

BRIEFING

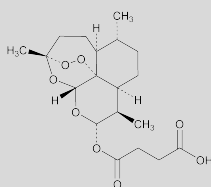
Artesunate. A new USP Non-U.S. Standards Monograph, based on submitted data, is being proposed. The HPLC procedures in the *Assay* and in the test for *Organic Impurities* are based on analyses performed with the Kromasil C18 brand of L1 column. The typical retention times for the artesunate peak in the *Assay* and in the test for *Organic Impurities* is about 15 min.

(MD-AA: L. Santos, B. Davani.) RTS—C75291

Add the following:

▶ **Artesunate**

Draft 1



C₁₉H₂₈O₈ 384.42
Butanedioic acid, mono[(3*R*,5*aS*,6*R*,8*aS*,9*R*,10*S*,12*R*,12*aR*)-decahydro-3,6,9-trimethyl-3,12-epoxy-12*H*-pyrano[4,3-*j*]-1,2-benzodioxepin-10-yl] ester;
(3*R*,5*aS*,6*R*,8*aS*,9*R*,10*S*,12*R*,12*aR*)-decahydro-3,6,9-trimethyl-3,12-epoxy-12*H*-pyrano[4,3-*j*]-1,2-benzodioxepin-10-yl hydrogen succinate [182824-33-5].

DEFINITION

Artesunate contains NLT 98.0% and NMT 102.0% of C₁₉H₂₈O₈, calculated on the anhydrous basis.

IDENTIFICATION

- A. INFRARED ABSORPTION** (197K)
- B.** The retention time of artesunate peak from the *Sample solution* corresponds to that from the *Standard solution*, as obtained in the *Assay*.

ASSAY

- PROCEDURE**
- Buffer:** 1.36 g/L of potassium dihydrogen phosphate in water. Adjust with phosphoric acid to a pH of 3.
- Mobile phase:** Acetonitrile and *Solution A* (12:13)
- Standard solution:** 4.0 mg/mL of USP Artesunate RS in acetonitrile
- Sample solution:** 4 mg/mL in acetonitrile
- System suitability solution:** 0.1 mg/mL of USP Artesunate RS and 0.1 mg/mL of USP Artemether Related Compound A RS in acetonitrile
- Chromatographic system**
(See *Chromatography* (621), *System Suitability*.)
- Mode:** LC
- Detector:** UV 216 nm
- Column:** 4.6-mm × 25-cm; 5-μm packing L1
- Flow rate:** 1 mL/min
- Injection size:** 20 μL
- Column temperature:** 30°
- System suitability**
- Samples:** *Standard solution* and *System suitability solution*
- Suitability requirements**
- Resolution:** NLT 1.5 between artesunate and β-dihydroartemisinin, *System suitability solution*

Relative standard deviation: NMT 2%, *Standard solution Analysis*

Samples: *Standard solution* and *Sample solution*
Calculate the percentage of C₁₉H₂₈O₈ in the portion of Artesunate taken:

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

- r_U = peak response of artesunate from the *Sample solution*
- r_S = peak response of artesunate from the *Standard solution*
- C_S = concentration of USP Artesunate RS in the *Standard solution* (mg/mL)
- C_U = concentration of Artesunate in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

Inorganic Impurities

- RESIDUE ON IGNITION** (281): NMT 0.1%
- HEAVY METALS, Method II** (231): NMT 20 ppm

Organic Impurities

PROCEDURE

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

Analysis

Sample: *Sample solution*

[NOTE—The relative retention times are listed in *Impurity Table 1*.]

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

$$\text{Result} = (r_U/r_T) \times 100$$

- r_U = peak response of each impurity in the *Sample solution*
- r_T = sum of peak responses in the *Sample solution*

Acceptance criteria

Individual impurities: See *Impurity Table 1*.
Total impurities: NMT 1.0%

Impurity Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
α-Dihydroartemisinin ^a	0.6	0.5
β-Dihydroartemisinin ^b	0.9	
Artesunate	1.0	—
Anhydrodihydroartemisinin ^c	2.7	0.5
Individual unspecified impurity ^d	—	0.5

^a (3*R*,5*aS*,6*R*,8*aS*,9*R*,12*S*,12*aR*)-Octahydro-3,6,9-trimethyl-3,12-epoxy-12*H*-pyrane[4,3-*j*]-1,2-coumaron-10(3*H*)alcohol.

^b (3*R*,5*aS*,6*R*,8*aS*,9*R*,12*S*,12*aR*)-Octahydro-3,6,9-trimethyl-3,12-epoxy-12*H*-pyrane [4,3-*j*]-1,2-coumaron-10(3*H*)alcohol.

^c (3*R*,5*aS*,6*R*,8*aS*,12*R*,12*aR*)-3,4,5,5*a*,6,7,8,8*a*-Octahydro-3,6,9-trimethyl-3,12-epoxy-12*H*-pyrano[4,3-*j*]-1,2-benzodioxepin.

^d Disregard peak response less than 0.05%.

SPECIFIC TESTS

- OPTICAL ROTATION, Specific Rotation** (781S): +4.5° to +6.5°
Sample solution: 40 mg/mL, in methylene chloride
- WATER DETERMINATION, Method I** (921): NMT 0.5%
- PH** (791): 3.5–4.5, aqueous suspension of 1% artesunate

ADDITIONAL REQUIREMENTS

- PACKAGING AND STORAGE:** Preserve in well-closed, light-resistant containers and store in a cool place.
- USP REFERENCE STANDARDS** (11)
USP Artemether Related Compound A RS
USP Artesunate RS₁ (1-Mar-2010)