

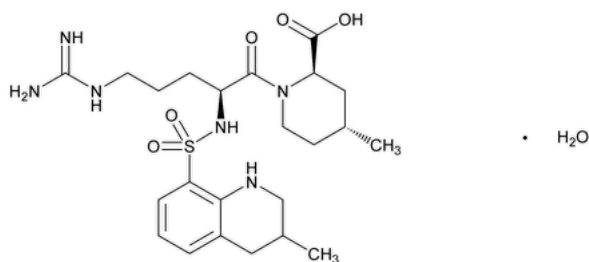
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Change to read:

Argatroban

▲



▲ (ERR 1-Mar-2019)

$C_{23}H_{36}N_6O_5 \cdot H_2O$ 526.65

2-Piperidinecarboxylic acid, 1-[(S)-5-[(aminoiminomethyl)amino]-1-oxo-2-[(1,2,3,4-tetrahydro-3-methyl-8-quinolyl)sulfonyl]amino]pentyl]-4-methyl-, (2R,4R)-monohydrate;

(2R,4R)-4-Methyl-1-{N²-[(1,2,3,4-tetrahydro-3-methyl-8-quinolyl)sulfonyl]-L-arginyl}pipecolic acid, monohydrate CAS RN[®]: 141396-28-3; UNII: IY90U61Z3S.

DEFINITION

Argatroban contains NLT 98.0% and NMT 102.0% of argatroban ($C_{23}H_{36}N_6O_5$), calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

Change to read:

- A. ▲ [SPECTROSCOPIC IDENTIFICATION TESTS <197>](#), *Infrared Spectroscopy*: **197K** ▲ (CN 1-MAY-2020)
- B. The retention times of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the Assay.

ASSAY

• PROCEDURE

[NOTE—It is recommended to keep all solutions containing argatroban at about 4°.]

Solution A: 10 mM ammonium acetate and 5 mM sodium 1-heptanesulfonate

Solution B: Acetonitrile and methanol (500:300)

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	60	40
20	60	40
35	50	50
50	20	80
60	20	80
60.1	60	40
72.1	60	40

Standard solution: 4 mg/mL of [USP Argatroban RS](#) in methanol

Sample solution: 4 mg/mL of Argatroban in methanol

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 259 nm

Column: 4.6-mm × 25-cm; 3-μm packing L1

Temperatures

Column: 50°

Autosampler: 4°

Flow rate: 0.6 mL/min

Injection volume: 10 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5 for both peaks

Relative standard deviation: NMT 1.0% for the sum of the peak responses of (R)-argatroban and (S)-argatroban

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of argatroban ($C_{23}H_{36}N_6O_5S$) in the portion of Argatroban taken:

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

r_U = sum of the peak responses of (R)-argatroban and (S)-argatroban from the *Sample solution*

r_S = sum of the peak responses of (R)-argatroban and (S)-argatroban from the *Standard solution*

C_S = concentration of [USP Argatroban RS](#) in the *Standard solution* (mg/mL)

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

Acceptance criteria: 98.0%–102.0% on the anhydrous and solvent-free basis

IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#): NMT 0.1%

• **ORGANIC IMPURITIES**

[NOTE—It is recommended to keep all solutions containing argatroban at about 4°.]

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

Sensitivity solution: 2 μg/mL of [USP Argatroban RS](#) in methanol

Standard solution: 4 μg/mL each of [USP Argatroban RS](#), [USP Argatroban Related Compound A RS](#), and [USP Argatroban Related Compound B RS](#) in methanol

System suitability

Samples: *Sensitivity solution* and *Standard solution*

Suitability requirements

Resolution: NLT 1.2 between (R)-argatroban and (S)-argatroban, *Standard solution*

Signal-to-noise ratio: NLT 10 for (R)-argatroban, *Sensitivity solution*

Relative standard deviation: NMT 5% for all peaks. For argatroban, use the sum of the peak responses of (R)-argatroban and (S)-argatroban, *Standard solution*.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of argatroban related compound A and argatroban related compound B in the portion of Argatroban taken:

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

r_U = peak response of argatroban related compound A or argatroban related compound B from the *Sample solution*

r_S = peak response of argatroban related compound A or argatroban related compound B from the *Standard solution*

C_S = concentration of [USP Argatroban Related Compound A RS](#) or [USP Argatroban Related Compound B RS](#) in the *Standard solution* (mg/mL)

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

Calculate the percentage of any unspecified impurity in the portion of Argatroban taken:

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