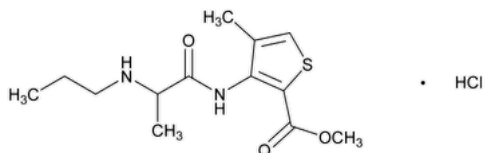


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Articaine Hydrochloride

Change to read:



$C_{13}H_{20}N_2O_3S \cdot HCl$ ▲320.83

2-Thiophenecarboxylic acid, 4-methyl-3-[(1-oxo-2-(propylamino)propyl)amino]-, methyl ester, monohydrochloride; ▲ (CN 1-Aug-2024)

Methyl 4-methyl-3-[2-(propylamino)propionamido]-2-thiophenecarboxylate, monohydrochloride CAS RN®: 23964-57-0; UNII: QS9014Q792.

DEFINITION

Articaine Hydrochloride contains NLT 98.5% and NMT 101.0% of $C_{13}H_{20}N_2O_3S \cdot HCl$, calculated on the dried basis.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy: 197F**

Standard solution: 12 mg/mL of [USP Articaine RS](#) in methylene chloride. Transfer 20 µL of this solution onto a 300-mg disk.

Sample solution: Dissolve 100 mg of Articaine Hydrochloride in 5 mL of water. Add 3 mL of a saturated solution of sodium bicarbonate, and shake twice with 2 mL of methylene chloride. Combine the methylene chloride layers, dilute with methylene chloride to 5.0 mL, and dry over anhydrous sodium sulphate. Transfer 20 µL of this solution onto a 300-mg disk.

- **B. IDENTIFICATION TESTS—GENERAL, Chloride(191)**

ASSAY

PROCEDURE

Sample solution: 250 mg of Articaine Hydrochloride to a 250-mL conical flask. Add 5.0 mL of 0.01 M hydrochloric acid and 50 mL of alcohol. Stir to dissolve.

Analysis: Titrate with 0.1 M sodium hydroxide VS, determining the endpoint potentiometrically, using a glass electrode. Calculate the volume of sodium hydroxide consumed by reading the volume added between the two points of inflection. Each mL of 0.1 M sodium hydroxide is equivalent to 32.08 mg of $C_{13}H_{20}N_2O_3S \cdot HCl$.

Acceptance criteria: 98.5%–101.0% on the dried basis.

IMPURITIES

INORGANIC IMPURITIES

- **RESIDUE ON IGNITION (281)**

Sample: 1 g

Acceptance criteria: NMT 0.1%

ORGANIC IMPURITIES

PROCEDURE

Buffer solution: 2.02 g of sodium 1-heptanesulfonate and 4.08 g of potassium dihydrogen phosphate in 1 L of water. Adjust with phosphoric acid to a pH of 2.0.

Mobile phase: Acetonitrile and *Buffer solution* (1:3)

Standard solution: 2 µg/mL of USP Articaine Related Compound A, and 1 µg/mL each of [USP Articaine Related Compound E RS](#) and [USP Articaine Hydrochloride RS](#) in *Mobile phase*. [NOTE—This solution is also used to determine the reporting threshold limit.]

Sample solution: 1.0 mg/mL of Articaine Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 276 nm

Column: 4.6-mm × 25-cm; packing L1

Temperature: 45°

Flow rate: 1 mL/min

Injection size: 10 µL

System suitability**Sample:** *Standard solution***Suitability requirements****Resolution:** NLT 1.2 between articaine related compound A and articaine related compound E**Analysis****Samples:** *Standard solution and Sample solution.* [NOTE—Run time is 5 times the retention time of articaine.]

Calculate the percentage of any articaine related compound A in the portion of Articaine Hydrochloride taken:

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

 r_U = response of articaine related compound A from the *Sample solution* r_S = response of articaine related compound A from the *Standard solution* C_S = concentration of [USP Articaine Related Compound A RS](#) in the *Standard solution* (mg/mL) C_U = concentration of Articaine Hydrochloride in the *Sample solution* (mg/mL)

Calculate the percentage of each individual impurity in the portion of Articaine Hydrochloride 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 hydrochloride from the *Standard solution* C_S = concentration of [USP Articaine Hydrochloride RS](#) in the *Standard solution* (mg/mL) C_U = concentration of Articaine Hydrochloride in the *Sample solution* (mg/mL)

[NOTE—Disregard any peak below 0.05%.]

Acceptance criteria**Individual impurities:** See [Impurity Table 1](#).**Total impurities:** NMT 0.5%. [NOTE—Excluding articaine related compound A.]**Impurity Table 1**

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Articaine acid ^a	0.6	0.1
Ethylarticaine ^b	0.7	0.1
Articaine related compound A ^c	0.8	0.2
Articaine related compound E ^d	0.86	0.1
Articaine acid-propionamide ^e	0.9	0.1
Articaine	1.0	—
Butylarticaine ^f	1.7	0.1
Dipropylarticaine ^g	2.1	0.1
3-Aminoarticaine ^h	2.6	0.1
Articaine isopropyl ester ⁱ	3.6	0.1
Bromo compound ^j	4.0	0.1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Any other individual impurity	—	0.10

- a 4-Methyl-3-[[[(2*RS*)-2-(propylamino)propanoyl]amino]thiophene-2-carboxylic acid.
- b Methyl 3-[[[(2*RS*)-2-(ethylamino)propanoyl]amino]-4-methylthiophene-2-carboxylate.
- c Methyl 4-methyl-3-[2-(propylamino)acetamido]thiophene-2-carboxylate.
- d Methyl 3-[2-(isopropylamino)propanamido]-4-methylthiophene-2-carboxylate.
- e 4-Methyl-*N*-propyl-3-[[[(2*RS*)-2-(propylamino)propanoyl]amino]thiophene-2-carboxamide.
- f Methyl 3-[[[(2*RS*)-2-(butylamino)propanoyl]amino]-4-methylthiophene-2-carboxylate.
- g Methyl 3-[[[(2*RS*)-2-(dipropylamino)propanoyl]amino]-4-methylthiophene-2-carboxylate.
- h Methyl 3-amino-4-methylthiophene-2-carboxylate.
- i 1-Methylethyl 4-methyl-3-[[[(2*RS*)-2-(propylamino)propanoyl]amino]thiophene-2-carboxylate.
- j Methyl 3-[[[(2*RS*)-2-bromopropanoyl]amino]-4-methylthiophene-2-carboxylate.

SPECIFIC TESTS

- [Loss on Drying \(731\)](#): Dry at 105° for 5 h: it loses NMT 0.5% of its weight.
- [pH \(791\)](#).
- Sample solution: 10 mg/mL
- Acceptance criteria: 4.2–5.2

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in light-resistant containers.

Change to read:

- [USP REFERENCE STANDARDS \(11\)](#).
- [USP Articaine RS](#)
- [USP Articaine Hydrochloride RS](#)
- [USP Articaine Related Compound A RS](#)
- ▲Methyl 4-methyl-3-[2-(propylamino) acetamido]thiophene-2-carboxylate hydrochloride.
 $C_{12}H_{18}N_2O_3S \cdot HCl$ 306.81 ▲ (CN 1-Aug-2024)
- [USP Articaine Related Compound E RS](#)
- Methyl 3-[2-(isopropylamino) propanamido]-4-methylthiophene-2-carboxylate.
 $C_{13}H_{20}N_2O_3S$ 284.37

Auxiliary Information - Please [check for your question in the FAQs](#) before contacting USP.

Topic/Question	Contact	Expert Committee
ARTICAINE HYDROCHLORIDE	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](#)

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