Oxycodone Hydrochloride Extended-Release Tablets

DEFINITION
Oxycodone Hydrochloride Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of oxycodone hydrochloride (C₁₈H₂₁NO₄ ∙ HCl).

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.

ASSAY
• PROCEDURE
Buffer solution: 2 g/L of sodium heptanesulfonate in water. Add 13.3 mL/L of glacial acetic acid, and adjust with 5 N sodium hydroxide solution to a pH of 3.50 ± 0.05.
Mobile phase: Acetonitrile and Buffer solution (1:3)
Standard solution: 0.036 mg/mL of USP Oxycodone RS in Acetonitrile and 2 g/L of sodium heptanesulfonate in (See Mobile phase).
Sample stock solution: Transfer 10 Tablets into an appropriate volumetric flask, and add a volume of a mixture of methanol and acetonitrile (1:1) equivalent to 50% of the volumetric flask volume. Sonicate for 10 min, and stir for 20 min. Dilute with Buffer solution to volume.
Sample solution: 0.04 mg/mL of oxycodone hydrochloride from the Sample stock solution, diluted with Mobile phase to volume. Pass through a suitable filter.

Chromatographic system
(See Chromatography (621), System Suitability.)
Mode: LC
Detector: UV 280 nm
Column: 4.6-mm × 15-cm; packing L1
Flow rate: 1.0 mL/min
Injection volume: 20 µL
System suitability
Sample: Standard solution
Suitability requirements
Column efficiency: NLT 4000 theoretical plates
Tailing factor: NMT 2.0
Relative standard deviation: NMT 2.0%
Analysis
Samples: Standard solution and Sample solution
Calculate the concentration (Ci) of oxycodone hydrochloride (C₁₈H₂₁NO₄ ∙ HCl) in the sample withdrawn at time point (i): Result = (A0/Ai) × Ci × D × (M₁/M₂)

PERFORMANCE TESTS

Change to read:

• DISSOLUTION (711)
Test 1
Medium: Simulated gastric fluid (without enzymes); 900 mL
Apparatus 1: 100 rpm
Time: 1, 2, 4, 6, and 8 h for Tablets labeled to contain 10, 20, or 40 mg; 1, 2, 4, and 6 h for Tablets labeled to contain 80 mg
Standard stock solution
Tablets labeled to contain 10 mg: 398 µg/mL of USP Oxycodone RS in Medium
Tablets labeled to contain 20, 40, or 80 mg: 796 µg/mL of USP Oxycodone RS in Medium
Standard solution: Dilute the appropriate Standard stock solution with Medium to obtain solutions containing (L/900) mg/mL, with L as the label claim in mg/Tablet.
Sample solution: Pass a portion of the solution under test through a suitable filter. Dilute with Medium, if necessary.

Instrumental conditions
(See Spectrophotometry and Light-Scattering (851))
Mode: UV
Analytical wavelength: About 226 nm (shoulder)
Cell
For Tablets labeled to contain 10, 20, or 40 mg: 1.0 cm
For Tablets labeled to contain 80 mg: 0.5 cm
Blank: Medium
Analysis
Samples: Standard solution and Sample solution
Calculate the concentration (Ci) of oxycodone hydrochloride (C₁₈H₂₁NO₄ ∙ HCl) in the sample withdrawn from the vessel at each time point (i):

Result = (CI × VS) / (C₁ × L) × 100

Result2 = [(CI × (V – VS))] / (C₁ × VS) × (1/L) × 100

Result3 = [(CI × [V – (2 × VS)]) + (CI × VS)] / (1/L) × 100

Result4 = [(CI × [V – (3 × VS)]) + (CI × 2 × VS)] / (1/L) × 100

Result5 = [(CI × [V – (4 × VS)]) + (CI × 3 × VS)] / (1/L) × 100

Acceptance criteria: 90.0%–110.0%
For Tablets labeled to contain 80 mg, calculate the labeled amount of oxycodone hydrochloride (C₁₈H₂₁NO₄·HCl) released at each time point (i):

Result₃ = Cᵢ × V × (1/L) × 100

Result₂ = ((Cᵢ × (V − 2 × Vᵢ)) + (Cᵢ × Vᵢ)) × (1/L) × 100

Result₁ = ((Cᵢ × [V − (2 × Vᵢ)]) + [(Cᵢ + Cᵢ) × Vᵢ]) × (1/L) × 100

Cᵢ = concentration of oxycodone hydrochloride in the portion of sample withdrawn at time point i (mg/mL)

V = volume of Medium, 900 mL

L = label claim (mg/Tablet)

Vᵢ = volume of the Sample solution withdrawn from the Medium (mL)

Tolerances: See Table 1 for Tablets labeled to contain 10, 20, or 40 mg; see Table 2 for Tablets labeled to contain 80 mg.

### Table 1

<table>
<thead>
<tr>
<th>Time Point (i)</th>
<th>Time (h)</th>
<th>Amount Released (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>20–40</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>35–55</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>55–75</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>70–90</td>
</tr>
<tr>
<td>5</td>
<td>8</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of oxycodone hydrochloride (C₁₈H₂₁NO₄·HCl) released at the times specified, conform to Acceptance Table 2 in Dissolution (711).

Test 2: If the product complies with this test, the labeling indicates that the product meets USP Dissolution Test 2.

Medium: Simulated gastric fluid (without enzymes); 900 mL

Apparatus 1: 100 rpm

Time: 1, 4, and 12 h

0.85% phosphoric acid: 10 mL/L of phosphoric acid in water

Mobile phase: Weigh 23.1 g of monobasic potassium phosphate into a 4-L flask, and dissolve with 3400 mL of water. Add 4 mL of triethylamine, and adjust with 0.85% phosphoric acid to a pH of 3.0 ± 0.1. Add 600 mL of methanol and 20 mL of tert-butyl methyl ether, and mix well.

Standard stock solution: 0.9 mg/mL of USP Oxy- codone RS in 0.85% phosphoric acid

### Table 2

<table>
<thead>
<tr>
<th>Time Point (i)</th>
<th>Time (h)</th>
<th>Amount Released (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>25–45</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>45–65</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>65–85</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

Standard solution: Dilute the Standard stock solution, quantitatively and stepwise, with Medium to obtain a solution having a concentration of 40% of the Tablet label claim. [NOTE—This solution is stable for two weeks at room temperature.]

Sample solution: Pass the solution under test through a suitable filter of 0.45-µm pore size.

**Chromatographic system**

(See Chromatography (621), System Suitability.)

Mode: LC

Detector: UV 230 nm

Column: 3.9-mm × 30-cm; 10-µm packing L1

Column temperature: 60°

Flow rate: 1 mL/min

Injection volume: 50 µL

System suitability

Sample: Standard solution

Suitability requirements

Capacity factor: NLT 0.5

Tailing factor: 0.75–1.5

Relative standard deviation: NMT 2%

Analysis

Samples: Standard solution and Sample solution

Calculate the concentration (C) of oxycodone hydrochloride (C₁₈H₂₁NO₄·HCl) in the sample withdrawn from the vessel at each time point (i):

Result₄ = \((rᵢ/rᵢ) \times Cᵢ \times (Mᵢ/M₂)\)

rᵢ = peak response from the Sample solution

rᵢ = peak response from the Standard solution

Cᵢ = concentration of the Standard solution (mg/mL)

Mᵢ = molecular weight of oxycodone hydrochloride, 351.82

M₂ = molecular weight of oxycodone base, 315.37

Calculate the labeled amount of oxycodone hydrochloride (C₁₈H₂₁NO₄·HCl) released at each time point (i):

Result₃ = Cᵢ × V × (1/L) × 100

Result₂ = ((Cᵢ × (V − 2 × Vᵢ)) + (Cᵢ × Vᵢ)) × (1/L) × 100

Result₁ = ((Cᵢ × [V − (2 × Vᵢ)]) + [(Cᵢ + Cᵢ) × Vᵢ]) × (1/L) × 100

Cᵢ = concentration of oxycodone hydrochloride in the portion of sample withdrawn at time point i (mg/mL)

V = volume of Medium, 900 mL

L = label claim (mg/Tablet)

Vᵢ = volume of the Sample solution withdrawn from the Medium (mL)

Tolerances: See Table 3 for Tablets labeled to contain 10 mg; see Table 4 for Tablets labeled to contain 20 mg; see Table 5 for Tablets labeled to contain 40 mg; see Table 6 for Tablets labeled to contain 80 mg.

### Table 3

<table>
<thead>
<tr>
<th>Time Point (i)</th>
<th>Time (h)</th>
<th>Amount Released (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>29–49</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>58–78</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>NLT 85</td>
</tr>
</tbody>
</table>
The percentages of the labeled amount of oxycodone hydrochloride (C₁₈H₂₁NO₄ · HCl), released at the times specified, conform to Acceptance Table 2 in Dissolution (711).

**UniforMity of Dosage Units (905):** Meet the requirements

**Impurities**

- **Limit of Oxycodone Related Compound B (Oxycodone N-Oxide):**
  - Diluent: 10 mL/L of phosphoric acid in water
  - Buffer: 6.8 g/L of monobasic potassium phosphate. Add 1.2 mL of triethylamine, and adjust with Diluent to a pH of 3.0 ± 0.1.
  - Mobile phase: Methanol, tert-butyl methyl ether, and Buffer (30:1:170)
  - Standard solution: 0.18 mg/mL of USP Oxycodone RS and 0.002 mg/mL of USP Oxycodone Related Compound B RS in Diluent [Note—Prepare fresh daily.]
  - Sample stock solution: Transfer 10 Tablets into a 500-mL volumetric flask, add 50 mL of Diluent and 50 mL of alcohol, and sonicate for 90 min to extract the active ingredient. Dilute with Diluent to volume.

Sample solution: 0.2 mg/mL of oxycodone hydrochloride from the Sample stock solution in Diluent. Pass a portion of the solution through a suitable filter, and use the filtrate.

**Chromatographic system**

(See Chromatography (621), System Suitability.)

- **Mode:** LC
- **Detector:** UV 230 nm
- **Column:** 3.9-mm × 30-cm; 10-µm packing L1
- **Column temperature:** 60°C
- **Flow rate:** 1.0 mL/min
- **Injection volume:** 50 μL
- **System suitability**
  - Sample: Standard solution
  - Suitability requirements
    - Resolution: NLT 4.5 between the oxycodone and oxycodone related compound B peaks
    - Relative standard deviation: NMT 3.0% for oxycodone related compound B

**Analysis**

Samples: Standard solution and Sample solution

Calculate the percentage of oxycodone related compound B in the portion of the Tablets taken:

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

- \(r_U\) = peak area of oxycodone related compound B (USP 1-Nov-2013) from the Sample solution
- \(r_S\) = peak area of oxycodone related compound B (USP 1-Nov-2013) from the Standard solution
- \(C_S\) = concentration of USP Oxycodone Related Compound B RS in the Standard solution (mg/mL)
- \(C_U\) = nominal concentration of oxycodone hydrochloride (USP 1-Nov-2013) in the Sample solution (mg/mL)

Acceptance criteria: NMT 1%

**Additional requirements**

- **Packaging and Storage:** Preserve in tight, light-resistant containers, and store at controlled room temperature.
- **Labeling:** When more than one Dissolution Test is given, the labeling states the Dissolution Test used only if Test 1 is not used.
- **USP Reference Standards (11)**
  - USP Oxycodone RS
  - USP Oxycodone Related Compound B RS
  - 4,5a-Epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one N-oxide.
  - C₁₈H₂₁NO₄ 331.36