Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-May-2018
Document Type: USP Monographs
DocId: GUID-C69CAD6C-0CD7-47AE-BC69-BAB8EC0A78F9_3_en-US
DOI: https://doi.org/10.31003/USPNF_M2413_03_01
DOI Ref: o38af

Articaine Hydrochloride and Epinephrine Injection

DEFINITION

Articaine Hydrochloride and Epinephrine Injection is a sterile solution of Articaine Hydrochloride and Epinephrine, in Water for Injection, and contains NLT 95.0% and NMT 105.0% of the labeled amount of articaine hydrochloride ($C_{13}H_{20}N_2O_3S \cdot HCl$) and NLT 90.0% and NMT 115.0% of the labeled amount of epinephrine ($C_9H_{13}NO_3$).

IDENTIFICATION

• **A.** The retention times of the articaine and epinephrine peaks from the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assays* for *Articaine Hydrochloride* and *Epinephrine*, respectively.

ASSAY

• **Articaine Hydrochloride**

Buffer: Glacial acetic acid and water (50:930). Adjust with 2 N sodium hydroxide to a pH of 3.4.

Mobile phase: Acetonitrile and *Buffer* (22:78)

Standard stock solution: 40 mg/mL of USP Articaine Hydrochloride RS in water

Standard solution: 0.8 mg/mL of USP Articaine Hydrochloride RS in *Mobile phase* from *Standard stock solution*

Sample solution: Equivalent to 0.8 mg/mL of articaine hydrochloride in *Mobile phase* from a portion of Injection

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 270 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection size: 10 µL

Run time: 2.5 times the retention time of articaine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.2

Relative standard deviation: NMT 1.0%, from six injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of articaine hydrochloride ($C_{13}H_{20}N_2O_3S \cdot HCl$) in the portion of Injection taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Articaine Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of articaine hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 95.0%–105.0%

• **Epinephrine**

Mobile phase: Mix 50 mL of glacial acetic acid and 930 mL of water. Adjust with 2 N sodium hydroxide to a pH of 3.4. In this solution, dissolve 1.2 g of sodium 1-heptanesulfonate, and add 1.0 mL of 0.1 M edetate disodium and 0.298 g of potassium chloride. Add 150 mL of methanol.

Diluent: 0.5 mg/mL potassium metabisulfite in water

System suitability solution: 22 µg/mL of epinephrine from USP Epinephrine Bitartrate RS and 20 µg/mL of norepinephrine from USP Norepinephrine Bitartrate RS in *Diluent*

Standard stock solution: 0.55 mg/mL of epinephrine from USP Epinephrine Bitartrate RS in *Diluent*

Standard solution: Dilute a suitable volume of the *Standard stock solution* with *Diluent* to obtain a final concentration of *L* mg/mL of epinephrine, where *L* is the label claim of epinephrine in the Injection.

Sample solution: Use the Injection directly.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: Amperometric electrochemical

Reference electrode: Silver/silver chloride

Working electrode: Glassy carbon

Potential: +650 mV

Detector temperature: 28 ± 2°

Column: 4.0-mm × 25-cm; 5-µm packing L7

Flow rate: 1 mL/min

Injection size: 2 µL

Run time: 1.7 times the retention time of epinephrine

System suitability

Sample: *System suitability solution*

[Note—The relative retention times for norepinephrine and epinephrine are 0.90 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between the norepinephrine and epinephrine peaks

Tailing factor: NMT 2.0 for the epinephrine peak

Relative standard deviation: NMT 1.0% for the epinephrine peak, from six injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of epinephrine ($C_9H_{13}NO_3$) in the portion of Injection taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

Acceptance criteria: 90.0%–115.0%

PERFORMANCE TESTS

• **Deliverable Volume ⟨698⟩**

For Articaine Hydrochloride and Epinephrine Injection packaged in single-dose containers: Meets the requirements

IMPURITIES

• **Organic Impurities, Limit of Articaine Related Compounds**

Mobile phase, Standard stock solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay* for *Articaine Hydrochloride*.

Standard solution: 0.8 mg/mL of USP Articaine Hydrochloride RS from *Standard stock solution* and 40 µg/mL of USP Articaine Related Compound B RS in *Mobile phase*

System suitability

Sample: *Standard solution*

[Note—See *Table 1* for relative retention times.]

Suitability requirements

Tailing factor: NMT 2.2 for the articaine peak

Resolution: NLT 1.25 between the articaine related compound B and articaine peaks

Relative standard deviation: NMT 1.0% for the articaine peak

Analysis

Samples: *Standard solution* and *Sample solution*

[Note—Articaine related compounds elute at relative retention times of NMT 2.0 with respect to the articaine peak.]

Calculate the percentage of articaine related compounds and any other individual impurity in the portion of Injection taken:

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

r_U = response of each individual impurity from the *Sample solution*

r_S = response of articaine from the *Standard solution*

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

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

[NOTE—Disregard any peak below 0.05%.]

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Articaine related compound B	0.6	0.5
Articaine	1.0	—
Any other individual impurity	—	0.2
Total impurities	—	0.5

• **ORGANIC IMPURITIES, LIMIT OF EPINEPHRINE RELATED COMPOUNDS**

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

Analysis

Samples: *Standard solution* and *Sample solution*

[NOTE—Epinephrine related compounds elute between relative retention times of 0.35 and 1.0, with respect to the epinephrine peak.]

Calculate the percentage of epinephrine related compounds and any other individual impurity in the portion of Injection taken:

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

r_U = response of each individual impurity from the *Sample solution*

r_S = response of epinephrine from the *Standard solution*

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

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

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Epinephrine sulfonate[a]	0.46	7.5
Specified impurity	0.52	8
Epinephrine	1.0	—
Any other individual impurity	—	1
Total impurities	—	10

[a] 1-(3,4-Dihydroxyphenyl)-2-(methylamino)ethanesulfonic acid.

SPECIFIC TESTS

• **pH** ⟨791⟩**:** 2.7–5.2

• **BACTERIAL ENDOTOXINS TEST** ⟨85⟩**:** NMT 0.7 USP Endotoxin Unit/mg of articaine hydrochloride

• **STERILITY TESTS** ⟨71⟩**:** It meets the requirements when tested as directed for *Test for Sterility of the Product to Be Examined, Membrane Filtration*.

• **PARTICULATE MATTER IN INJECTIONS** ⟨788⟩**:** Meets the requirements

• **Other Requirements:** It meets the requirements under *Injections and Implanted Drug Products* ⟨1⟩.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in single-dose containers, preferably of Type I glass. Store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Articaine Hydrochloride RS

USP Articaine Related Compound B RS

4-Methyl-3-{[2-(propylamino)propanoyl]amino}thiophene-2-carboxylic acid.

$C_{12}H_{18}N_2O_3S$ 270.35

USP Epinephrine Bitartrate RS

USP Norepinephrine Bitartrate RS

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

Topic/Question	Contact	Expert Committee
ARTICAINE HYDROCHLORIDE AND EPINEPHRINE INJECTION	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 37(3)

Current DocID: GUID-C69CAD6C-0CD7-47AE-BC69-BAB8EC0A78F9_3_en-US
Previous DocID: GUID-C69CAD6C-0CD7-47AE-BC69-BAB8EC0A78F9_1_en-US
DOI: https://doi.org/10.31003/USPNF_M2413_03_01
DOI ref: o38af