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Oseltamivir Phosphate Capsules

DEFINITION
Oseltamivir Phosphate Capsules contain Oseltamivir Phosphate equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of oseltamivir ($C_{16}H_{28}N_2O_4$).

IDENTIFICATION
The retention time of the major peaks of the *Sample solution* corresponds to those of the *Standard solution,* as obtained in the *Assay.*

ASSAY
Change to read:

• **Oseltamivir**

Solution A: Dissolve 6.8 g of potassium dihydrogen phosphate in 980 mL of water. Adjust with 1 M potassium hydroxide solution to a pH of 6.0, and dilute with water to 1 L.

Mobile phase: Methanol, acetonitrile, and *Solution A* (245:135:620)

Diluent: Methanol, acetonitrile, and 0.01 N phosphoric acid (245:135:620)

Standard solution: 1 mg/mL of USP Oseltamivir Phosphate RS in *Diluent*

Sample solution: Weigh the contents of 20 Capsules, and mix. Prepare the equivalent of about 1 mg of oseltamivir phosphate per mL, based on the label claim, by first dispersing a suitable portion of the powder in about 40% of the flask volume of *Diluent* using an ultrasonic bath for about 20 min, and diluting with *Diluent* to volume. Centrifuge an aliquot of this solution, and use the supernatant.

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

Mode: LC

Detector: UV 207 nm

Column: 4.6-mm × 25-cm; packing L7

Column temperature: 50°

Flow rate: 1.2 mL/min

Injection size: 15 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 labeled amount of oseltamivir ($C_{16}H_{28}N_2O_4$) in the portion of Capsules taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

M_{r1} = molecular weight of oseltamivir, ▲312.41▲ (CN 1-Aug-2024)

M_{r2} = molecular weight of oseltamivir phosphate, 410.40

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Test 1

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 20 min

Detector: UV 240 nm

Standard solution: Prepare a solution in *Medium* having a known concentration of about 0.11 mg/mL of USP Oseltamivir Phosphate RS. Quantitatively dilute a portion of this solution with *Medium* to obtain a solution having a known concentration similar to the expected concentration in the solution under test.

Sample solution: Pass a portion of the solution under test through a suitable filter of 1-µm pore size.

Excipients solution: Suspend an amount of the placebo mixture equivalent to the weight of the excipients in one dosage unit and one empty Capsule shell in 900 mL of *Medium*. Heat to 37°, and filter.

Analysis

Samples: *Medium*, *Standard solution*, *Sample solution*, and *Excipients solution*

Determine the amount of oseltamivir phosphate ($C_{16}H_{28}N_2O_4 \cdot H_3PO_4$) dissolved by measuring the absorbance at about 240 nm of the *Sample solution* and *Excipients solution* in comparison with the *Standard solution*, using the *Medium* as the blank. Calculate the percentage of oseltamivir phosphate dissolved:

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

A_U = absorbance of the *Sample solution*

A_E = absorbance of the *Excipients solution*

C_S = concentration of USP Oseltamivir Phosphate RS in the *Standard solution*

V = volume of *Medium*, 900 mL

A_S = absorbance of the *Standard solution*

L = label claim for oseltamivir phosphate (mg/Capsule)

Tolerances: NLT 75% (Q) of the labeled amount of oseltamivir phosphate is dissolved.

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

Medium: 0.1 N hydrochloric acid; 500 mL, deaerated

Apparatus 2: 50 rpm

Time: 30 min

Buffer: 6.8 g/L of monobasic potassium phosphate in water. Adjust with 8 N potassium hydroxide solution to a pH of 6.0.

Mobile phase: Acetonitrile and *Buffer* (25:75)

Standard solution: (L/500) mg/mL of oseltamivir from USP Oseltamivir Phosphate RS in *Medium*, where L is the label claim in mg/Capsule. Sonicate to dissolve, if necessary.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 207 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 50°

Flow rate: 1.2 mL/min

Injection volume: 15 µL

Run time: NLT 1.5 times the retention time of oseltamivir

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 labeled amount of oseltamivir ($C_{16}H_{28}N_2O_4$) dissolved:

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

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

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

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

V = volume of the *Medium*, 500 mL

M_{r1} = molecular weight of oseltamivir, ▲312.41▲ (CN 1-Aug-2024)

M_{r2} = molecular weight of oseltamivir phosphate, 410.40

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of oseltamivir ($C_{16}H_{28}N_2O_4$) is dissolved.

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

IMPURITIES

Change to read:

• **Organic Impurities**

Solution A, Mobile phase, Diluent, Standard solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of individual impurities in the portion of Capsules 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 each individual impurity from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

F = relative response factor from *Table 1*

M_{r1} = molecular weight of oseltamivir, ▲312.41▲ (CN 1-Aug-2024)

M_{r2} = molecular weight of oseltamivir phosphate, 410.40

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
▲Oseltamivir acid analog▲ (CN 1-Aug-2024) [a]	0.18	1.4	2.0
▲Oseltamivir phenol analog▲ (CN 1-Aug-2024) [b]	0.49	2.7	0.3
Oseltamivir phosphate	1.00	1.0	—
▲5-Acetyloseltamivir▲ (CN 1-Aug-2024) [c]	1.45	0.9	0.5
Individual unidentified impurity	—	1.0	0.2
Total unidentified impurities	—	1.0	0.5
Total impurities	—	1.0	3.0

a ▲(3*R*,4*R*,5*S*)-4-Acetylamino-5-amino-3-(pentan-3-yloxy)-1-cyclohexene-1-carboxylic acid.▲ (CN 1-Aug-2024)

b ▲Ethyl 4-acetylamino-3-hydroxy-benzoate.▲ (CN 1-Aug-2024)

c ▲Ethyl (3*R*,4*R*,5*S*)-5-acetylamino-4-amino-3-(pentan-3-yloxy)-1-cyclohexene-1-carboxylate.▲ (CN 1-Aug-2024)

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature.
- **Labeling:** When more than one *Dissolution* test is given, the labeling states the test used only if *Test 1* is not used.
- **USP Reference Standards** ⟨11⟩
  USP Oseltamivir Phosphate RS

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

Topic/Question	Contact	Expert Committee
OSELTAMIVIR PHOSPHATE CAPSULES	Documentary Standards Support	SM12020 Small Molecules 1
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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