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Atovaquone Oral Suspension

DEFINITION
Atovaquone Oral Suspension contains NLT 90.0% and NMT 110.0% of the labeled amount of atovaquone ($C_{22}H_{19}ClO_3$).

IDENTIFICATION

Change to read:

• **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: **197U**▲ (CN 1-May-2020)

Medium: Methanol and water (1:1)

Standard solution: Dilute 5 mL of *Standard solution* from the *Assay* with *Medium* to 50 mL.

Sample solution: Dilute 5 mL of *Sample solution* from the *Assay* with *Medium* to 50 mL.

Acceptance criteria: Meets the requirements

• **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**

Mobile phase: Acetonitrile, methanol, water, and phosphoric acid (480:160:360:5)

System suitability solution: 0.09 mg/mL of USP Atovaquone RS and 0.01 mg/mL of USP Atovaquone Related Compound A RS in 0.1 M methanolic sodium hydroxide. Store in a low-actinic glass container.

Standard stock solution: 3 mg/mL of USP Atovaquone RS in a low-actinic, appropriately sized volumetric flask. Add 20% water and 60% 0.1 M methanolic sodium hydroxide. Sonicate for 5 min or until the material has dissolved. Allow to cool, and dilute with 0.1 M methanolic sodium hydroxide to volume.

Standard solution: 0.09 mg/mL of USP Atovaquone RS from *Standard stock solution*. Transfer to an appropriately sized, low-actinic volumetric flask in a mixture of methanol and water (1:1). Minimize exposure of this solution to light.

Sample stock solution: Nominally 3 mg/mL from a known volume of well-mixed Oral Suspension NLT 750 mg of atovaquone prepared as follows. In an appropriately sized, low-actinic volumetric flask, add 20% volume of water, swirl for 5 min, add 60% volume of 0.1 M methanolic sodium hydroxide, and sonicate for 15 min. Allow to cool, and dilute with 0.1 M methanolic sodium hydroxide to volume. Immediately filter a 20-mL portion, discarding the first 5 mL of the filtrate.

Sample solution: 0.09 mg/mL of atovaquone from the clear filtrate of the *Sample stock solution.* Transfer to an appropriately sized, low-actinic volumetric flask, and dilute with a mixture of methanol and water (1:1) to volume. Minimize exposure of this solution to light.

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 12.5-cm; packing L1

Flow rate: 3 mL/min

Injection volume: 20 µL

System suitability

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

[Note—The relative retention times for atovaquone related compound A and atovaquone are 0.86 and 1.0, respectively.]

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of atovaquone ($C_{22}H_{19}ClO_3$) in the portion of Oral Suspension taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Uniformity of Dosage Units ⟨905⟩:** Meets the requirements for oral suspension packaged in single-unit containers

• **Deliverable Volume ⟨698⟩:** Meets the requirements for oral suspension packaged in multiple-unit containers

IMPURITIES

• **Organic Impurities**

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

Analysis

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

Using the chromatograms of the *System suitability solution* and the *Sample solution*, calculate the percentage of atovaquone related compounds in the portion of Oral Suspension taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = individual peak response of an atovaquone related compound, if any, from the *Sample solution*

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

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

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

F = relative response factor of an individual atovaquone related compound relative to the response of atovaquone (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Photodegradation peak[a]	0.3	—	—
Atovaquone impurity	0.65	1.08	0.5
Atovaquone related compound A	0.86	0.85	1.0
Atovaquone impurity	0.88	1.0	0.3
Atovaquone	1.0	1.0	—
Any other atovaquone related compound	—	1.0	0.2
Total impurities	—	—	2.0

[a] Disregard any peak having a relative retention time of 0.3, which is due to photodegradation during preparation of the *Sample solution*.

SPECIFIC TESTS

• **pH ⟨791⟩:** 3.5–7.0

• **Sedimentation**

For oral suspension packaged in multiple-unit containers

Analysis: Transfer 50 mL of well-mixed Oral Suspension to a glass-stoppered graduated cylinder, and allow to stand for 16 h. Measure the volume, if any, of clear liquid observed in the cylinder.

Acceptance criteria: NMT 1 mL of clear liquid

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers.

• **USP Reference Standards** ⟨11⟩

USP Atovaquone RS

USP Atovaquone Related Compound A RS

cis-2-[4-(4-Chlorophenyl)cyclohexyl]-3-hydroxy-1,4-naphthoquinone.

$C_{22}H_{19}ClO_3$ 366.84

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

Topic/Question	Contact	Expert Committee
ATOVAQUONE ORAL SUSPENSION	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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