Oxymorphone Hydrochloride Tablets

Type of Posting	Revision Bulletin
Posting Date	18–Nov–2016
Official Date	01–Dec–2016
Expert Committee	Chemical Medicines Monographs 2
Reason for Revision	Compliance

In accordance with the Rules and Procedures of the 2015-2020 Council of Experts, the Chemical Medicines Monographs 2 Expert Committee has revised the Oxymorphone Hydrochloride Tablets monograph. The purpose for the revision is to add *Dissolution Test 2* for a generic product approved by the FDA.

Dissolution Test 2 was validated using a Luna C8 brand of L7 column. The typical retention time for oxymorphone is about 4.5 min.

The Oxymorphone Hydrochloride Tablets Revision Bulletin supersedes the currently official monograph. The Revision Bulletin will be incorporated in the *Second Supplement* to *USP 40–NF 35*.

Should you have any questions, please contact Hillary Cai, Ph.D., Scientific Liaison (301-230-3379 or hzc@usp.org)

Oxymorphone Hydrochloride Tablets

DEFINITION

Oxymorphone Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of oxymorphone hydrochloride ($C_{17}H_{19}NO_4 \cdot HCl$).

IDENTIFICATION

- **A.** The retention time of the oxymorphone peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B.** The UV absorption spectra of the oxymorphone 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**

Protect all solutions containing oxymorphone from light and use clear glass HPLC vials.

Solution A: Dissolve 2.02 g of sodium 1-heptanesulfonate in 900 mL of water and add 100 mL of acetonitrile. Adjust with phosphoric acid to a pH of 2.1.

Solution B: Dissolve 2.02 g of sodium 1-heptanesulfonate in 750 mL of water and add 250 mL of acetonitrile. Adjust with phosphoric acid to a pH of 2.1.

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
3	100	0
35	0	100
40	0	100
40.1	100	0
50.1	100	0

Standard solution: 0.14 mg/mL of USP Oxymorphone RS in *Solution A*. Sonicate to dissolve if necessary.

Sample solution: Nominally 0.16 mg/mL of oxymorphone hydrochloride in *Solution A* prepared as follows. Transfer NLT 8 Tablets to a suitable volumetric flask and add about 50% of the final volume of *Solution A*. Sonicate for at least 15 min with occasional vigorous shaking until the Tablets disintegrate completely. Then shake for at least 20 min. Immediately dilute with *Solution A* to volume, and mix well. Immediately pass the solution through a suitable filter of 0.45-µm pore size, discard the first 5 mL of the filtrate, and use the filtrate for analysis.

Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)
Mode: LC
Detectors
Assay: UV 230 nm
Identification test B: Diode array UV 200–360 nm
Column: 4.6-mm × 7.5-cm; 3.5-µm packing L1
Column temperature: 40°
Flow rate: 1.0 mL/min
Injection volume: 30 µL
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 oxymorphone hydrochloride ($C_{17}H_{19}NO_4 \cdot HCl$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of oxymorphone from the *Sample solution*
r_S = peak response of oxymorphone from the *Standard solution*
C_S = concentration of USP Oxymorphone RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of oxymorphone hydrochloride in the *Sample solution* (mg/mL)
M_{r1} = molecular weight of oxymorphone hydrochloride, 337.80
M_{r2} = molecular weight of oxymorphone, 301.34

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- **DISSOLUTION** ⟨**711**⟩

Test 1 (RB 1-Dec-2016)
Medium: 0.1 N hydrochloric acid; 900 mL
Apparatus 2: 50 rpm
Time: 30 min
Mobile phase: Dissolve 2.02 g of sodium 1-heptanesulfonate in 800 mL of water and add 200 mL of acetonitrile. Adjust with phosphoric acid to a pH of 2.1.
Standard stock solution: 0.1 mg/mL of USP Oxymorphone RS in 0.1 N hydrochloric acid
Standard solution: (*L*/1000) mg/mL of USP Oxymorphone RS in water from the *Standard stock solution*, where *L* is the label claim in mg/Tablet
Sample solution: Pass a portion of 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: 4.6-mm × 7.5-cm; 3.5-µm packing L1
Column temperature: 40°
Flow rate: 1.0 mL/min
Injection volume: 60 µL
Run time: NLT 2.7 times the retention time of oxymorphone

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 oxymorphone hydrochloride ($C_{17}H_{19}NO_4 \cdot HCl$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (M_{r1}/M_{r2}) \times (1/L) \times 100$$

r_U = peak response of oxymorphone from the *Sample solution*
r_S = peak response of oxymorphone from the *Standard solution*
C_S = concentration of USP Oxymorphone RS in the *Standard solution* (mg/mL)
V = volume of *Medium*, 900 mL
M_{r1} = molecular weight of oxymorphone hydrochloride, 337.80
M_{r2} = molecular weight of oxymorphone, 301.34
L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of oxymorphone hydrochloride ($C_{17}H_{19}NO_4 \cdot HCl$) is dissolved.

• **Test 2:** If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 2*.
Medium: 0.1 N hydrochloric acid; 900 mL
Apparatus 2: 50 rpm
Time: 20 min
Buffer: Dissolve 26.4 g of dibasic ammonium phosphate in 2 L of water.
Mobile phase: Acetonitrile, methanol, and *Buffer* (5:25:70)
Diluent: *Buffer*
Standard stock solution: 0.05 mg/mL of USP Oxymorphone RS in *Medium*
Standard solution: 0.0025 mg/mL of USP Oxymorphone RS in *Diluent* from *Standard stock solution*
Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Dilute this solution with *Diluent* to obtain a solution with a similar concentration as that of the *Standard solution*.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 212 nm
Column: 4.6-mm × 15-cm; 5-µm packing L7
Column temperature: 40°
Flow rate: 1.5 mL/min
Injection volume: 50 µL
Run time: NLT 1.6 times the retention time of oxymorphone
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 oxymorphone hydrochloride ($C_{17}H_{19}NO_4 \cdot HCl$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (M_{r1}/M_{r2}) \times (1/L) \times 100$$

r_U = peak response of oxymorphone from the *Sample solution*
r_S = peak response of oxymorphone from the *Standard solution*
C_S = concentration of USP Oxymorphone RS in the *Standard solution* (mg/mL)
V = volume of *Medium*, 900 mL
M_{r1} = molecular weight of oxymorphone hydrochloride, 337.80
M_{r2} = molecular weight of oxymorphone, 301.34
L = label claim (mg/Tablet)

Tolerances: NLT 85% (Q) of the labeled amount of oxymorphone hydrochloride ($C_{17}H_{19}NO_4 \cdot HCl$) is dissolved.● (RB 1-Dec-2016)

• **UNIFORMITY OF DOSAGE UNITS ⟨905⟩:** Meet the requirements

IMPURITIES

• **ORGANIC IMPURITIES**
Protect all solutions containing oxymorphone from light and use clear glass HPLC vials.
Solution A, Solution B, Mobile phase, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay.*
System suitability stock solution A: 0.2 mg/mL of USP Oxymorphone Related Compound A RS prepared as follows. Transfer an amount of USP Oxymorphone Related Compound A RS to a suitable volumetric flask. Dissolve with 24% of the flask volume of 0.1 N hydrochloric acid and dilute with acetonitrile to volume.
System suitability stock solution B: 0.02 mg/mL of USP Oxymorphone Related Compound A RS in acetonitrile from *System suitability stock solution A*
System suitability stock solution C: 0.14 mg/mL of USP Oxymorphone RS in *Solution A*
System suitability solution: 0.0008 mg/mL of USP Oxymorphone Related Compound A RS in *System suitability stock solution C* from *System suitability stock solution B*
Standard solution: 0.00014 mg/mL of USP Oxymorphone RS in *Solution A* from *System suitability stock solution C*
System suitability
Samples: *System suitability solution* and *Standard solution*
Suitability requirements
Resolution: NLT 2 between oxymorphone related compound A and oxymorphone, *System suitability solution*
Relative standard deviation: NMT 10%, *Standard solution*
Analysis
Sample: *Sample solution*
Calculate the percentage of each individual degradation product in the portion of Tablets taken:

$$\text{Result} = (r_U/r_T) \times (1/F) \times 100$$

r_U = peak response of each individual degradation product from the *Sample solution*
r_T = sum of peak responses from the *Sample solution*
F = relative response factor of each individual degradation product (see *Table 2*)

Acceptance criteria: See *Table 2*. Disregard any peaks less than 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
10-Hydroxyoxymorphone[a]	0.58	1.00	0.2
Oxymorphone related compound A (oxymorphone *N*-oxide)	0.81	1.09	0.2
Oxymorphone	1.00	1.00	—
10-Ketooxymorphone[b]	1.42	0.93	0.2
Oxycodone[c]	2.11	—	—
1-Bromooxymorphone[c,d]	2.22	—	—
2,2′-Bisoxymorphone[e]	2.36	1.61	0.2
Any individual unspecified degradation product	—	1.00	0.2
Total degradation products	—	—	1.5

[a] 4,5α-Epoxy-3,10,14-trihydroxy-17-methylmorphinan-6-one.
[b] 4,5α-Epoxy-3,14-dihydroxy-17-methylmorphinan-6,10-dione.
[c] Process impurities, not included in the total degradation products.
[d] 1-Bromo-4,5α-epoxy-3,14-dihydroxy-17-methylmorphinan-6-one.
[e] 2,2′-Bioxymorphone.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers. Store at 25°, excursions permitted between 15° and 30°.

Add the following:

- **LABELING:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used. (RB 1-Dec-2016)
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Oxymorphone RS
  USP Oxymorphone Related Compound A RS
  4,5α-Epoxy-3,14-dihydroxy-17-methylmorphinan-6-one *N*-oxide.
  $C_{17}H_{19}NO_5$ 317.34