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Add the following:

^Argatroban Injection

DEFINITION

Argatroban Injection is a sterile solution of Argatroban. It contains NLT 90.0% and NMT 110.0% of the labeled amount of argatroban ($C_{23}H_{36}N_6O_5S \cdot H_2O$).

IDENTIFICATION

- **A.** The retention times of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the Assay.
- **B.** The UV spectra of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the Assay.

ASSAY

• **PROCEDURE**

Protect solutions containing argatroban from light.

Buffer: Dissolve 1 g of [ammonium acetate](#) in 750 mL of [water](#). Adjust with [glacial acetic acid](#) to a pH of 5.5. Dilute with [water](#) to 1000 mL.

Solution A: [Methanol](#) and Buffer (50:50)

Solution B: [Methanol](#)

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

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
40	100	0
65	50	50
69	50	50
70	100	0
80	100	0

Standard solution: 2 mg/mL of [USP Argatroban RS](#) prepared as follows. Transfer a quantity of [USP Argatroban RS](#) to a suitable volumetric flask, and add 5% of the flask volume of [methanol](#) to dissolve. Dilute with *Solution A* to volume.

Sample solution: Nominally 2 mg/mL of argatroban (monohydrate) prepared as follows. Transfer a volume of the Injection to a suitable volumetric flask, and dilute with *Solution A* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 259 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 25-cm; 5-µm packing [L1](#)

Column temperature: 50°

Flow rate: 1.0 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for argatroban (*R*-isomer) and argatroban (*S*-isomer) are 1.00 and 1.06, respectively.]

Suitability requirements

Resolution: NLT 1.3 between argatroban (*R*-isomer) and argatroban (*S*-isomer)

Tailing factor: NMT 1.5 for argatroban (*R*-isomer) and argatroban (*S*-isomer)

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of argatroban ($C_{23}H_{36}N_6O_5S \cdot H_2O$) in the portion of Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

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

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

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

C_U = nominal concentration of argatroban (monohydrate) in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of argatroban (monohydrate), 526.65

M_{r2} = molecular weight of argatroban (anhydrous), 508.63

Acceptance criteria: 90.0%–110.0%

IMPURITIES

• ORGANIC IMPURITIES

Protect solutions containing argatroban from light.

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

Sensitivity solution: 2.0 µg/mL of [USP Argatroban RS](#) from the *Standard solution* diluted with *Solution A*

System suitability

Samples: *Standard solution* and *Sensitivity solution*

Suitability requirements

Resolution: NLT 1.3 between argatroban (R-isomer) and argatroban (S-isomer), *Standard solution*

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

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of dehydroargatroban and any unspecified degradation product in the portion of the Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times (1/F) \times 100$$

r_U = peak response of dehydroargatroban or any unspecified degradation product from the *Sample solution*

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

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

C_U = nominal concentration of argatroban (monohydrate) in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of argatroban (monohydrate), 526.65

M_{r2} = molecular weight of argatroban (anhydrous), 508.63

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 ^a	Acceptance Criteria, NMT (%)
Dehydroargatroban ^b	0.22	0.4	1.5
Argatroban (R-isomer) ^c	1.00	—	—



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