak response of naproxen from the *Standard solution*
C_S = concentration of USP Naproxen Sodium RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of naproxen sodium in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

- **DISSOLUTION ⟨711⟩**
  Buffer: 0.1 M of a phosphate buffer with a pH of 7.4, containing 2.62 g/L of monobasic sodium phosphate and 11.50 g/L of anhydrous dibasic sodium phosphate in water
  Medium: *Buffer*; 900 mL
  Apparatus 2: 50 rpm
  Time: 45 min
  Standard solution: 50 µg/mL of USP Naproxen Sodium RS in *Medium*
  Sample solution: Dilute a filtered portion of the solution under test with *Medium* as necessary to obtain a nominal concentration of 50 µg/mL of naproxen sodium ($C_{14}H_{13}NaO_3$).
  Instrumental conditions
  Mode: UV
  Analytical wavelength: About 332 nm (maximum absorbance)
  Analysis
  Samples: *Standard solution* and *Sample solution*
  Calculate the percentage of the labeled amount of naproxen sodium ($C_{14}H_{13}NaO_3$) dissolved.
  Tolerances: NLT 80% (*Q*) of the labeled amount of naproxen sodium ($C_{14}H_{13}NaO_3$) is dissolved.
- **UNIFORMITY OF DOSAGE UNITS ⟨905⟩:** Meet the requirements

IMPURITIES

Change to read:

- **ORGANIC IMPURITIES**
  Solution A: Dissolve 1.36 g of monobasic potassium phosphate in 1 L of water. Adjust with triethylamine to a pH of 6.5. Pass through a suitable filter of 0.45-µm pore size.
  Solution B: Acetonitrile
  Diluent: Acetonitrile and *Solution A* (50:50)
  Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	85	15
5	85	15
25	60	40
45	50	50
50	85	15
60	85	15

Standard stock solution 1: 0.05 mg/mL (IRA 1-May-2018) of USP Naproxen Sodium RS in *Diluent* (IRA 1-May-2018)
Standard stock solution 2: 0.01 mg/mL of USP Naproxen Related Compound A RS in methanol
Standard stock solution 3: 0.01 mg/mL of USP Naproxen Related Compound L RS in methanol
System suitability solution: 0.5 mg/mL of USP Naproxen Sodium RS and 0.5 µg/mL of USP Naproxen Related Compound A RS in *Diluent*, from *Standard*

stock solution 1 and *Standard stock solution 2*, respectively

Standard solution: 1.0 µg/mL of USP Naproxen Sodium RS, and 0.5 µg/mL each of USP Naproxen Related Compound A RS and USP Naproxen Related Compound L RS in *Diluent*, from *Standard stock solution 1*, *Standard stock solution 2*, and *Standard stock solution 3*, respectively

●**Sample stock solution:** Nominally 1.0 mg/mL of naproxen sodium from Tablets prepared as follows. Transfer an appropriate amount of naproxen sodium from NLT 20 Tablets, finely powdered, to a suitable volumetric flask. Add 15% of the volume of water and sonicate for 5 min. Add 50% of the volume of *Mobile phase* described in the *Assay* and sonicate for an additional 30 min, shaking intermittently. Allow the solution to cool to room temperature and then dilute with *Mobile phase* described in the *Assay* to volume. Centrifuge or pass a portion of this solution through a suitable filter.● (IRA 1-May-2018)

Sample solution: Nominally equivalent to 0.55 mg/mL of naproxen sodium in *Diluent* from the *Sample stock solution*

Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 236 nm
Column: 4.6-mm × 15-cm; 5-µm packing L7
Column temperature: 40°
Flow rate: 1.0 mL/min
Injection volume: 10 µL

System suitability
Samples: *System suitability solution* and *Standard solution*
Suitability requirements
Resolution: NLT 6.0 between naproxen related compound A and naproxen, *System suitability solution*
Relative standard deviation: NMT 5.0% for naproxen, naproxen related compound A, and naproxen related compound L, *Standard solution*

Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of naproxen related compound A and naproxen related compound L in the portion of Tablets taken:

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

r_U = peak response of naproxen related compound A or naproxen related compound L from the *Sample solution*
r_S = peak response of naproxen related compound A or naproxen related compound L from the *Standard solution*
C_S = concentration of USP Naproxen Related Compound A RS or USP Naproxen Related Compound L RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of naproxen sodium in the *Sample solution* (mg/mL)

Calculate the percentage of naproxen methyl ester and any individual unspecified degradation product in the portion of Tablets taken:

●$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$● (IRA 1-May-2018)

r_U = peak response of naproxen methyl ester or any individual unspecified degradation product from the *Sample solution*
r_S = peak response of naproxen from the *Standard solution*
C_S = concentration of USP Naproxen Sodium RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of naproxen sodium in the *Sample solution* (mg/mL)

●● (IRA 1-May-2018)

Acceptance criteria: See *Table 2*. Disregard any peaks below LOQ (0.004% for naproxen methyl ester and any individual unspecified degradation product, 0.002% for naproxen related compound A, and 0.006% for naproxen related compound L).

Table 2

Name	Relative Retention Time	●● (IRA 1-May-2018)	Acceptance Criteria, NMT (%)
Naproxen related compound A[a]	0.63	●● (IRA 1-May-2018)	0.2
Naproxen	1.00	●● (IRA 1-May-2018)	—
Naproxen related compound L[b]	2.32	●● (IRA 1-May-2018)	0.2
Naproxen methyl ester[c]	3.19	●● (IRA 1-May-2018)	0.2
Any individual unspecified degradation product	—	●● (IRA 1-May-2018)	0.2
Total impurities	—	●● (IRA 1-May-2018)	1.5

[a] 6-Methoxy-2-naphthoic acid.
[b] 1-(6-Methoxynaphthalen-2-yl)ethanone.
[c] (*S*)-Methyl 2-(6-methoxynaphthalen-2-yl)propanoate.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers.
- **USP REFERENCE STANDARDS** ⟨11⟩
  USP Naproxen Sodium RS
  USP Naproxen Related Compound A RS
  6-Methoxy-2-naphthoic acid.
  $C_{12}H_{10}O_3$ 202.21
  USP Naproxen Related Compound L RS
  1-(6-Methoxynaphthalen-2-yl)ethanone.
  $C_{13}H_{12}O_2$ 200.23