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Ondansetron Tablets

DEFINITION

Ondansetron Tablets contain Ondansetron Hydrochloride equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of ondansetron ($C_{18}H_{19}N_3O$).

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**

Sample: Transfer a portion of the powder from finely powdered Tablets, equivalent to 100 mg of ondansetron hydrochloride, to a suitable conical flask. Add 50 mL of alcohol, and swirl. Pass the liquid through a PTFE filter of 0.45-µm pore size into a 50-mL beaker. Evaporate the solvent on a rotary evaporator. Dry the precipitate in an air oven for 1 h at 105°. Prepare a suitable dispersion of the residue in potassium bromide, and record the spectra of the *Sample* and the standard specimen in the spectral range 3800–650 cm^{-1}. [Note—It is recommended that a solution of USP Ondansetron Hydrochloride RS in alcohol be prepared at a concentration of 2 mg/mL before the evaporation, followed by the drying steps.]

Acceptance criteria: The *Sample* shows strong bands at 1621, 1481, 1281, and 758 cm^{-1}, similar to the potassium bromide dispersion of USP Ondansetron Hydrochloride RS.

• **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

• **Procedure**

Buffer: 2.7 g/L of monobasic potassium phosphate. Adjust with 1 N sodium hydroxide to a pH of 5.4.

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

Diluent: Acetonitrile and *Buffer* (1:1)

Standard solution: 0.05 mg/mL of ondansetron (free base) in *Diluent* from USP Ondansetron Hydrochloride RS

Sample stock solution: Weigh and finely powder NLT 20 Tablets. Transfer a portion of the powder, equivalent to 50 mg of ondansetron, based on the label claim, to a 100-mL volumetric flask. Add 70 mL of *Diluent*, and sonicate for about 20 min. Dilute with *Diluent* to volume. Centrifuge a portion of the solution.

Sample solution: Quantitatively dilute the supernatant with *Diluent* to obtain a solution having a nominal concentration of 0.05 mg/mL of ondansetron, based on the label claim. Pass through a suitable nylon filter of 0.45-µm pore size, and use the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 216 nm

Column: 4.6-mm × 25-cm; 5-µm packing L10

Flow rate: 1.5 mL/min

Injection size: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the label claim 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 ondansetron (free base) 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

• **Dissolution ⟨711⟩**

Test 1

Medium: Water; 500 mL, deaerated

Apparatus 2: 50 rpm

Time: 15 min

Standard solution: USP Ondansetron Hydrochloride RS in *Medium* in a concentration similar to the one expected in the *Sample solution*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, and dilute, if necessary, with *Medium*.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: UV

Analytical wavelength: 310 nm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

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

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times (M_{r1}/M_{r2}) \times V \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

L = label claim (mg/Tablet)

M_{r1} = molecular weight of ondansetron, 293.36

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

V = volume of *Medium*, 500 mL

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

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

Medium, Apparatus 2, Standard solution, Sample solution, Instrumental conditions, and **Analysis:** Proceed as directed for *Test 1*.

Time: 30 min

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

Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

Medium: 0.01 N hydrochloric acid; 500 mL, deaerated

Apparatus 2: 50 rpm

Time: 30 min

Standard solution: Known concentration of USP Ondansetron Hydrochloride RS in *Medium*, close to the expected concentration of the *Sample solution*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, and dilute, if necessary, with *Medium*.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: UV

Analytical wavelength: 248 nm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

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

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times (M_{r1}/M_{r2}) \times V \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

L = label claim (mg/Tablet)

M_{r1} = molecular weight of ondansetron, 293.36

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

V = volume of *Medium*, 500 mL

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

Test 4: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 4*.

Medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 2: 50 rpm

Time: 30 min

Standard stock solution: 450 µg/mL of USP Ondansetron Hydrochloride RS in *Medium*

Standard solution: Dilute the *Standard stock solution* quantitatively and stepwise, if necessary, with *Medium* to obtain a final concentration of about (L/500) mg/mL, where L is the Tablet label claim, in mg.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: 249 nm

Cell path: 1 cm for Tablets labeled to contain 4 or 8 mg; 0.2 cm for Tablets labeled to contain 16 or 24 mg

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

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

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times (M_{r1}/M_{r2}) \times V \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

L = label claim (mg/Tablet)

M_{r1} = molecular weight of ondansetron, 293.36

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

V = volume of *Medium*, 500 mL

Tolerances: NLT 80% (Q) of the labeled amount of ondansetron is dissolved.

Test 5: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 5*.

Medium, Apparatus 2, Standard solution, Sample solution, Instrumental conditions, and **Analysis:** Proceed as directed for *Test 1*.

Time: 30 min

Tolerances: NLT 70% (*Q*) of the labeled amount of ondansetron is dissolved.

Test 6: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 6*.

Medium: Water; 500 mL, deaerated

Apparatus 2: 50 rpm

Time: 30 min

Buffer: 3.12 g/L of monobasic sodium phosphate dihydrate. Adjust with 1 N sodium hydroxide to a pH of 5.4.

Mobile phase: Acetonitrile and *Buffer* (40:60)

Standard solution

For Tablets labeled to contain 4 or 24 mg: 0.01 mg/mL of USP Ondansetron Hydrochloride RS in *Medium*

For Tablets labeled to contain 8 mg: 0.02 mg/mL of USP Ondansetron Hydrochloride RS in *Medium*

Sample solution

For Tablets labeled to contain 4 or 8 mg: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

For Tablets labeled to contain 24 mg: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Further dilute 4.0 mL of this solution with *Medium* to 25.0 mL.

Chromatographic system

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

Mode: LC

Detector: UV 216 nm

Column: 4.6-mm × 15-cm; 5-µm packing L10

Flow rate: 2.0 mL/min

Injection size: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

r_U = peak response of the *Sample solution*

r_S = peak response of the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

L = label claim (mg/Tablet)

M_{r1} = molecular weight of ondansetron, 293.36

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

V = volume of *Medium*, 500 mL

D = dilution factor of the *Sample solution*

Tolerances: NLT 75% (*Q*) of the labeled amount of ondansetron is dissolved.

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

IMPURITIES

Change to read:

- **Organic Impurities**

Buffer and **Mobile phase:** Proceed as directed in the *Assay*.

System suitability solution: 0.05 and 0.1 mg/mL of USP Ondansetron Related Compound A RS and USP Ondansetron Hydrochloride RS, respectively, in *Mobile phase*

Standard stock solution: Use the *Standard solution* in the *Assay*.

Standard solution: 1.5 µg/mL of ondansetron in *Mobile phase* from the *Standard stock solution*

Sample solution: Weigh and crush NLT 20 Tablets. Transfer a quantity of powder, equivalent to 50 mg of ondansetron, to a 100-mL volumetric flask. Add about 70 mL of *Mobile phase*, and sonicate for about 20 min. Dilute with *Mobile phase* to volume. Centrifuge the solution. Pass a portion of the solution through a suitable nylon filter of 0.45-µm pore size, and use the filtrate.

Chromatographic system: Proceed as directed in the *Assay*.

Run time: At least 45 min for the *Sample solution*

System suitability

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

Suitability requirements

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

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each 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 response of each individual impurity from the *Sample solution*

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

C_S = concentration of ondansetron (free base) in the *Standard solution* (mg/mL)

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

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
2-Methyl imidazole[a]	0.22	0.53	0.2
Ondansetron related compound C[b]	0.40	1.2	0.2
Ondansetron related compound D[c]	0.47	1.3	0.1
Ondansetron related compound A[d]	0.87	0.90	0.2
Desmethylondansetron[a,e]	0.90	0.91	0.2
Ondansetron	1.0	—	—
Any other individual, unspecified degradation product	—	1.0	0.2
Total impurities	—	—	1.0

[a] Not to be included in total impurities.

▲[b] 9-Methyl-1,2,3,9-tetrahydro-4*H*-carbazol-4-one.▲ (ERR 1-Apr-2022)

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

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

▲e 3-[(1*H*-Imidazol-1-yl)methyl]-9-methyl-1,2,3,9-tetrahydro-4*H*-carbazol-4-one.▲ (ERR 1-Apr-2022)

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at controlled room temperature.

• **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Ondansetron Hydrochloride 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-Apr-2022)

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

Topic/Question	Contact	Expert Committee
ONDANSETRON 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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