Add the following:

▲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

- 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**

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: Transfer the contents of NLT 10 Capsules into a suitable container, weigh, and mix. Transfer an accurately weighed portion of the powder, equivalent to 120 mg of orlistat, into a 200-mL volumetric flask. Add 140 mL 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 mL of filtrate.

Chromatographic system

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

Mode: LC

Detector: 195 nm

Column: 3.9-mm × 15-cm; packing L1

Flow rate: 1.0 mL/min

Injection size: 20 µL

System suitability

Sample: *Standard solution*

System 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 from the *Sample solution*
r_S = peak response 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: 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 (860:140)

Standard solution: Transfer about 13 mg of USP Orlistat RS to a 100-mL volumetric flask. Dissolve in 2 mL 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 size: 50 µL

System suitability

Sample: *Standard solution*

System suitability requirements

Relative standard deviation: NMT 2.0%

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 from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of 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 is dissolved.

- **UNIFORMITY OF DOSAGE UNITS** ⟨905⟩**:** Meet the requirements

IMPURITIES

Organic Impurities

- **PROCEDURE**

Mobile phase, Standard solution, and **Sample solution:** Prepare as directed in the *Assay.*

System suitability solution: 0.025 mg/mL of USP Orlistat Related Compound D RS in *Mobile phase.* Transfer 1 mL of this solution to a 50-mL volumetric flask, and dilute with *Standard solution* to volume.

Chromatographic system

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

System suitability

Sample: *System suitability solution*

System suitability requirements

Resolution: NLT 1.4 between USP Orlistat RS and USP Orlistat Related Compound D RS

Relative standard deviation: NMT 2.0% for the orlistat peak

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 in the *Sample solution*
r_S = peak response of orlistat in 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 *Impurity Table 1*)

Acceptance criteria: See *Impurity Table 1.*

Impurity 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

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

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

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

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

Impurity Table 1 *(Continued)*

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Henicosenyl leucinate[d]	4.7	2.3	0.3
Any other identified impurity	—	—	0.3
Individual unidentified impurity	—	1.0	0.2
Total impurities	—	—	3.0

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

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

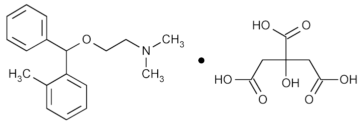
[c] (*S*)-3-Hexyl-5,6-dihydro-6-undecyl-2*H*-pyran-2-one.

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

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers, and store at 25°, excursions permitted between 15° and 30°.
- **USP REFERENCE STANDARDS** ⟨11⟩
  USP Orlistat RS
  USP Orlistat Related Compound D RS▲*USP35*

Orphenadrine Citrate



$C_{18}H_{23}NO \cdot C_6H_8O_7$ 461.50
Ethanamine, *N*,*N*-dimethyl-2-[(2-methylphenyl)phenylmethoxy]-, (±)-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1).
(±)-*N*,*N*-Dimethyl-2-[(*o*-methyl-α-phenylbenzyl)oxy]ethylamine citrate (1:1) [4682-36-4].

» Orphenadrine Citrate contains not less than 98.0 percent and not more than 101.5 percent of $C_{18}H_{23}NO \cdot C_6H_8O_7$, calculated on the dried basis.

Packaging and storage—Preserve in tight, light-resistant containers.

USP Reference standards ⟨11⟩—
USP Orphenadrine Citrate RS

Clarity and color of solution—Mix 1 g of it with 10 mL of a 1 in 28 solution of hydrochloric acid in alcohol: the solution is clear and its absorbance at 436 nm is not greater than 0.050.

Identification—

A: *Infrared Absorption* ⟨197M⟩.

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 500 µg per mL.

Medium: alcohol.

Absorptivities at 264 nm, calculated on the dried basis, do not differ by more than 3.0%.

Melting range ⟨741⟩: between 134° and 138°.

Loss on drying ⟨731⟩—Dry it at 105° for 3 hours: it loses not more than 0.5% of its weight.

Residue on ignition ⟨281⟩: not more than 0.1%.

Related compounds—

0.05 M Ammonium phosphate buffer, Mobile phase, System sensitivity solution, and *Chromatographic system*—Prepare as directed in the *Assay.*

Standard solution—Use the *Standard preparation,* prepared as directed in the *Assay.*

Test solution—Use the *Assay preparation,* prepared as directed in the *Assay.*

Procedure—Separately inject equal volumes (about 20 µL) of the *Test solution* and the *Standard solution* into the chromatograph, record the chromatogram for at least 2.5 times the retention time of orphenadrine citrate, and measure all of the peak areas. Calculate the percentage of each impurity in the portion of Orphenadrine Citrate taken by the formula:

$$5000F(C/W)(r_i / r_S)$$

in which *C* is the concentration, in mg per mL, of USP Orphenadrine Citrate RS in the *Standard solution; W* is the weight, in mg, of the sample taken to prepare the *Test solution; F* is the relative response factor described in the table below; r_i is the peak area for each impurity in the *Test solution;* and r_S is the peak area of Orphenadrine Citrate in the *Standard solution:* not more than 0.5% of total impurities is found.

Compound name	Relative Retention Time	Relative Response Factor
Ethyldimethyl [2-(2-methylbenzhydryloxy)ethyl] ammonium chloride	0.25	0.75
2-Methylbenzhydrol	0.51	0.41
Orphenadrine Citrate	1.0	—
N,*N*-Dimethyl-2-(*o*-tolyl-*o*-xylyloxy)ethylamine	1.54	0.52
Others	—	1.0

Isomer content—

Solvent—Use carbon tetrachloride.

NMR reference—Use tetramethylsilane.

Test preparation—Place about 1 g of Orphenadrine Citrate and 10 mL of water in a 60-mL separator, slowly add about 20 drops of sodium hydroxide solution (1 in 2), with swirling, to obtain a solution having a pH of about 10, and extract with three 15-mL portions of ether. Combine the ether extracts in a beaker, discarding the aqueous phase, and evaporate to about one-half the volume by warming on a steam bath under a stream of nitrogen. Transfer to a 60-mL separator, wash with three 20-mL portions of water, and dry the ether solution with about 15 g of anhydrous sodium sulfate in a 125-mL conical flask for 1 hour, with intermittent swirling. Decant the dried ether solution through a pledget of glass wool into a small beaker. Rinse the sodium sulfate with two 10-mL portions of ether, and add the rinsings to the beaker. Evaporate most of the ether by warming under a stream of nitrogen, and remove the last traces of ether by drying at a pressure not exceeding 2 mm of mercury at 60°. Transfer 400 mg of the orphenadrine so obtained to a small weighing bottle, add 0.5 mL of carbon tetrachloride and 1 drop of tetramethylsilane, and swirl to dissolve.

Procedure—Proceed as directed for *Relative Method of Quantitation* under *Nuclear Magnetic Resonance* ⟨761⟩, using the calculation formula given therein, in which A_1 is the sum of the average areas of the combined methine peaks associated with the *meta-* and *para*-methylbenzyl isomers, appearing at about 5.23 ppm, and A_2 is the area of the methine peak associated with the *ortho*-methylbenzyl isomer, appearing at about 5.47 ppm, with reference to the tetramethylsilane singlet at 0 ppm, and both n_1 and n_2 are equal to 1: the limit of combined *meta-* and *para*-methylbenzyl isomers is 3.0%.

Assay—

0.05 M Ammonium phosphate buffer—Dissolve 5.8 g of monobasic ammonium phosphate in 1000 mL of water, and adjust with ammonium hydroxide or phosphoric acid to a pH of 7.9 ± 0.05.