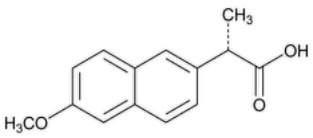
Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-Aug-2024
Document Type: USP Monographs
DocId: GUID-F8F7140C-EDAF-4BE3-B47E-7A28F414BCD9_5_en-US
DOI: https://doi.org/10.31003/USPNF_M55760_05_01
DOI Ref: e8kpc

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 CAS RN®: 22204-53-1; UNII: 57Y76R9ATQ.

Change to read:

DEFINITION

Naproxen contains ▲NLT 98.0% and NMT 102.0%▲ (USP 1-Aug-2024) of naproxen ($C_{14}H_{14}O_3$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K ▲or 197A▲ (USP 1-Aug-2024)

Change to read:

• **B.** ▲The retention time of the major peak of the *Sample solution* corresponds to that of the naproxen peak in the *System suitability solution*, as obtained in the *Enantiomeric Purity Test*.▲ (USP 1-Aug-2024)

ASSAY

Change to read:

• **Procedure**

▲**Solution A:** 0.1% glacial acetic acid in water

Solution B: 0.01% glacial acetic acid in methanol

Mobile phase: See *Table 1*. The recommended equilibration time after the gradient is 5–10 min.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	45	55
20	45	55
27	20	80
32	20	80
32.1	45	55
35	45	55

Diluent: Acetonitrile and water (50:50)

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

Sample solution: 0.1 mg/mL of Naproxen in *Diluent*

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 272 nm

Column: 4.6-mm × 15-cm; 3.5-µm packing L1
Column temperature: 35°
Flow rate: 1 mL/min
Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0
Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of naproxen ($C_{14}H_{14}O_3$) in the portion of Naproxen 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 = concentration of Naproxen in the *Sample solution* (mg/mL)

▲ (USP 1-Aug-2024)

Acceptance criteria: ▲98.0%–102.0%▲ (USP 1-Aug-2024) on the dried basis

IMPURITIES

Change to read:

• **Organic Impurities**

▲**Solution A, Solution B, Mobile phase,** and **Diluent:** Prepare as directed in the *Assay*.

System suitability solution: 100 µg/mL of USP Naproxen RS and 0.5 µg/mL each of USP Naproxen Related Compound K RS, USP Naproxen Related Compound A RS, and USP Naproxen Related Compound L RS in *Diluent*

Standard solution: 0.1 µg/mL each of USP Naproxen RS, USP Naproxen Related Compound A RS, USP Naproxen Related Compound L RS, and USP Naproxen Related Compound E RS in *Diluent*

Sensitivity solution: 0.05 µg/mL each of USP Naproxen RS, USP Naproxen Related Compound A RS, USP Naproxen Related Compound L RS, and USP Naproxen Related Compound E RS in *Diluent* from *Standard solution*

Sample solution: 100 µg/mL of Naproxen in *Diluent*

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC
Detector: UV 240 nm
Column: 4.6-mm × 15-cm; 3.5-µm packing L1
Column temperature: 35°
Flow rate: 1 mL/min
Injection volume: 20 µL

System suitability

Samples: *System suitability solution*, *Standard solution*, and *Sensitivity solution*

[Note—See *Table 2* for the relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between naproxen related compound K and naproxen related compound A; NLT 2.0 between naproxen related compound L and naproxen, *System suitability solution*
Relative standard deviation: NMT 5.0% for each peak, *Standard solution*
Signal-to-noise ratio: NLT 10 for each peak, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of naproxen related compound E, naproxen related compound A, and naproxen related compound L in the portion of Naproxen taken:

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

r_U = peak response of naproxen related compound E, naproxen related compound A, or naproxen related compound L from the *Sample solution*

r_S = peak response of naproxen related compound E, naproxen related compound A, or naproxen related compound L from the *Standard solution*

C_S = concentration of USP Naproxen Related Compound E RS, USP Naproxen Related Compound A RS, or USP Naproxen Related Compound L RS in the *Standard solution* (µg/mL)

C_U = concentration of Naproxen in the *Sample solution* (µg/mL)

Calculate the percentage of naproxen related compound K and any unspecified impurity in the portion of Naproxen taken:

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

r_U = peak response of naproxen related compound K or any unspecified 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* (µg/mL)

C_U = concentration of Naproxen in the *Sample solution* (µg/mL)

F = relative response factor, 0.64 for naproxen related compound K and 1.0 for unspecified impurity

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Naproxen related compound K, if present	0.66	0.07
Naproxen related compound A	0.71	0.07
Naproxen related compound L	0.88	0.1
Naproxen	1.0	—
Naproxen related compound E	1.64	0.1
Any unspecified impurity	—	0.07
Total impurities	—	0.5▲ (USP 1-Aug-2024)

Add the following:

▲• **Enantiomeric Purity Test**

[Note—Protect solutions containing naproxen from light.]

Mobile phase: Hexane, isopropanol, acetonitrile, and glacial acetic acid (84.5: 10: 5: 0.5)

System suitability stock solution: 250 µg/mL each of USP Naproxen RS and USP Naproxen Related Compound G RS in tetrahydrofuran

System suitability solution: 25 µg/mL each of USP Naproxen RS and USP Naproxen Related Compound G RS in *Mobile phase* from *System suitability stock solution*

Standard solution: 1.25 µg/mL of USP Naproxen Related Compound G RS in *Mobile phase*

Sample stock solution: 500 µg/mL of Naproxen in tetrahydrofuran

Sample solution: 50 µg/mL of Naproxen in *Mobile phase* from *Sample stock solution*

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 263 nm

Column: 4.6-mm × 25-cm; 5-µm packing L102

Flow rate: 2 mL/min

Injection volume: 20 µL

Run time: NLT 1.5 times the retention time of naproxen

System suitability

Samples: *System suitability solution* and *Standard solution*

[Note—The relative retention times for naproxen related compound G and naproxen are approximately 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 3.0 between naproxen related compound G and naproxen, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of naproxen related compound G in the portion of Naproxen taken:

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

r_U = peak response of naproxen related compound G from the *Sample solution*

r_S = peak response of naproxen related compound G from the *Standard solution*

C_S = concentration of USP Naproxen Related Compound G RS in the *Standard solution* (µg/mL)

C_U = concentration of Naproxen in the *Sample solution* (µg/mL)

Acceptance criteria: NMT 2.5%▲ (USP 1-Aug-2024)

SPECIFIC TESTS

Delete the following:

▲• **Optical Rotation** ⟨781S⟩, *Procedures, Specific Rotation*▲ (USP 1-Aug-2024)

• **Loss on Drying** ⟨731⟩

Analysis: Dry at 105° for 3 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

Change to read:

• **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 E RS

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

$C_{15}H_{16}O_3$ 244.29

USP Naproxen Related Compound G RS

(*R*)-2-(6-Methoxynaphthalen-2-yl)propanoic acid.

$C_{14}H_{14}O_3$ 230.26

USP Naproxen Related Compound K RS

1-(6-Methoxynaphthalen-2-yl)ethanol.

$C_{13}H_{14}O_2$ 202.25

USP Naproxen Related Compound L RS

1-(6-Methoxynaphthalen-2-yl)ethanone.

$C_{13}H_{12}O_2$ 200.24▲ (USP 1-Aug-2024)

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 47(4)

Current DocID: GUID-F8F7140C-EDAF-4BE3-B47E-7A28F414BCD9_5_en-US

DOI: https://doi.org/10.31003/USPNF_M55760_05_01

DOI ref: e8kpc