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Ondansetron Injection

DEFINITION

Ondansetron Injection is a sterile solution of Ondansetron Hydrochloride in Water for Injection or of Ondansetron in Water for Injection prepared with the aid of Hydrochloric Acid. It may contain suitable buffers and/or tonicity adjusting agents. It contains an amount of Ondansetron Hydrochloride equivalent to NLT 95.0% and NMT 105.0% of the labeled amount of ondansetron ($C_{18}H_{19}N_3O$).

IDENTIFICATION

• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

Add the following:

▲• **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-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
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: Nominally 0.1 mg/mL of ondansetron from Injection in *Diluent*

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 216 nm. For *Identification B*, use a diode array detector in the range of 200–400 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 1.0%▲ (USP 1-May-2024)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ondansetron ($C_{18}H_{19}N_3O$) in the portion of Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

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

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

C_S = concentration▲ (USP 1-May-2024) of USP Ondansetron Hydrochloride RS in the *Standard solution* (mg/mL)

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

M_{r1} = molecular weight of ondansetron, ▲293.37▲ (USP 1-May-2024)

M_{r2} = molecular weight of anhydrous ondansetron hydrochloride, 329.83

Acceptance criteria: 95.0%–105.0%

IMPURITIES

Delete the following:

▲• **Limit of Ondansetron Related Compound D**▲ (USP 1-May-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 Hydrochloride RS and 0.002 mg/mL of USP Ondansetron Related Compound G in *Diluent*

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

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

Sample solution: Nominally 1.0 mg/mL of ondansetron from Injection 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

Name	Relative Retention Time
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]	1.1
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 hydrochloride.

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

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 Injection 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 = nominal concentration of ondansetron in the *Sample solution* (mg/mL)

Calculate the percentage of any other specified or unspecified degradation product in the portion of Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of any other specified or any unspecified degradation product 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 = nominal concentration of ondansetron in the *Sample solution* (mg/mL)

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

M_{r1} = molecular weight of ondansetron, 293.37

M_{r2} = molecular weight of anhydrous ondansetron hydrochloride, 329.83

Acceptance criteria: See *Table 3*. The reporting threshold is 0.1%.

Table 3

Name	Relative Response Factor	Acceptance Criteria, NMT (%)
Ondansetron related compound A	1.0	0.2
Ondansetron related compound C	1.5	0.2
Ondansetron related compound D	—	0.12
Any unspecified degradation product	1.0	0.2
Total degradation products	—	0.5

▲ (USP 1-May-2024)

SPECIFIC TESTS

Change to read:

• **Bacterial Endotoxins Test** ⟨85⟩**:** ▲Meets the requirements▲ (USP 1-May-2024)

Add the following:

▲• **Sterility Tests** ⟨71⟩**:** Meets the requirements▲ (USP 1-May-2024)

• **pH** ⟨791⟩**:** 3.3–4.0

• **Particulate Matter in Injections** ⟨788⟩**:** Meets the requirements for small-volume injections

• **Other Requirements:** It meets the requirements under *Injections and Implanted Drug Products* ⟨1⟩.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in single-dose or in multiple-dose containers, preferably of Type I glass, at a temperature between 2° and 30°, protected from light.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Ondansetron Hydrochloride RS

▲▲ (USP 1-May-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-May-2024)

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

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

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