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Orlistat Capsules

DEFINITION
Orlistat Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of orlistat ($C_{29}H_{53}NO_5$).

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⟩, *Infrared Spectroscopy*:** 197A or 197K

ASSAY
Change to read:
- **Procedure**

Mobile phase: Acetonitrile, phosphoric acid, and water (860: 0.05: 140)

Standard solution: 0.6 mg/mL of USP Orlistat RS in *Mobile phase*

Sample solution: Nominally 0.6 mg/mL of orlistat in *Mobile phase* prepared as follows. Transfer a quantity of orlistat from the contents of Capsules (NLT 10) to a suitable volumetric flask. Add 70% of the final volume of *Mobile phase* and sonicate for 1 min. Shake the resulting solution mechanically for 15 min and dilute with *Mobile phase* to volume. Pass a portion of this solution through a filter of 0.45-µm or finer pore size, discarding the first few milliliters of filtrate.

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

Mode: LC

Detector: UV 195 nm

Column: 3.9-mm × 15-cm; 4-µm packing L1

Flow rate: 1.0 mL/min

Injection volume: 20 µL

▲**Run time:** NLT 5.5 times the retention time of orlistat▲ (IRA 1-Jan-2022)

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of orlistat ($C_{29}H_{53}NO_5$) in the portion of Capsules taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS
- **Dissolution ⟨711⟩**

Medium: 3% sodium lauryl sulfate and 0.5% sodium chloride in water. To each 10 L of media, add 1–2 drops of *n*-octanol, and adjust with phosphoric acid to a pH of 6.0; 900 mL

Apparatus 2: 75 rpm, with coil wire sinker

Time: 45 min

Mobile phase: Acetonitrile and water (86:14)

Standard solution: 0.13 mg/mL of USP Orlistat RS prepared as follows. Transfer a quantity of USP Orlistat RS to a suitable volumetric flask. Dissolve in 2% of the final volume of acetonitrile, and dilute with *Medium* to volume.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.2-µm pore size.

Chromatographic system

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

Mode, Detector, and **Column:** Proceed as directed in the *Assay*.

Flow rate: 2.0 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of orlistat ($C_{29}H_{53}NO_5$) dissolved:

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

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

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

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

L = label claim (mg/Capsule)

V = volume of *Medium*, 900 mL

Tolerances: NLT 75% (Q) of the labeled amount of orlistat ($C_{29}H_{53}NO_5$) is dissolved.

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

IMPURITIES

Change to read:

• **Organic Impurities**

Mobile phase, Standard solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution: ▲0.6 mg/mL of USP Orlistat RS and 0.5 µg/mL of orlistat related compound D prepared by dissolving a suitable amount of USP Orlistat RS and diluting USP Orlistat Related Compound D Solution RS in *Mobile phase*▲ (IRA 1-Jan-2022)

System suitability

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

Suitability requirements

Resolution: NLT 1.4 between orlistat and orlistat related compound D, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Capsules 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 orlistat from the *Standard solution*

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

C_U = nominal concentration of orlistat 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 (%)
Orlistat open-ring epimer[a]	0.45	1.0	1.5
Orlistat open ring[b]	0.5	1.0	0.3
Orlistat related compound D	0.9	1.0	1.0
Orlistat	1.0	—	—
Hexyl undecyl pyranone[c]	2.0	1.0	0.2
Henicosenyl leucinate[d]	4.7	2.3	0.3
Any other identified impurity	—	1.0	0.3
Any unidentified impurity	—	1.0	0.2
Total impurities	—	—	3.0

[a] (2*S*,3*R*,5*S*)-5-[(Formyl-L-leucyl)oxy]-2-hexyl-3-hydroxyhexadecanoic acid.

[b] (2*S*,3*S*,5*S*)-5-[(Formyl-L-leucyl)oxy]-2-hexyl-3-hydroxyhexadecanoic acid.

[c] (*S*)-3-Hexyl-6-undecyl-5,6-dihydro-2*H*-pyran-2-one.

[d] (*S*,*E*)-Henicos-7-en-10-yl formyl-L-leucinate.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store at 25°, excursions permitted between 15° and 30°.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Orlistat RS

▲ USP Orlistat Related Compound D Solution RS

Orlistat related compound D;
(3*S*,4*R*,6*S*)-3-Hexyl-2-oxo-6-undecyltetrahydro-2*H*-pyran-4-yl formyl-L-leucinate.

$C_{29}H_{53}NO_5$ 495.75▲ (IRA 1-Jan-2022)

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

Topic/Question	Contact	Expert Committee
ORLISTAT CAPSULES	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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