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

Oxycodone Prolonged-release Tablets

General Notices

Prolonged-release Oxycodone Tablets

Oxycodone Prolonged-release Tablets from different manufacturers, whilst complying with the requirements of the monograph, are not interchangeable unless otherwise justified and authorised.

Oxycodone Prolonged-release Tablets that have a tamper-resistant formulation, whilst complying with the requirements of the monograph, may require different methods of sample preparation where justified and authorised.

Action and use

Opioid receptor agonist; analgesic.

DEFINITION

Oxycodone Prolonged-release Tablets contain Oxycodone Hydrochloride.

PRODUCTION

A suitable dissolution test is carried out to demonstrate the appropriate release of oxycodone. The dissolution profile reflects the *in vivo* performance which in turn is compatible with the dosage schedule recommended by the manufacturer.

The tablets comply with the requirements stated under Tablets 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

Mix a quantity of the powdered tablets containing 50 mg of Oxycodone Hydrochloride with 25 mL of *water*, filter and add sufficient *dilute ammonia R1* to make the solution alkaline. Allow the mixture to stand until a precipitate is formed. Filter and wash the precipitate with 10 mL of cold *water*. The *infrared absorption spectrum* of the dried residue, Appendix II A, is concordant with the *reference spectrum* of oxycodone hydrochloride *(RS 457)*.

TESTS

Related substances

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

(1) Shake with the aid of ultrasound a quantity of the powdered tablets 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 1 volumes of solution (2) to 5 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
06-62	50→100	50→0	linear gradient
62-70	100	0	re-equilibration

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 impurity D is at least 3.0.

LIMITS

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

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity F 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 peaks due to impurity D and impurity E is not more 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

Weigh and powder 20 tablets. 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 powdered tablets containing 25 mg of Oxycodone Hydrochloride add sufficient 0.02M *acetic acid* to produce 50 mL and filter. Dilute 1 volume of the filtrate to 100 volumes with 0.02M *acetic acid*.
(2) 0.0005% w/v of *oxycodone hydrochloride BPCRS*.
(3) 0.0005% 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 oxycodone hydrochloride (retention time, about 6 minutes).

MOBILE PHASE

100 volumes of *acetonitrile*, 200 volumes of *methanol* and 700 volumes of a solution containing 0.11% w/v of *sodium heptane sulfonate 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 (3), the *resolution* between the peaks due to oxycodone hydrochloride and 14-hydroxycodeinone is at least 2.0.

DETERMINATION OF CONTENT

Calculate the total content of $C_{18}H_{21}NO_4$,HCl in the tablets using the declared content of $C_{18}H_{21}NO_4$,HCl in *oxycodone hydrochloride BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities D, E and F listed under Oxycodone Hydrochloride.