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Naproxen Tablets

DEFINITION
Naproxen Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of naproxen ($C_{14}H_{14}O_3$).

IDENTIFICATION
• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
• **B.** 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
• **Procedure**

Mobile phase: Acetonitrile, water, and glacial acetic acid (450:540:10)

Standard solution: 0.1 mg/mL of USP Naproxen RS in *Mobile phase*

Sample stock solution: Nominally equivalent to 1 mg/mL of naproxen in *Mobile phase*. Transfer an amount equivalent to about 500 mg of naproxen, from NLT 10 finely powdered Tablets, to a 500-mL volumetric flask. Add about 300 mL of *Mobile phase*, and sonicate for 30 min. Cool to room temperature, and dilute with *Mobile phase* to volume.

Sample solution: Nominally equivalent to 0.1 mg/mL of naproxen in *Mobile phase* from *Sample stock solution*. Pass through a suitable filter of 0.45-µm of pore size.

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 ($C_{14}H_{14}O_3$) 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 RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of naproxen in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS
• **Dissolution ⟨711⟩**

Buffer: 0.1 M of pH 7.4 phosphate buffer prepared as follows. 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: *Buffer*; 900 mL

Apparatus 2: 50 rpm

Time: 45 min

Standard solution: A known concentration of USP Naproxen RS in *Buffer*

Sample solution: Filter portions of the solution under test, and suitably dilute with *Buffer*.

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 ($C_{14}H_{14}O_3$) dissolved.

Tolerances: NLT 80% (*Q*) of the labeled amount of naproxen ($C_{14}H_{14}O_3$) is dissolved.

- **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

Change to read:

- **Organic Impurities**

Buffer: 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.

Diluent: Acetonitrile and *Buffer* (50:50)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Buffer (%)	Acetonitrile (%)
0	85	15
5	85	15
25	60	40
45	50	50
50	85	15
60	85	15

Standard stock solution 1: Prepare 5 mg/mL of USP Naproxen RS in *Diluent*. Further dilute this solution with *Diluent* to obtain 0.05 mg/mL of USP Naproxen RS in *Diluent*.

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 µg/mL of USP Naproxen Related Compound A RS from *Standard stock solution 2* and 0.5 mg/mL of USP Naproxen RS in *Diluent*▲ (ERR 1-Oct-2018)

Standard solution: 1.0 µg/mL of USP Naproxen RS, 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 solution: Nominally equivalent to 0.5 mg/mL of naproxen from NLT 10 finely powdered Tablets. Transfer nominally equivalent to about 500 mg of naproxen to a 1000-mL volumetric flask. Add 600 mL of *Diluent*, and sonicate for 30 min with intermittent shaking. Cool to room temperature, and dilute with *Diluent* to volume. Mix, and allow to settle for 5 min. Pass through a suitable filter of 0.45-µm pore size.

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 in the *Sample solution* (mg/mL)

Calculate the percentage of any other individual impurity in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of any other individual impurity from the *Sample solution*

r_S = peak response of naproxen from the *Standard solution*

C_S = concentration of USP Naproxen RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of naproxen in the *Sample solution* (mg/mL)

F = relative response factor of each individual impurity (see *Table 2*)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Naproxen related compound A[a]	0.63	—	0.10
Naproxen	1.00	—	—
Naproxen related compound L[b]	2.32	—	0.10
Naproxen methyl ester[c]	3.19	1.0	0.10
Any other individual impurity	—	1.0	0.10
Total impurities[d]	—	—	0.50

[a] 6-Methoxy-2-naphthoic acid.

[b] 1-(6-Methoxynaphthalen-2-yl)ethanone.

[c] (*S*)-Methyl 2-(6-methoxynaphthalen-2-yl)propanoate.

[d] Disregard any peaks below LOQ (0.004% for any other individual impurity and naproxen methyl ester, 0.002% for naproxen related compound A, and 0.006% for naproxen related compound L).

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers.
- **USP Reference Standards** ⟨11⟩

USP Naproxen 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

Topic/Question	Contact	Expert Committee
NAPROXEN TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

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