Naproxen Sodium Tablets

DEFINITION
Naproxen Sodium Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of naproxen sodium (C14H13NaO3).

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 Tablets prepared under System suitability, 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.
  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 (C14H13NaO3) in the portion of Tablets taken:
\[
\text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_S}{C_U} \right) \times 100
\]

\( r_U \) = 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
  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 (C14H13NaO3).

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 (C14H13NaO3) dissolved.
Tolerances: NLT 80% (Q) of the labeled amount of naproxen sodium (C14H13NaO3) 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>
<thead>
<tr>
<th>Time (min)</th>
<th>Solution A (%)</th>
<th>Solution B (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>85</td>
<td>15</td>
</tr>
<tr>
<td>5</td>
<td>85</td>
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<tr>
<td>25</td>
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<tr>
<td>50</td>
<td>85</td>
<td>15</td>
</tr>
<tr>
<td>60</td>
<td>85</td>
<td>15</td>
</tr>
</tbody>
</table>

Standard stock solution 1: 0.05 mg/mL (IRA 1-May-2018) of USP Naproxen Sodium 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 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.

**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

**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:

\[ \text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_S}{C_U} \right) \times 100 \]

\( r_U \) = 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 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)

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**

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naproxen related compound A</td>
<td>0.63</td>
<td>0.2</td>
</tr>
<tr>
<td>Naproxen related compound L</td>
<td>2.32</td>
<td>0.2</td>
</tr>
<tr>
<td>Naproxen methyl ester</td>
<td>3.19</td>
<td>0.2</td>
</tr>
<tr>
<td>Any individual unspecified degradation product</td>
<td>—</td>
<td>0.2</td>
</tr>
<tr>
<td>Total impurities</td>
<td>—</td>
<td>1.5</td>
</tr>
</tbody>
</table>

**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.
  - USP Naproxen Related Compound L RS
  - 1-(6-Methoxynaphthalen-2-yl)ethanone.
  - USP Related Compound L RS
  - (5)-Methyl 2-(6-methoxynaphthalen-2-yl)propanoate.

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