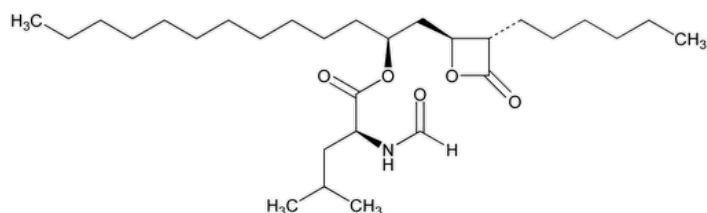


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Orlistat

Change to read:



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

L-Leucine, N-formyl-, 1-[(3-hexyl-4-oxo-2-oxetan-2-yl)methyl]dodecyl ester, [2S-[2 α (R*), 3 β]];

N-Formyl-L-leucine, ester with (3S,4S)-3-hexyl-4-[(2S)-2-hydroxytridecyl]-2-oxetanone;

Δ (S)-1-[(2S,3S)-3-Hexyl-4-oxooxetan-2-yl]tridecan-2-yl formyl-L-leucinate Δ (IRA 1-Jan-2022) CAS RN[®]: 96829-58-2; UNII: 95M8R751W8.

DEFINITION

Orlistat contains NLT 98.0% and NMT 101.5% of orlistat ($C_{29}H_{53}NO_5$), calculated on the anhydrous, solvent-free basis.

IDENTIFICATION

Change to read:

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197K or Δ 197A Δ (IRA 1-Jan-2022)
- **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

Change to read:

• PROCEDURE

[NOTE—Avoid the use of plastic flasks for the preparation or containment of any solution in this analysis.]

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

Standard solution: 0.5 mg/mL of [USP Orlistat RS](#) in *Mobile phase*. Inject immediately after preparation or store at 5°.

Sample solution: 0.5 mg/mL of Orlistat in *Mobile phase*. Inject immediately after preparation or store at 5°.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 195 Δ nm Δ (IRA 1-Jan-2022)

Column: 3.9-mm $\times$ 15-cm; 4- μ m packing [L1](#)

Flow rate: 1.0 mL/min

Injection volume: 20 μ L

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

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT Δ 1.0% Δ (IRA 1-Jan-2022)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of orlistat ($C_{29}H_{53}NO_5$) in the portion of Orlistat 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 = concentration of Orlistat in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–101.5% on the anhydrous, solvent-free basis

IMPURITIES

- [RESIDUE ON IGNITION \(281\)](#): NMT 0.1%

• LIMIT OF ORLISTAT RELATED COMPOUND A

Standard solution: 0.1 mg/mL of [USP Orlistat Related Compound A RS](#) in [acetone](#)

Sample solution: 50 mg/mL of Orlistat in [acetone](#)

Chromatographic system

(See [Chromatography \(621\), General Procedures, Thin-Layer Chromatography](#).)

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 10 µL

Developing solvent system: [Toluene](#) and [ethyl acetate](#) (4:1)

Detection solution: Transfer 2.5 g of [phosphomolybdic acid](#) and 1 g of [ceric sulfate](#) into a 100-mL volumetric flask, and dissolve in and dilute with [methanol](#) to volume.

Analysis

Samples: *Standard solution* and *Sample solution*

Remove the plate, and air-dry it thoroughly. Spray the dried plate with *Detection solution*, and place the plate in an oven at 120° for 30 min.

Acceptance criteria: Any secondary spot from the *Sample solution* corresponding to orlistat related compound A is not more intense than the corresponding spot from the *Standard solution* (0.2%).

• LIMIT OF ORLISTAT RELATED COMPOUND B

Standard solution: 0.025 mg/mL of [USP Orlistat Related Compound B RS](#) in [methylene chloride](#)

Sample solution: 50 mg/mL of Orlistat in [methylene chloride](#)

Spiked sample solution: 50 mg/mL of Orlistat in *Standard solution*

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: GC

Detector: Flame ionization

Column: 0.32-mm × 30-m fused silica, coated with a 0.25-µm [G27](#) stationary phase

Temperatures

Injector: 270°

Detector: 280°

Column: See [Table 1](#).

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
50	4	170	—
170	30	300	30

Carrier gas: Helium

Flow rate: 1 mL/min

Injection type: Split, split ratio 20:1

Injection volume: 2 µL

System suitability**Sample:** *Standard solution***Suitability requirements****Relative standard deviation:** NMT 10.0%**Analysis****Samples:** *Standard solution, Sample solution, and Spiked sample solution*

Calculate the percentage of orlistat related compound B in the portion of Orlistat taken:

$$\text{Result} = \{r_U/[r_{SP} - r_U \times (C_T/C_U)]\} \times (C_S/C_U) \times 100$$

 r_U = peak response of orlistat related compound B from the *Sample solution* r_{SP} = peak response of orlistat related compound B from the *Spiked sample solution* C_T = concentration of Orlistat in the *Spiked sample solution* (mg/mL) C_U = concentration of Orlistat in the *Sample solution* (mg/mL) C_S = concentration of [USP Orlistat Related Compound B RS](#) in the *Standard solution* (mg/mL)**Acceptance criteria:** NMT 0.05%**Change to read:****• ORGANIC IMPURITIES**

[NOTE—Avoid the use of plastic flasks for the preparation or containment of any solution in this analysis.]

Mobile phase, Standard solution, and Sample solution: Prepare as directed in the Assay.**System suitability solution:** 10 µg/mL of [USP Orlistat RS](#) and 0.1 µg/mL of [USP Orlistat Related Compound C RS](#) in *Mobile phase***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:** *System suitability solution***Suitability requirements****Relative standard deviation:** NMT ▲5.0% ▲ (IRA 1-Jan-2022) for the orlistat peak**Signal-to-noise ratio:** NLT 3 for orlistat related compound C**Analysis****Samples:** *Standard solution and Sample solution*

Calculate the percentage of each impurity other than orlistat related compound A, orlistat related compound B, orlistat related compound D, orlistat open ring amide, and orlistat related compound E in the portion of Orlistat 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 = concentration of Orlistat in the *Sample solution* (mg/mL) F = relative response factor (see [Table 2](#))**Acceptance criteria:** See [Table 2](#).**Table 2**