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Ondansetron Orally Disintegrating Tablets

DEFINITION

Ondansetron Orally Disintegrating Tablets contain the equivalent of NLT 90.0% and NMT 110.0% 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*.

• **B.** **Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: 197U** [Note—Alternatively, the UV spectra of the major peaks of the *Sample solution* and the *Standard solution*, as obtained in the *Assay*, may be used to meet the *Acceptance criteria*.]

Diluent: 0.1 N hydrochloric acid

Standard solution: 8 µg/mL of USP Ondansetron RS in *Diluent*

Sample solution: Nominally 8 µg/mL of ondansetron from Tablets in *Diluent*. Pass a portion of the solution through a suitable filter of 0.45-µm pore size, discarding the first few milliliters of the filtrate.

Wavelength range: 200–400 nm

Cell: 1 cm

Blank: *Diluent*

Acceptance criteria: The UV absorption spectrum of the *Sample solution* exhibits maxima and minima at the same wavelengths as those of the *Standard solution*.

ASSAY

• **Procedure**

Diluent: 0.01 N hydrochloric acid

Buffer: 2.72 g/L of monobasic potassium phosphate in water. Adjust with 1 N sodium hydroxide or 0.5 N sodium hydroxide to a pH of 5.4.

Mobile phase: Acetonitrile and *Buffer* (48:52)

System suitability solution: 0.02 mg/mL of USP Ondansetron Related Compound A RS and 0.006 mg/mL of USP Ondansetron RS in *Diluent*

Standard solution: 40 µg/mL of USP Ondansetron RS in *Diluent*

Sample stock solution: Nominally equivalent to 400 µg/mL of ondansetron prepared as follows. Transfer 10 Tablets to a suitable volumetric flask. Add *Diluent* to fill about 60% of the flask volume. Shake by mechanical means for about 5 min, and dilute with *Diluent* to volume. Pass a portion of this solution through a polypropylene membrane of 0.45-µm pore size, discarding the first 5 mL of the filtrate.

Sample solution: Nominally 40 µg/mL of ondansetron in *Diluent*, from the *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 216 nm. If the procedure is used for *Identification B*, use a diode array detector set at 200–400 nm.

Column: 4.6-mm × 25-cm; packing L10

Flow rate: 1.5 mL/min

Injection volume: 10 µL

System suitability

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

[Note—The relative retention times for ondansetron and ondansetron related compound A are 1.0 and 1.1, respectively.]

Suitability requirements

Resolution: NLT 1.5 between ondansetron related compound A and ondansetron, *System suitability solution*

Tailing factor: NMT 2.0 for the ondansetron peak, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

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 Tablets taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Disintegration ⟨701⟩**

Test 1

Time: NMT 10 s

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Disintegration Test 2*.

Time: NMT 60 s

• **Dissolution ⟨711⟩**

Medium: 0.1 N hydrochloric acid; 500 mL, deaerated

Apparatus 2: 50 rpm

Time: 10 min

Detector: UV 310 nm

Cell

For 4- and 8-mg Tablets: 1 cm

For 16-mg Tablets: 0.5 cm

For 24-mg Tablets: 0.2 cm

Standard solution: (L/500) mg/mL of USP Ondansetron RS in *Medium*, where L is the label claim in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ondansetron ($C_{18}H_{19}N_3O$) dissolved:

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times V \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

L = label claim (mg/Tablet)

V = volume of *Medium*, 500 mL

Tolerances: NLT 80% (Q) of the labeled amount of ondansetron ($C_{18}H_{19}N_3O$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

• **Organic Impurities**

Buffer: Prepare as directed in the *Assay*.

Mobile phase: Acetonitrile and *Buffer* (1:4)

System suitability solution: 2 µg/mL each of USP Ondansetron Related Compound D RS, 2-methylimidazole, and USP Ondansetron RS in *Mobile phase*. [Note—First dissolve in acetonitrile, and then dilute with *Mobile phase* to volume.]

Standard solution: 2 µg/mL of USP Ondansetron RS in *Mobile phase*

Sensitivity solution: 0.2 µg/mL of USP Ondansetron RS, from the *Standard solution* in *Mobile phase*

Sample solution: Nominally equivalent to 400 µg/mL of ondansetron prepared as follows. Transfer 10 Tablets to a suitable volumetric flask. Add *Mobile phase* to fill about 60% of the flask volume. Shake by mechanical means for about 5 min, and dilute with *Mobile phase* to

volume. Centrifuge a portion of this solution at 3000 rpm for 10 min. Use the supernatant.

Chromatographic system

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

Mode: LC

Detector: UV 216 nm

Column: 4.6-mm × 25-cm; packing L10

Flow rate: 1.5 mL/min

Injection volume: 20 µL

Run time: About 60 min

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between ondansetron and any adjacent peak, *System suitability solution*

Column efficiency: NLT 8000 theoretical plates for ondansetron, *System suitability solution*

Tailing factor: NMT 2.0 for the ondansetron peak, *System suitability solution*

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

Signal-to-noise ratio: NLT 15, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual impurity in the portion of Tablets taken:

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

r_U = peak area of each individual impurity from the *Sample solution*

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

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

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

F = relative response factor for each impurity (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
2-Methylimidazole	0.16	0.5	0.2
Ondansetron related compound D	0.45	1.2	0.12
Ondansetron	1.0	—	—
Individual unknown impurity	—	1.0	0.2
Total impurities	—	—	0.5

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in light-resistant containers. Store at controlled room temperature.
- **Labeling:** The labeling states the *Disintegration* test used only if *Test 1* is not used.

Change to read:

- **USP Reference Standards ⟨11⟩**

USP Ondansetron RS

USP Ondansetron Related Compound A RS

▲3-[(Dimethylamino)methyl]-9-methyl-1,2,3,9-tetrahydro-4*H*-carbazol-4-one hydrochloride.▲ (ERR 1-Feb-2022)

$C_{16}H_{20}N_2O \cdot HCl$ ▲292.81▲ (ERR 1-Feb-2022)

USP Ondansetron Related Compound D RS

▲9-Methyl-3-methylene-1,2,3,9-tetrahydro-4*H*-carbazol-4-one.▲ (ERR 1-Feb-2022)

$C_{14}H_{13}NO$ 211.26

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

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

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