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Tramadol Prolonged-release Capsules

Prolonged-release Tramadol Capsules

Details for the public consultation of this monograph are as follows:

EAG/Panel/Working Party	Medicinal Chemicals 1
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Deadline for Comment	30 June 2021
Target Publication Date (subject to change)	BP 2023
Notes	Revised monograph If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required. Related substances quantitative limits introduced Impurities amended to exclude impurity E

Tramadol Prolonged-release Capsules 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 (OP₃, MOR) agonist; noradrenaline reuptake inhibitor; analgesic.

DEFINITION

Tramadol Prolonged-release Capsules 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 capsules comply with the requirements stated under Capsules and with the following requirements.

Content of tramadol hydrochloride, C₁₆H₂₅NO₂.HCl

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the powdered capsule contents containing 50 mg of Tramadol Hydrochloride with 25 mL of [methanol](#) for 5 minutes, filter and evaporate the filtrate to dryness. The [infrared absorption spectrum](#) of the dried residue, [Appendix II A](#), is concordant with the *reference spectrum* of tramadol hydrochloride ([RS 465](#)).

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 capsule contents 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 2 volumes of solution (1) to 100 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

For system suitability, use solution (4):

the [resolution](#) between 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 all other impurities, use the concentration of tramadol hydrochloride in solution (2).

Tramadol retention time: about 5 minutes.

Relative retention: impurity A, about 0.9.

LIMITS

Impurity A: 0.3%.

Unspecified impurities: 0.2%.

Total impurities: 1.0%.

Reporting threshold: 0.1%.

ASSAY

Weigh the contents of 20 capsules. Mix and powder if necessary. 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 capsule contents containing 50 mg of Tramadol Hydrochloride with 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 $C_{16}H_{25}NO_2 \cdot HCl$ in the capsules using the declared content of $C_{16}H_{25}NO_2 \cdot HCl$ in [tramadol hydrochloride BPCRS](#).

IMPURITIES

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