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## Tramadol Injection

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

EAG/Panel/Working Party	Medicinal Chemicals 1
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Notes	New monograph If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required.

### Action and use

$\mu$ -Opioid receptor (OP<sub>3</sub>, MOR) agonist and noradrenaline reuptake inhibitor; analgesic.

### DEFINITION

Tramadol Injection contains Tramadol Hydrochloride.

The Injection complies with the requirements stated under [Parenteral Preparations](#) and with the following requirements.

### Content of tramadol hydrochloride, C<sub>16</sub>H<sub>25</sub>NO<sub>2</sub>.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

### Acidity or alkalinity

pH of a 5% w/v solution, 6.0 to 7.0, [Appendix V L](#).

### Clarity and colour of solution

The solution for injection is *clear*, [Appendix IV A](#), and *colourless*, [Appendix IV B](#), Method I.

### Related substances

Carry out the method for [liquid chromatography](#), [Appendix III D](#), using the following solutions.

- (1) Dilute the injection with sufficient mobile phase to produce a solution containing 0.05% 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) 0.005% w/v each of [tramadol hydrochloride BPCRS](#) and [tramadol impurity A BPCRS](#) in the mobile phase.

### CHROMATOGRAPHIC CONDITIONS

- (a) Use a stainless steel column (25 cm × 4.6 mm) packed with [end-capped octadecylsilyl silica gel for chromatography](#) (5 µm) (Nucleosil 100-5 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 270 nm.
- (f) Inject 20 µL of each solution.
- (g) For solution (1) allow the chromatography to proceed for five times the retention time of the principal peak.

### MOBILE PHASE

295 volumes of [acetonitrile](#) and 705 volumes of 0.2% w/v of [trifluoroacetic acid](#) in [water](#).

### 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 5 minutes.

Relative retention: impurity D, about 0.7; impurity A, about 0.9; impurity 1, about 1.2; impurity 2, about 1.9; impurity C, about 2.4; impurity B, about 2.7 and impurity 3, about 4.2.

## LIMITS

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 the injection with sufficient mobile phase to produce a solution containing 0.05% w/w of Tramadol Hydrochloride.
- (2) 0.05% w/v of [tramadol hydrochloride BPCRS](#) in the mobile phase.
- (3) 0.005% w/v each of [tramadol hydrochloride BPCRS](#) and [tramadol impurity A BPCRS](#) in the mobile phase.

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 injection from the chromatograms obtained and 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](#) and:

 1. [ (N-oxide impurity) ]

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 2. [ (cyclization product) ]

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 3. [ (anisole) ]

3. [ (anisole) ]

