

BRIEFING

Artesunate Tablets. A new USP Non-U.S. Standards monograph, based on validated methods, is being proposed. The HPLC procedure in the *Assay* and in the test for *Organic Impurities* is based on analysis performed with the Waters XBridge C18 brand of column. [NOTE—The Kromasil C18 column is a suitable alternative.] The typical retention time of artesunate in the *Assay* and in the test for *Organic Impurities* is 15 min.

(MD-AA: L. Santos, B. Davani. BPC: M. Marques.) RTS—
C75303

Add the following:

▶Artesunate Tablets

Draft 1

DEFINITION

Artesunate Tablets contain NLT 93.0% and NMT 107.0% of the labeled amount of artesunate (C₁₉H₂₈O₈).

IDENTIFICATION

- **A. INFRARED ABSORPTION** (197K)
- **B.** The retention time of the artesunate peak from the *Sample solution* corresponds of 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 3.0.

Mobile phase: Acetonitrile and *Buffer* (12:13). Pass the solution through a suitable 0.45-μm filter.

Standard solution: 4.0 mg/mL of USP Artesunate RS in acetonitrile

Sample solution: Transfer an equivalent to 100 mg of artesunate from finely powdered Tablets (NLT 20) to a 25-mL volumetric flask. Add acetonitrile to dissolve and dilute with acetonitrile to volume. Pass the solution through a suitable 0.45-μm filter.

System suitability solution: 0.4 mg/mL of USP Artesunate RS and 0.4 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

Temperature: 30°

Flow rate: 1 mL/min

Injection size: 20 μL

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between artesunate and β-dihydroartemisinin, *System suitability solution*

Tailing factor: 0.95–1.05, *Standard solution*

Relative standard deviation: NMT 1.5%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of C₁₉H₂₈O₈ in the portion of Tablets taken:

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

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

Acceptance criteria: 93.0%–107.0%

PERFORMANCE TESTS

• **DISSOLUTION** (711)

Medium: Water, 900 mL

Apparatus 1: 100 rpm

Time: 30 min

Standard solution: Transfer 10 mg of USP Artesunate RS to a 250-mL volumetric flask, dissolve in 200 mL of *Medium* and 25 mL of 1 N sodium hydroxide. Dilute with *Medium* to volume.

Sample solution: Pass a portion of the solution under test through a suitable 0.45-μm filter. Transfer 20 mL of filtrate to a 25-mL volumetric flask, add 2.5 mL of 1 N sodium hydroxide solution, and dilute with *Medium* to volume.

Spectrometric conditions

(See *Spectrophotometry and Light-Scattering* (851).)

Mode: UV

Analytical wavelength: UV 289 nm

Blank: Transfer 2.5 mL of 1 N sodium hydroxide to a 25-mL volumetric flask, and dilute with *Medium* to volume.

Analysis: Warm the *Standard solution* and *Sample solution* to 50 ± 1° for 45 min, cool to room temperature immediately, and determine the absorbances of the solutions, using the *Blank* to zero the spectrophotometer.

Calculate the percentage of C₁₉H₂₈O₈ dissolved:

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times V \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

L = label claim (mg/Tablet)

V = volume of *Medium*, 900 mL

Tolerances: Not less than 85% (Q) of the labeled amount of artesunate is dissolved.

- **UNIFORMITY OF DOSAGE UNITS** (905): Meet the requirements

IMPURITIES

Organic Impurities

• **PROCEDURE**

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

Analysis

Sample: *Sample solution*

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

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

r_U = peak response for each impurity in the *Sample solution*

r_T = sum of all the peak responses in the *Sample solution*

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Impurity Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
α -Dihydroartemisinin ^a	0.6	1.0
β -Dihydroartemisinin ^b	0.9	
Artesunate	1.0	—
Anhydrodihydroartemisinin ^c	2.7	1.0
Individual unspecified impurity ^d	—	0.2

^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 any peak response less than 0.05%.

Acceptance criteria

Total impurities: NMT 2.0%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tightly closed, light-resistant containers at a temperature not exceeding 30°.

• **USP REFERENCE STANDARDS (11)**

USP Artesunate RS

USP Artemether Related Compound A RS^(1-Mar-2010)