Tramadol Oral Drops

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

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<thead>
<tr>
<th>EAG/Panel/Working Party</th>
<th>Medicinal Chemicals 1</th>
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<tbody>
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<td>Deadline for Comment</td>
<td>30 June 2021</td>
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<td>Target Publication Date (subject to change)</td>
<td>BP 2023</td>
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<td>Notes</td>
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<td>If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required.</td>
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Action and use

\(\mu\)-Opioid receptor (\(\text{OP}_3\), 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, \(\text{C}_{16}\text{H}_{25}\text{NO}_2\cdot\text{HCl}\)**

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