Status: Effectivity information can only be shown for content published to the website.

Update information can only be shown for content published to the website.

Tramadol Oral Drops

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

EAG/Panel/Working Party	Medicinal Chemicals 1
Contact Details	helen.corns@mhra.gov.uk laxsaan.elanganathan@mhra.gov.uk
Deadline for Comment	30 June 2021
Target Publication Date (subject to change)	BP 2023
Notes	New monograph If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required.

Action and use

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

DEFINITION

Tramadol Oral Drops contain Tramadol Hydrochloride in a suitable vehicle.

The Oral Drops comply with the requirements stated under Oral Liquids 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

In the Assay, record the UV spectrum of the principal peak in the chromatograms obtained with solutions (1) and (2) with a diode array detector in the range of 210 to 400 nm.

The UV spectrum of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2);

the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the 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.

(1) Dilute the oral drops with sufficient mobile phase to produce a solution containing 0.1% w/w of Tramadol Hydrochloride.

(2) Dilute 1 volume of solution (1) to 50 volumes with the mobile phase and further dilute 1 volume to 10 volumes with the mobile phase.

(3) 0.0002% w/v each of *tramadol hydrochloride BPCRS* and *tramadol impurity A BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *base-deactivated end-capped octylsilyl silica gel for chromatography* (5 µm) (LiChrospher 60 RP Select B 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 a column temperature of 40°.

(e) Use detection wavelengths of 213 nm and 273 nm.

(f) Inject 20 µL of each solution.

(g) Allow the chromatography to proceed for 6 times the retention time of tramadol.

MOBILE PHASE

15 volumes of *acetonitrile R1* and 85 volumes of a solution of 0.12% w/v of *diammonium hydrogen orthophosphate* in a mixture of 0.9 volumes of *triethylamine* and 100 volumes of *water*, adjusted to pH 3.0 with *orthophosphoric acid*.

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to tramadol (retention time about 4 minutes) are: impurity D, about 0.5; impurity A, about 0.9; impurity 1, about 1.1; impurity C, about 3.7 and impurity B, about 4.5.

SYSTEM SUITABILITY

For system suitability, use solution (3):

the *resolution* between impurity A and tramadol is at least 3.0.

CALCULATION OF IMPURITIES

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

Tramadol retention time: about 4 minutes.

Relative retention: impurity D, about 0.5; impurity A, about 0.9; impurity 1, about 1.1; impurity C, about 3.7 and impurity B, about 4.5.

LIMITS

At 213 nm

Impurities B and C: 0.2% of each.

At 273 nm

Unspecified impurities: 0.2%.

Total impurities: 1.0%.

Reporting threshold: 0.1%.

ASSAY

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

(1) Dilute a volume of the oral drops with sufficient mobile phase to produce a solution containing 0.1% w/v of Tramadol Hydrochloride.

(2) 0.1% w/v of *tramadol hydrochloride BPCRS* in the mobile phase.

(3) 0.0002% w/v each of *tramadol hydrochloride BPCRS* and *tramadol impurity A BPCRS* in the mobile phase.

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 oral drops from the chromatograms obtained and 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 - D listed under *Tramadol Hydrochloride* and:


1. 3-methoxyphenol

1. 3-methoxyphenol