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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	—	—

Name	Relative Retention Time	Relative Response Factor[a]	Acceptance Criteria, NMT (%)
Argatroban (*S*-isomer)[d]	1.06	—	—
Any unspecified degradation product	—	1.0	0.2
Total degradation products[e]	—	—	1.0

[a] The relative response factor is calculated relative to argatroban monohydrate.

[b] (2*R*,4*R*)-4-Methyl-1-{[(3-methylquinolin-8-yl)sulfonyl]-L-arginyl}piperidine-2-carboxylic acid.

[c] (2*R*,4*R*)-4-Methyl-1-{[((*R*)-3-methyl-1,2,3,4-tetrahydroquinolin-8-yl)sulfonyl]-L-arginyl}piperidine-2-carboxylic acid.

[d] (2*R*,4*R*)-4-Methyl-1-{[((*S*)-3-methyl-1,2,3,4-tetrahydroquinolin-8-yl)sulfonyl]-L-arginyl}piperidine-2-carboxylic acid.

[e] Excluding dehydroargatroban.

SPECIFIC TESTS

- **pH ⟨791⟩:** 6–8.5. [NOTE—This pH test is applicable to formulations which contain sorbitol.]
- **PARTICULATE MATTER IN INJECTIONS ⟨788⟩:** Meets the requirements
- **STERILITY TESTS ⟨71⟩:** Meets the requirements
- **BACTERIAL ENDOTOXINS TEST ⟨85⟩:** Meets the requirements
- **OTHER REQUIREMENTS:** Meets the requirements in *Injections and Implanted Drug Products ⟨1⟩*

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in Type 1 glass vials. Store at controlled room temperature. Protect from light. Do not freeze.
- **USP REFERENCE STANDARDS ⟨11⟩**
  USP Argatroban RS▲ (USP 1-Dec-2022)

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

Topic/Question	Contact	Expert Committee
ARGATROBAN INJECTION	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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