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

Ondansetron Injection

General Notices

Action and use

Serotonin 5HT$_3$ antagonist; treatment of nausea and vomiting.

DEFINITION

Ondansetron Injection is a sterile solution of Ondansetron Hydrochloride Dihydrate in Water for Injections.

The injection complies with the requirements stated under Parenteral Preparations and with the following requirements.

Content of ondansetron, $C_{18}H_{19}N_3O$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

To a volume of the injection containing the equivalent of 40 mg of ondansetron add 3 mL of 10M *sodium hydroxide*, shake and filter. Wash the precipitate with *water* and dry at 60° at a pressure of 2 kPa. The *infrared absorption spectrum* of the dried residue, Appendix II A, is concordant with the *reference spectrum* of ondansetron *(RS 418)*.

TESTS

Acidity

pH, 3.3 to 4.0, Appendix V L.

Impurity B

Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions in solution A.

Solution A: 0.5 volumes of 13.5M *ammonia*, 100 volumes of *ethanol (96%)* and 100 volumes of *methanol*.

(1) Dilute the injection, if necessary, to give a solution containing the equivalent of 0.2% w/v of ondansetron.
(2) Dilute 1 volume of solution (1) to 50 volumes and dilute 1 volume of the resulting solution to 5 volumes.
(3) 0.25% w/v solution of *ondansetron for TLC system suitability BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use *silica gel F_{254}* as the coating.
(b) Use the mobile phase described below.
(c) Apply 100 µL of each solution.
(d) Develop the plate to 15 cm.

(e) Remove the plate, dry in air and examine under *ultraviolet light (254 nm)*.

MOBILE PHASE

1 volume of 13.5M *ammonia*, 20 volumes of *methanol*, 25 volumes of *ethyl acetate* and 45 volumes of *dichloromethane*.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) shows three clearly separated spots (impurity A, Rf value of about 0.3; impurity B, Rf value of about 0.4; ondansetron, Rf value of about 0.6).

LIMITS

In the chromatogram obtained with solution (1):

any *secondary spot* corresponding to impurity B is not more intense than the spot obtained with solution (2) (0.4%).

Related substances

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

(1) Dilute the injection, if necessary, to give a solution containing the equivalent of 0.1% w/v of ondansetron.
(2) Dilute 1 volume of solution (1) to 50 volumes and further dilute 1 volume of the resulting solution to 10 volumes.
(3) 0.0004% w/v each of *ondansetron impurity E EPCRS* and *ondansetron impurity F EPCRS*.
(4) 0.05% w/v of *ondansetron impurity standard BPCRS*.
(5) 0.005% w/v of *ondansetron impurity A EPCRS* and 0.005% w/v of *ondansetron impurity G EPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *cyanosilyl silica gel for chromatography* (5 µm) (Spherisorb CN is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use ambient column temperature.
(e) Use a detection wavelength of 216 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

20 volumes of *acetonitrile R1* and 80 volumes of 0.02M *sodium dihydrogen orthophosphate dihydrate*, previously adjusted to pH 5.4 with 1M *sodium hydroxide*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution factor* between the peaks due to impurity C and D is at least 2.5.

LIMITS

Identify any peak corresponding to impurity C (the first eluting peak in solution (4)) and multiply the area of this peak by a correction factor of 0.6.

The peaks due to impurity E and impurity F in solution (3) and the peaks due to impurity A and impurity G in solution (5) may co-elute or may invert.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity D (the second eluting peak in solution (4)) is not greater than 0.75 times the area of the principal peak in the chromatogram obtained with solution (2) (0.15%);

the area of any peak corresponding to impurity C (the first eluting peak in solution (4)) is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of the peaks corresponding to impurities E and F is not greater than the area of the corresponding peaks in the chromatogram obtained with solution (3) (0.4%);

the sum of the areas of the peaks corresponding to impurities A and G is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (0.4%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of any *secondary peaks*, apart from any peaks corresponding to impurity C and impurity D, is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%).

Disregard any peak with an area less than 0.25 times the area of the principal peak in the chromatogram obtained with solution (2) (0.05%).

ASSAY

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

(1) Dilute the injection to give a solution containing the equivalent of 0.01% w/v of ondansetron.
(2) 0.0125% w/v of *ondansetron hydrochloride dihydrate BPCRS*.
(3) 0.05% w/v of *ondansetron impurity standard 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 C and impurity D is at least 2.5.

DETERMINATION OF CONTENT

Calculate the content of $C_{18}H_{19}N_3O$ in the injection using the declared content of $C_{18}H_{19}N_3O$ in *ondansetron hydrochloride dihydrate BPCRS*.

LABELLING

The quantity of active ingredient is stated in terms of the equivalent amount of ondansetron.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Ondansetron Hydrochloride Dihydrate.