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

Tramadol Prolonged-release Tablets

General Notices

Prolonged-release Tramadol Tablets

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

Action and use

μ-Opioid receptor (OP_3, MOR) agonist; noradrenaline reuptake inhibitor; analgesic.

DEFINITION

Tramadol Prolonged-release Tablets contain Tramadol Hydrochloride. They are formulated so that the medicament is released over a period of several hours.

PRODUCTION

A suitable dissolution test is carried out to demonstrate the appropriate release of Tramadol Hydrochloride. 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 tramadol hydrochloride, $C_{16}H_{25}NO_2,HCl$

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) Add 25 mL of *methanol* to a quantity of the powdered tablets containing 50 mg of Tramadol Hydrochloride, shake for 10 minutes and filter through a glass-fibre filter (Whatman GF/A is suitable).
(2) 0.2% w/v of *tramadol hydrochloride BPCRS* in *methanol*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel F* (Merck plates are suitable).
(b) Use the mobile phase as described below.
(c) Apply 10 μL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, allow it to dry in air, expose to iodine vapour until spots appear and examine in daylight.

MOBILE PHASE

1 volume of *anhydrous formic acid*, 50 volumes of *acetone* and 50 volumes of *methanol*.

CONFIRMATION

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

B. In the Assay, the retention time of the principal peak in the chromatogram obtained with solution (1) corresponds to that of the principal peak in the chromatogram obtained with solution (2).

TESTS

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in the mobile phase.

(1) Mix, with the aid of ultrasound, a quantity of the powdered tablets containing 0.5 g of Tramadol Hydrochloride with 80 mL, cool, add sufficient mobile phase to produce 100 mL and filter through a glass-fibre filter (Whatman GF/A is suitable).
(2) Dilute 1 volumes of solution (1) to 50 volumes and further dilute 1 volume to 10 volumes.
(3) 0.0015% w/v of *tramadol impurity A BPCRS*.
(4) 0.0015% w/v each of *tramadol hydrochloride BPCRS* and *tramadol impurity A BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Waters Symmetry C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.0 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 271 nm.
(f) Inject 20 µL of each solution.
(g) For solution (1) allow the chromatography to proceed for four times the retention time of the principal peak.

MOBILE PHASE

1 volume of *trifluoroacetic acid*, 30 volumes of *acetonitrile* and 69 volumes of *water*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution* between the peaks due to impurity A and tramadol is at least 3.0.

CALCULATION OF IMPURITIES

For impurity A, use the concentration of impurity A in solution (3).

For each unspecified impurity, use the concentration of tramadol hydrochloride in solution (2).

For the reporting threshold, use the concentration of tramadol hydrochloride in solution (2).

For peak identification, use solution (3).

Tramadol retention time: about 5 minutes.

Relative retention: impurity A, about 0.9.

LIMITS

— impurity A: not more than 0.3%;

— unspecified impurities: for each impurity, not more than 0.2%;

— total impurities: not more than 1.0%;

— reporting threshold: 0.1%.

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in the mobile phase.

(1) Mix, with the aid of ultrasound, a quantity of the powdered tablets containing 50 mg of Tramadol Hydrochloride in 150 mL, cool, add sufficient mobile phase to produce 200 mL and filter through a glass-fibre filter (Whatman GF/A is suitable).
(2) 0.025% w/v of *tramadol hydrochloride BPCRS*.
(3) 0.0015% w/v each of *tramadol hydrochloride BPCRS* and *tramadol impurity A BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity A and tramadol is at least 3.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{16}H_{25}NO_2$,HCl in the tablets using the declared content of $C_{16}H_{25}NO_2$,HCl in *tramadol hydrochloride BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities A to D listed under Tramadol Hydrochloride.