Edition: BP 2025 (Ph. Eur. 11.6 update)

Oxycodone Oral Solution

General Notices

Oxycodone Hydrochloride Oral Solution

Action and use

Opioid receptor agonist; analgesic.

DEFINITION

Oxycodone Oral Solution contains Oxycodone Hydrochloride in a suitable vehicle.

The oral solution complies with the requirements stated under Oral Liquids and with the following requirements.

Content of oxycodone hydrochloride, $C_{18}H_{21}NO_4,HCl$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Adjust the pH of a quantity of the oral solution containing 15 mg of Oxycodone Hydrochloride to pH 9.5 with 6M *ammonia*. Transfer the solution to a separating funnel and extract with two 5-mL quantities of *dichloromethane*. Combine the dichloromethane extracts and evaporate 2 mL of the extract to dryness. Dissolve the residue obtained in 1 mL of *dichloromethane*.
(2) Transfer 15 mL of a 0.1% w/v solution of *oxycodone hydrochloride BPCRS,* adjusted to pH 9.5 with 6M *ammonia*, to a separating funnel and extract with two 5-mL quantities of *dichloromethane*. Combine the dichloromethane extracts and evaporate 2 mL of the extract to dryness. Dissolve the residue obtained in 1 mL of *dichloromethane*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating substance *silica gel F_{254}* (Merck TLC silica gel 60 F_{254} plates are suitable).
(b) Use the mobile phase described below.
(c) Apply 20 µL of each solution.
(d) Develop the plate to 15 cm.
(e) Dry the plate in air and examine under *ultraviolet light (254 nm)*.

MOBILE PHASE

3 volumes of 13.5M *ammonia*, 10 volumes of *diethyl ether*, 40 volumes of *toluene* and 60 volumes of *acetone*.

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) corresponds in position and colour to that in the chromatogram obtained with solution (2).

B. In the Assay, the chromatogram obtained with solution (1) shows a peak with the same retention time as the principal peak in the chromatogram obtained with solution (2).

TESTS

Acidity

pH, 2.5 to 3.0, Appendix V L.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in 0.02M *acetic acid*.

(1) Shake, with the aid of ultrasound, a quantity of the oral solution containing 20 mg of Oxycodone Hydrochloride with 40 mL of 0.02M *acetic acid*, add sufficient 0.02M *acetic acid* to produce 50 mL and filter.
(2) Dilute 1 volume of solution (1) to 100 volumes.
(3) Dilute 2 volumes of solution (2) to 10 volumes.
(4) 0.0002% w/v of oxycodone impurity standard BPCRS.
(5) Dilute 1 volume of solution (3) to 4 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm x 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Kromasil C18 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 230 nm.
(f) Inject 100 µL of each solution.

MOBILE PHASE

Mobile phase A 70 volumes of *acetonitrile*, 100 volumes of *methanol* and 830 volumes of a 0.11% w/v solution of *sodium heptanesulfonate monohydrate* previously adjusted to pH 2.0 with 8M *orthophosphoric acid*.

Mobile phase B 150 volumes of *acetonitrile*, 250 volumes of *methanol* and 600 volumes of a 0.11% w/v solution of *sodium heptanesulfonate monohydrate* previously adjusted to pH 2.0 with 8M *orthophosphoric acid*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-60	100→50	0→50	linear gradient
60-62	50→100	50→0	linear gradient
62-70	100	0	isocratic

When the chromatograms are recorded using the prescribed conditions, the retention time of oxycodone is about 24 minutes. The retention times relative to oxycodone are: impurity D, about 1.18; impurity E, about 1.18 and impurity F, about 2.4.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution* between the peaks due to oxycodone and 14-hydroxycodeinone is at least 3.0.

LIMITS

Identify any peaks in the chromatogram obtained with solution (1) corresponding to thebaine and multiply the area of this peak by 0.5.

In the chromatogram obtained with solution (1):

the sum of the areas of any peaks corresponding to 14-hydroxycodeinone and hydrocodone is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (0.2%);

the sum of the areas of any *secondary peaks* is not greater than 1.5 times the area of the principal peak in the chromatogram obtained with solution (2) (1.5%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (5) (0.05%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in 0.02M *acetic acid*.

(1) To a quantity of the oral solution containing 25 mg of Oxycodone Hydrochloride add sufficient 0.02M *acetic acid* to produce 50 mL and filter.Dilute 1 volume of this solution to 100 volumes with 0.02M *acetic acid*.
(2) 0.0005% w/v of *oxycodone hydrochloride BPCRS*.
(3) 0.0002% w/v of *oxycodone impurity standard BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm x 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Kromasil C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 230 nm.
(f) Inject 100 µL of each solution.
(g) For solution (3) allow the chromatography to proceed for 4 times the retention time of the peak due to oxycodone.

MOBILE PHASE

100 volumes of *acetonitrile*, 200 volumes of *methanol* and 700 volumes of a solution containing 0.11% w/v of *sodium heptanesulfonate monohydrate* previously adjusted to pH 2.0 with 8M *orthophosphoric acid*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2), the *resolution* between the peaks due to oxycodone and 14-hydroxycodeinone is at least 2.0.

DETERMINATION OF CONTENT

Calculate the total content of oxycodone hydrochloride, $C_{18}H_{21}NO_4$,HCl, in the oral solution from the chromatograms obtained and using the declared content of $C_{18}H_{21}NO_4$,HCl in *oxycodone hydrochloride BPCRS*.

IMPURITIES

D. 7,8-didehydro-4,5α-epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one (14-hydroxycodeinone);
E. 4,5α-epoxy-3-methoxy-17-methylmorphinan-6-one (hydrocodone);
F. 6,7,8,14-tetradehydro-4,5α-epoxy-3-6-dimethoxy-17-methylmorphinan (thebaine).