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Oxymorphone Hydrochloride Injection

DEFINITION

Oxymorphone Hydrochloride Injection is a sterile solution of Oxymorphone Hydrochloride in Water for Injection. It contains NLT 93.0% and NMT 107.0% of the labeled amount of oxymorphone hydrochloride ($C_{17}H_{19}NO_4 \cdot HCl$).

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*.

• **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**

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. 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. 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

Diluent: Dissolve 2.02 g of anhydrous sodium 1-heptanesulfonate in 1000 mL of water. Adjust with phosphoric acid to a pH of 2.1.

Standard solution: 0.14 mg/mL of USP Oxymorphone RS prepared as follows. Transfer a suitable amount of USP Oxymorphone RS to a suitable volumetric flask. Add 50% of the flask volume of *Diluent*. Sonicate to dissolve, if necessary. Add 9% of the flask volume of acetonitrile. Cool to room temperature and dilute with *Diluent* to volume.

Sample solution: Nominally 0.15 mg/mL of oxymorphone hydrochloride from Injection prepared as follows. Transfer a suitable volume of the composite sample from NLT 20 ampules to a suitable volumetric flask. Dilute with *Solution A* to volume.

Chromatographic system

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

Mode: LC

Detector

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 Injection 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: 93.0%–107.0%

IMPURITIES

• **Organic Impurities**

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

Solution A, Solution B, Mobile phase, Diluent, 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 a suitable 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 prepared as follows. Transfer a suitable amount of USP Oxymorphone RS to a suitable volumetric flask. Add 50% of the flask volume of *Diluent*. Sonicate to dissolve if necessary. Add 9% of the flask volume of acetonitrile. Cool to room temperature and dilute with *Diluent* to volume.

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 prepared as follows. Dilute *System suitability stock solution C* with *Solution A*.

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 Injection taken:

$$\text{Result} = \{(r_U/F)/[r_S + \Sigma(r_U/F)]\} \times 100$$

r_U = peak response of each individual degradation product from the *Sample solution*

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

r_S = peak response of oxymorphone from the *Sample solution*

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]	0.59	1.0	0.20
Oxymorphone related compound A (oxymorphone *N*-oxide)	0.82	1.1	0.30
Oxymorphone	1.00	1.0	—
10-Ketooxymorphone[b]	1.37	0.83	0.30
Oxycodone[c]	1.97	1.0	—
1-Bromooxymorphone[c,d]	2.05	1.0	—
2,2'-Bisoxymorphone[e]	2.08	1.7	1.00
Any individual unspecified degradation product	—	1.0	0.50
Total degradation products	—	—	2.00

[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.

SPECIFIC TESTS

- **Bacterial Endotoxins Test ⟨85⟩:** NMT 238.1 USP Endotoxin Units/mg of oxymorphone hydrochloride
- **pH ⟨791⟩:** 2.7–4.5
- **Other Requirements:** It meets the requirements in *Injections and Implanted Drug Products ⟨1⟩*.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in single-dose or in multiple-dose containers of Type I glass. Store at 25°, excursions permitted between 15° and 30°, and protected from light.
- **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

Topic/Question	Contact	Expert Committee
OXYMORPHONE HYDROCHLORIDE INJECTION	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

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