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Lumefantrine

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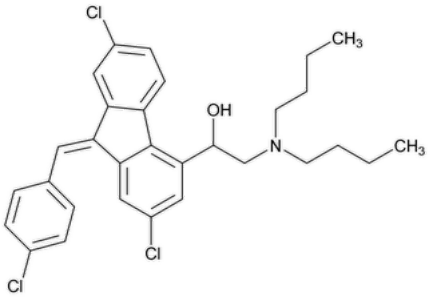

$C_{30}H_{32}Cl_3NO$ 528.94

(±)-2,7-Dichloro-9-[(*Z*)-*p*-▲chlorobenzylidene]-α-▲ (ERR 1-Sep-2021) [(dibutylamino)methyl]-fluorene-4-methanol CAS RN®: 82186-77-4; UNII: F38R0JR742.

DEFINITION
Lumefantrine contains NLT 98.0% and NMT 102.0% of lumefantrine ($C_{30}H_{32}Cl_3NO$).

IDENTIFICATION
• **A.** **Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**
• **B.** The retention time of the lumefantrine peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY
• **Procedure**
Buffer: Dissolve 5.65 g of sodium 1-hexanesulfonate and 2.75 g of monobasic sodium phosphate in 900 mL of water. Adjust with phosphoric acid to a pH of 2.3 before dilution with water to a final volume of 1000 mL.
Solution A: Acetonitrile and *Buffer* (300:700)
Solution B: Acetonitrile and 2-propanol (540:460)
Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	65	35
1.2	65	35
6.0	50	50
6.4	30	70
10.0	25	75
15.0	10	90
15.1	65	35
20.0	65	35

System suitability stock solution: 10 µg/mL of USP Lumefantrine Related Compound A RS prepared as follows. Transfer a suitable quantity of USP Lumefantrine Related Compound A RS to a volumetric flask, dissolve in 10% volume dichloromethane, and dilute with acetonitrile to volume.

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System suitability solution: 1 mg/mL of USP Lumefantrine RS and 1 µg/mL of USP Lumefantrine Related Compound A RS prepared as follows. Transfer 10 mg of USP Lumefantrine RS to a 10-mL volumetric flask, and dissolve in 1 mL of dichloromethane. Add 1.0 mL of the *System suitability stock solution*, and dilute with acetonitrile to volume.

Standard solution: 1 mg/mL of USP Lumefantrine RS prepared as follows. Transfer a suitable quantity of USP Lumefantrine RS to a volumetric flask, dissolve in 10% volume of dichloromethane, and dilute with acetonitrile to volume.

Sample solution: 1 mg/mL of Lumefantrine prepared as follows. Transfer a suitable quantity of Lumefantrine to a volumetric flask, dissolve in 10% volume of dichloromethane, and dilute with acetonitrile to volume.

Chromatographic system

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

Mode: LC

Detector: UV 265 nm

Column: 4.6-mm × 50-mm; 1.8-µm packing L1

Column temperature: Beginning of column, 50°; end of column, 35°

Flow rate: 2.5 mL/min

Injection volume: 2.5 µL

Run time: 20 min

System suitability

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

[Note—The relative retention times for lumefantrine related compound A and lumefantrine are 0.9 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.3 between lumefantrine and lumefantrine related compound A, *System suitability solution*

Tailing factor: NMT 2.1, *Standard solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of lumefantrine ($C_{30}H_{32}Cl_3NO$) in the portion of Lumefantrine 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 the *Standard solution* (mg/mL)

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

Acceptance criteria: 98.0%–102.0%

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Organic Impurities**

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

Standard stock solution: 50 µg/mL of USP Lumefantrine RS prepared as follows. Transfer a suitable quantity of USP Lumefantrine RS into a volumetric flask, dissolve in 10% volume of dichloromethane, and dilute with acetonitrile to volume.

Standard solution: 1 µg/mL of USP Lumefantrine RS in acetonitrile from the *Standard stock solution*

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of desbutyl lumefantrine or any other impurity in the portion of Lumefantrine taken:

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

r_U = peak response of desbutyl lumefantrine or any other impurity from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

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

F = relative response factor

Acceptance criteria: See *Table 2*. Disregard any peak less than 0.05%.

Table 2

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Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Desbutyl lumefantrine[a]	0.68	1.1	0.05
Lumefantrine	1.0	—	—
Any other individual impurity	—	1.0	0.10
Total impurities	—	—	0.3

[a] (*Z*)-2-(Butylamino)-1-(2,7-dichloro-9-(4-chlorobenzylidene)-9*H*-fluoren-4-yl)ethanol.

SPECIFIC TESTS

• **Clarity of Solution**

Hydrazine sulfate solution: Transfer 1.0 g of hydrazine sulfate to a 100-mL volumetric flask, and dissolve in and dilute with water to volume. Allow to stand for 4–6 h before use.

Methenamine solution: Transfer 2.5 g of methenamine to a 100-mL glass-stoppered flask, add 25 mL of water, insert the glass stopper, and mix to dissolve.

Primary opalescent suspension: Transfer 25.0 mL of *Hydrazine sulfate solution* to the *Methanamine solution* in the 100-mL glass-stoppered flask. Allow to stand for 24 h. This suspension is stable for 2 months, provided it is stored in a glass container free from surface defects. The suspension must not adhere to the glass and must be well mixed before use.

Stock opalescence suspension: Transfer 15.0 mL of the *Primary opalescent suspension* to a 1000-mL volumetric flask, and dilute with water to volume. This suspension should not be used beyond 24 h after preparation.

Sample solution: Dissolve 1.0 g of Lumefantrine in dichloromethane, and dilute with dichloromethane to 10.0 mL.

Standard suspension: Transfer 5.0 mL of *Stock opalescence suspension* to a 100-mL volumetric flask, and dilute with water to volume. Prepare only if the *Sample solution* is not as clear as water or dichloromethane.

Analysis

Samples: *Sample solution*, *Standard suspension*, water, and dichloromethane

Transfer a sufficient portion of the *Sample solution* to a test tube of colorless, transparent, neutral glass with a flat base and an internal diameter of 15–25 mm to obtain a depth of 40 mm. Similarly transfer portions of *Standard suspension* and dichloromethane to separate matching test tubes. Compare the *Sample solution*, *Standard suspension*, water, and dichloromethane in diffused daylight, viewing vertically against a black background. The diffusion of light must be such that the *Standard suspension* can readily be distinguished from dichloromethane. If the *Sample solution* is as clear as water or dichloromethane, it is not necessary to prepare the *Standard suspension*.

Acceptance criteria: The *Sample solution* shows the same or more clarity than water, dichloromethane, or the *Standard suspension*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at room temperature.

• **USP Reference Standards** ⟨11⟩

USP Lumefantrine RS

USP Lumefantrine Related Compound A RS

(*RS*,*Z*)-2-(Dibutylamino)-2-(2,7-dichloro-9-(4-chlorobenzylidene)-9*H*-fluoren-4-yl)ethanol.

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Topic/Question	Contact	Expert Committee
LUMEFANTRINE	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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