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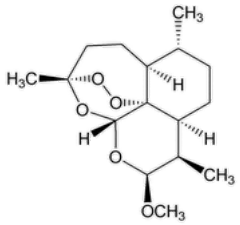
Add the following:

▲Artemether



$C_{16}H_{26}O_5$ 298.37

3,12-Epoxy-12*H*-pyrano[4,3-*j*]-1,2-benzodioxepin, decahydro-10-methoxy-3,6,9-trimethyl-, (3*R*,5a*S*,6*R*,8a*S*,9*R*,10*S*,12*R*,12a*R*); (3*R*,5a*S*,6*R*,8a*S*,9*R*,10*S*,12*R*,12a*R*)-Decahydro-10-methoxy-3,6,9-trimethyl-3,12-epoxy-12*H*-pyrano[4,3-*j*]-1,2-benzodioxepin CAS RN®: 71963-77-4; UNII: C7D6T3H22J.

DEFINITION

Artemether contains NLT 98.0% and NMT 102.0% of artemether ($C_{16}H_{26}O_5$).

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K

• **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**

Protect all solutions containing artemether from light.

Solution A: Acetonitrile and water (200:800)

Solution B: Acetonitrile and water (800:200)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
2	100	0
3	40	60
14	0	100
15.5	0	100
15.6	100	0
18	100	0

Diluent: Acetonitrile and water (50:50)

Standard solution: 0.5 mg/mL of USP Artemether RS in *Diluent*. Sonicate to dissolve if necessary.

Sample solution: 0.5 mg/mL of Artemether in *Diluent*. Sonicate to dissolve if necessary.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 15-cm; 1.8-µm packing L1

Temperatures

Autosampler: 5°

Column: 30°

Flow rate: 0.8 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of artemether ($C_{16}H_{26}O_5$) in the portion of Artemether taken:

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

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

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

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

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

Acceptance criteria: 98.0%–102.0%

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

• **Organic Impurities**

Protect all solutions containing artemether from light.

Solution A, Solution B, Mobile phase, Diluent, and **Chromatographic system:** Proceed as directed in the *Assay*.

Sensitivity solution: 5 µg/mL of USP Artemether RS in *Diluent*. Sonicate to dissolve if necessary.

Standard solution: 0.02 mg/mL of USP Artemether RS in *Diluent*. Sonicate to dissolve if necessary.

Sample solution: 10 mg/mL of Artemether in *Diluent*. Sonicate to dissolve if necessary.

System suitability

Samples: *Sensitivity solution* and *Standard solution*

Suitability requirements

Relative standard deviation: NMT 5%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Artemether taken:

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

r_U = peak response of each impurity from the *Sample solution*

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

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

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

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Cyclohexanone propanal derivative isomer 1[a,b]	0.50	5	0.2
Cyclohexanone propanal derivative isomer 2[a,b]	0.53	5	
Dihydroartemisinin (artenimol)[c]	0.55	1.0	0.2
Artimisitene[d]	0.65	35.7	0.10
Furoisochromen derivative[e]	0.78	0.36	0.2
Artemether related compound B (α-artemether)[f]	0.86	1.0	0.2
Artemether	1.0	—	—
Any individual unspecified impurity	—	1.0	0.10
Total impurities	—	—	1.0

[a] 2-(4-Methyl-2-oxo-3-(3-oxobutyl)cyclohexyl)propanal.

[b] The chromatographic system resolves two isomers. The sum of the values is reported.

[c] (3*R*,5a*S*,6*R*,8a*S*,9*R*,12*R*,12a*R*)-3,6,9-Trimethyldecahydro-3,12-epoxy[1,2]dioxepino[4,3-*i*]isochromen-10-ol.

[d] (3*R*,5a*S*,6*R*,8a*S*,12*S*,12a*R*)-Octahydro-3,6-dimethyl-9-methylene-3,12-epoxy-12*H*-pyrano[4,3-*j*]-1,2-benzodioxepin-10(3*H*)-one.

[e] (3a*S*,4*R*,6a*S*,7*R*,8*S*,10*R*,10a*S*)-8-Methoxy-4,7-dimethyldecahydrofuro[3,2-*i*]isochromen-10-yl acetate.

[f] (3*R*,5a*S*,6*R*,8a*S*,9*R*,10*R*,12*R*,12a*R*)-Decahydro-10-methoxy-3,6,9-trimethyl-3,12-epoxy-12*H*-pyrano[4,3-*j*]-1,2-benzodioxepin.

SPECIFIC TESTS

• **Optical Rotation** ⟨781S⟩, *Procedures, Specific Rotation*

Sample solution: 10 mg/mL in dehydrated alcohol

Acceptance criteria: +166° to +173° measured at 20°

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed, light-resistant containers. Store in a refrigerator.

• **USP Reference Standards** ⟨11⟩

USP Artemether RS▲ (USP 1-May-2023)

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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