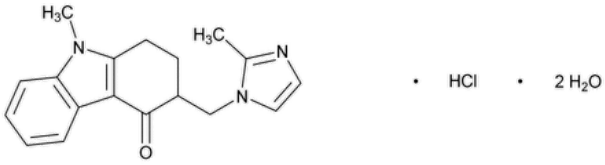
Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-Aug-2024
Document Type: USP Monographs
DocId: GUID-28EE3481-B13C-45F7-9B5C-D91BD991EF73_7_en-US
DOI: https://doi.org/10.31003/USPNF_M58650_07_01
DOI Ref: x06em

Ondansetron Hydrochloride

Change to read:



$C_{18}H_{19}N_3O \cdot HCl \cdot 2H_2O$ ▲365.86▲ (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]-, monohydrochloride, (±)-, dihydrate;
▲9-Methyl-3-[(2-methyl-1*H*-imidazol-1-yl)methyl]-1,2,3,9-tetrahydro-4*H*-carbazol-4-one hydrochloride dihydrate▲ (USP 1-Aug-2024) CAS RN®: 103639-04-9; UNII: NMH84OZK2B.

DEFINITION

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

IDENTIFICATION

Change to read:

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** ▲197A, 197K, or▲ (USP 1-Aug-2024) 197M

• **B. Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Chloride***

Sample solution: Dissolve 20 mg in 2 mL of water, add 1 mL of 2 M nitric acid, and filter.

Acceptance criteria: Meets the requirements.

Add the following:

▲• **C.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution,* as obtained in the *Assay.*▲ (USP 1-Aug-2024)

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

Time (min)	Solution A (%)	Solution B (%)
25	35	65
27	30	70
33	30	70
35	95	5
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 Hydrochloride RS in *Diluent*

Sample solution: 0.1 mg/mL of Ondansetron Hydrochloride 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 hydrochloride ($C_{18}H_{19}N_3O \cdot HCl$) in the portion of Ondansetron Hydrochloride 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 Hydrochloride RS in the *Standard solution* (mg/mL)

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

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

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

Delete the following:

▲• **Organic Impurities, Method I**▲ (USP 1-Aug-2024)

Add the following:

▲• **Limit of Methylene Bisondansetron**

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 Hydrochloride RS in *Mobile phase*

Sensitivity solution: 0.001 mg/mL of USP Ondansetron Hydrochloride RS from the *Standard solution* in *Mobile phase*

Sample solution: 1.0 mg/mL of Ondansetron Hydrochloride 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 Hydrochloride 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 Hydrochloride RS in the *Standard solution* (mg/mL)

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

F = relative response factor, 0.75

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

Delete the following:

▲• **ORGANIC IMPURITIES, METHOD II**▲ (USP 1-AUG-2024)

Delete the following:

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

Add the following:

▲• **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 Hydrochloride RS and 0.001 mg/mL of USP Ondansetron Related Compound G in *Diluent*

Standard solution: 0.001 mg/mL each of USP Ondansetron Hydrochloride RS and USP Ondansetron Related Compound D RS, and 0.002 mg/mL of USP Imidazole RS in *Diluent*

Sensitivity solution: 0.5 µg/mL each of USP Ondansetron Hydrochloride RS and USP Ondansetron Related Compound D RS, and 0.001 mg/mL of USP Imidazole RS from the *Standard solution* in *Diluent*

Sample solution: 1.0 mg/mL of Ondansetron Hydrochloride 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	0.28
Ondansetron related compound F[a]	0.33
Ondansetron related compound A[b]	0.94
Ondansetron	1.00
Ondansetron related compound G	1.04
Ondansetron related compound C[c]	1.11
Methylene bisondansetron[d]	1.13
Ondansetron related compound D	1.2

[a] 2-Methyl-1*H*-imidazole.

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

[c] 9-Methyl-1,2,3,9-tetrahydro-4*H*-carbazol-4-one.

[d] 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 or imidazole in the portion of Ondansetron Hydrochloride taken:

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

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

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

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

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

Calculate the percentage of any other specified or unspecified impurity in the portion of Ondansetron Hydrochloride taken:

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

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

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

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

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

F = relative response factor (see *Table 3*)

Acceptance criteria: See *Table 3*. The reporting threshold is 0.05%.

Table 3

Name	Relative Response Factor	Acceptance Criteria, NMT (%)
Imidazole	—	0.2
Ondansetron related compound F	0.65	0.2
Ondansetron related compound A	1.0	0.2
Ondansetron related compound C	1.5	0.2
Ondansetron related compound D	—	0.10
Any unspecified impurity	1.0	0.1
Total impurities	—	0.5

▲ (USP 1-Aug-2024)

SPECIFIC TESTS

• **Water Determination** ⟨921⟩, *Method I, Method Ia*: 9.0%–10.5%

Add the following:

▲• **Bacterial Endotoxins Test** ⟨85⟩: Where the label states that Ondansetron Hydrochloride must be subjected to further processing during the preparation of injectable dosage forms, the level of bacterial endotoxins are such that the requirement under the relevant dosage form monograph(s) in which Ondansetron Hydrochloride is used can be met.▲ (USP 1-Aug-2024)

Add the following:

▲• **Microbial Enumeration Tests** ⟨61⟩: The total aerobic microbial count does not exceed 10^2 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. Store at 25°, excursions permitted between 15° and 30°.

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 Imidazole RS

1*H*-Imidazole.

$C_3H_4N_2$ 68.08▲ (USP 1-Aug-2024)

USP Ondansetron Hydrochloride 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.

▲$C_{14}H_{13}NO$ 211.26

USP Ondansetron Related Compound G

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

$C_{17}H_{17}N_3O$ 279.34▲ (USP 1-Aug-2024)

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.

$C_{16}H_{20}N_2O \cdot HCl$ 292.81

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}.

$C_{37}H_{38}N_6O_2$ 598.75▲ (USP 1-Aug-2024)

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
ONDANSETRON HYDROCHLORIDE	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

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 48(5)

Current DocID: GUID-28EE3481-B13C-45F7-9B5C-D91BD991EF73_7_en-US

DOI: https://doi.org/10.31003/USPNF_M58650_07_01

DOI ref: x06em