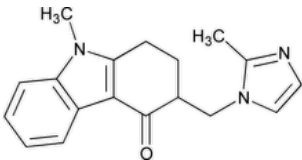


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Ondansetron

Change to read:



$C_{18}H_{19}N_3O$ ▲293.37▲ (USP 1-Aug-2024)
4*H*-Carbazol-4-one, 1,2,3,9-tetrahydro-9-methyl-3-[(2-methyl-1*H*-imidazol-1-yl)methyl]- (±);
▲9-Methyl-3-[(2-methyl-1*H*-imidazol-1-yl)methyl]-1,2,3,9-tetrahydro-4*H*-carbazol-4-one▲ (USP 1-Aug-2024) CAS RN®: 99614-02-5; UNII: 4AF302ESOS.

DEFINITION
Ondansetron contains NLT 98.0% and NMT 102.0% of ondansetron ($C_{18}H_{19}N_3O$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** ▲197A or▲ (USP 1-Aug-2024) 197K
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY

Change to read:

• **PROCEDURE**

▲**Solution A:** 2.4 g/L of [monobasic sodium phosphate, anhydrous](#) and 0.6 g/L of [sodium 1-heptanesulfonate](#) in [water](#). Adjust with [0.5 N sodium hydroxide](#) to a pH of 5.4.

Solution B: [Acetonitrile](#)

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	95	5
5	95	5
8	80	20
25	35	65
27	30	70
33	30	70
35	95	5

Time (min)	Solution A (%)	Solution B (%)
40	95	5

Diluent: [Acetonitrile](#) and [water](#) (30:70). To each liter of this solution add 1 mL of [formic acid](#).

Standard solution: 0.1 mg/mL of [USP Ondansetron RS](#) in *Diluent*

Sample solution: 0.1 mg/mL of Ondansetron in *Diluent*

Chromatographic system

(See [Chromatography \(621\), System Suitability.](#))

Mode: LC

Detector: UV 216 nm

Column: 4.6-mm × 25-cm; 5-μm packing [L11](#)

Temperatures

Autosampler: 15°

Column: 40°

Flow rate: 1 mL/min

Injection volume: 10 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%▲ (USP 1-Aug-2024)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ondansetron (C₁₈H₁₉N₃O) in the portion of Ondansetron taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of ondansetron from the *Sample solution*

r_S = peak response of ondansetron from the *Standard solution*

C_S = concentration of [USP Ondansetron RS](#) in the *Standard solution* (mg/mL)

C_U = concentration of Ondansetron in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

- [RESIDUE ON IGNITION \(281\)](#): NMT 0.1%

Change to read:

- [CHLORIDE AND SULFATE \(221\)](#), *Chloride*

▲ **Sample:** 1 g

Acceptance criteria: The turbidity produced in the *Sample* does not exceed that produced in 0.3 mL of 0.020 N [hydrochloric acid](#) (NMT 0.02%).▲ (USP 1-Aug-2024)

Delete the following:

- ▲ **LIMIT OF ONDANSETRON RELATED COMPOUND D**▲ (USP 1-Aug-2024)

Change to read:

- **ORGANIC IMPURITIES**

▲ **Solution A, Solution B, Mobile phase, Diluent, and Chromatographic system:** Proceed as directed in the Assay.

System suitability solution: 1 mg/mL of [USP Ondansetron RS](#) and 0.001 mg/mL of [USP Ondansetron Related Compound G](#) in *Diluent*

Standard solution: 0.001 mg/mL each of [USP Ondansetron RS](#) and [USP Ondansetron Related Compound D RS](#) in *Diluent*

Sensitivity solution: 0.5 μg/mL each of [USP Ondansetron RS](#) and [USP Ondansetron Related Compound D RS](#) from the *Standard solution* in *Diluent*

Sample solution: 1.0 mg/mL of Ondansetron in *Diluent*

System suitability

Samples: *System suitability solution, Standard solution, and Sensitivity solution*

[NOTE—The relative retention times in [Table 2](#) are provided as information that could aid in peak assignment.]

Table 2

Name	Relative Retention Time
Imidazole ^a	0.28
Ondansetron related compound F ^b	0.33
Ondansetron related compound A ^c	0.94
Ondansetron	1.00
Ondansetron related compound G	1.04
Ondansetron related compound C ^d	1.11
Methylene bisondansetron ^e	1.13
Ondansetron related compound D	1.2

^a 1*H*-Imidazole.

^b 2-Methyl-1*H*-imidazole.

^c 3-[(Dimethylamino)methyl]-9-methyl-1,2,3,9-tetrahydro-4*H*-carbazol-4-one.

^d 9-Methyl-1,2,3,9-tetrahydro-4*H*-carbazol-4-one.

^e Disregard the peak corresponding to methylene bisondansetron. Quantified in the test for *Limit of Methylene Bisondansetron*.

Suitability requirements

Resolution: NLT 2.0 between ondansetron and ondansetron related compound G, *System suitability solution*

Relative standard deviation: NMT 5.0% for ondansetron, *Standard solution*

Signal-to-noise ratio: NLT 10 for ondansetron, *Sensitivity solution*

Analysis

Samples: *Standard solution and Sample solution*

Calculate the percentage of ondansetron related compound D in the portion of Ondansetron taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of ondansetron related compound D from the *Sample solution*

r_S = peak response of ondansetron related compound D from the *Standard solution*

C_S = concentration of [USP Ondansetron Related Compound D RS](#) in the *Standard solution* (mg/mL)

C_U = concentration of Ondansetron in the *Sample solution* (mg/mL)

Calculate the percentage of any unspecified impurity in the portion of Ondansetron taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of any unspecified impurity from the *Sample solution*

r_S = peak response of ondansetron from the *Standard solution*

C_S = concentration of [USP Ondansetron RS](#) in the *Standard solution* (mg/mL)

C_U = concentration of Ondansetron in the *Sample solution* (mg/mL)

Acceptance criteria: See [Table 3](#). The reporting threshold is 0.05%.

Table 3

Name	Acceptance Criteria, NMT (%)
Ondansetron related compound D	0.10
Any unspecified impurity	0.1
Total impurities	0.5

▲ (USP 1-Aug-2024)

Add the following:

▲ • **LIMIT OF METHYLENE BISONDANSETRON (If Present)**

Buffer: 2.4 g/L of [monobasic sodium phosphate, anhydrous](#) in [water](#). Adjust with [0.5 N sodium hydroxide](#) to a pH of 6.5.

Mobile phase: [Acetonitrile](#) and *Buffer* (65:35)

Peak identification solution: 1 mg/mL of [USP Ondansetron Resolution Mixture RS](#) in *Mobile phase*

Standard solution: 0.002 mg/mL of [USP Ondansetron RS](#) in *Mobile phase*

Sensitivity solution: 0.001 mg/mL of [USP Ondansetron RS](#) from the *Standard solution* in *Mobile phase*

Sample solution: 1.0 mg/mL of Ondansetron in *Mobile phase*

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 216 nm

Column: 4.6-mm × 25-cm; 5-μm packing [L10](#)

Temperatures

Autosampler: 15°

Column: 35°

Flow rate: 1.5 mL/min

Injection volume: 20 μL

Run time: NLT 5 times the retention time of ondansetron

System suitability

Samples: *Standard solution* and *Sensitivity solution*

[NOTE—The relative retention times for ondansetron and methylene bisondansetron are 1.0 and 3.7, respectively. These relative retention times are provided as information that could aid in peak assignment.]

Suitability requirements

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of methylene bisondansetron in the portion of Ondansetron taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of methylene bisondansetron from the *Sample solution*

r_S = peak response of ondansetron from the *Standard solution*

C_S = concentration of [USP Ondansetron RS](#) in the *Standard solution* (mg/mL)

C_U = concentration of Ondansetron in the *Sample solution* (mg/mL)

F = relative response factor, 0.63

Acceptance criteria: NMT 0.4%▲ (USP 1-Aug-2024)

SPECIFIC TESTS

- [WATER DETERMINATION \(921\), Method I, Method Ia](#): NMT 3.0%

Add the following:

- ▲• [BACTERIAL ENDOTOXINS TEST \(85\)](#): Where the label states that Ondansetron must be subjected to further processing during the preparation of injectable dosage forms, the level of bacterial endotoxins is such that the requirement under the relevant dosage form monograph(s) in which Ondansetron is used can be met.▲ (USP 1-Aug-2024)

Add the following:

- ▲• [MICROBIAL ENUMERATION TESTS \(61\)](#): The total aerobic microbial count does not exceed 10² cfu/g and the total combined molds and yeast count does not exceed 50 cfu/g.▲ (USP 1-Aug-2024)

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers at room temperature.

Add the following:

- ▲• **LABELING:** Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms.▲ (USP 1-Aug-2024)

Change to read:

- [USP REFERENCE STANDARDS \(11\)](#).

[USP Ondansetron RS](#)

▲▲ (USP 1-Aug-2024)

[USP Ondansetron Related Compound D RS](#)

9-Methyl-3-methylene-1,2,3,9-tetrahydro-4*H*-carbazol-4-one.



[USP Ondansetron Related Compound G](#)

3-[(1*H*-Imidazol-1-yl)methyl]-9-methyl-1,2,3,9-tetrahydro-4*H*-carbazol-4-one.



[USP Ondansetron Resolution Mixture RS](#)

Contains a mixture of the following 3 compounds:

Ondansetron hydrochloride.

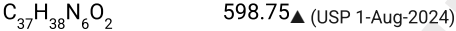
Ondansetron related compound A;

3-[(Dimethylamino)methyl]-9-methyl-1,2,3,9-tetrahydro-4*H*-carbazol-4-one hydrochloride.



Methylene bisondansetron;

6,6'-Methylenebis{9-methyl-3-[(2-methyl-1*H*-imidazol-1-yl)methyl]-1,2,3,9-tetrahydro-4*H*-carbazol-4-one}.



Auxiliary Information - Please [check for your question in the FAQs](#) before contacting USP.

Topic/Question	Contact	Expert Committee
ONDANSETRON	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: [Chromatographic Database](#)

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