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NF 34

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USP
U.S. Pharmacopeial Convention
Global Expertise
Trusted Standards
Improved Health

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

Change to read:

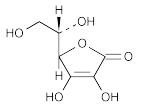
- **•STERILITY TESTS ⟨71⟩•** (CN 1-May-2016)**:** It meets the requirements when tested as directed for *Test for Sterility of the Product to Be Examined, Membrane Filtration*.
- **PARTICULATE MATTER IN INJECTIONS ⟨788⟩:** Meets the requirements

Change to read:

- **OTHER REQUIREMENTS:** It meets the requirements under •*Injections and Implanted Drug Products* ⟨1⟩.• (CN 1-May-2016)

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 Endotoxin RS
USP Epinephrine Bitartrate RS
USP Norepinephrine Bitartrate RS

Ascorbic Acid



$C_6H_8O_6$ 176.12
L-Ascorbic acid [50-81-7].

DEFINITION
Ascorbic Acid contains NLT 99.0% and NMT 100.5% of $C_6H_8O_6$.

IDENTIFICATION
- **A. INFRARED ABSORPTION ⟨197K⟩**
- **B.** A 20-mg/mL solution reduces alkaline cupric tartrate TS slowly at room temperature but more readily upon heating.

ASSAY
- **PROCEDURE**
Sample: 400 mg of Ascorbic Acid
Titrimetric system
(See *Titrimetry* ⟨541⟩.)
Mode: Direct titration
Titrant: 0.1 N iodine VS
Endpoint detection: Visual
Blank: 100 mL of water and 25 mL of 2 N sulfuric acid. Add 3 mL of starch TS.
Analysis: Dissolve the *Sample* in a mixture of 100 mL of water and 25 mL of 2 N sulfuric acid. Add 3 mL of starch TS, and titrate immediately with *Titrant* until a persistent violet-blue color is obtained.
Calculate the percentage of ascorbic acid ($C_6H_8O_6$) in the portion of Ascorbic Acid taken:

$$\text{Result} = [(V - B) \times N \times F \times 100]/W$$

V = sample titrant volume (mL)
B = blank titrant volume (mL)
N = titrant normality (mEq/mL)
F = equivalency factor, 88.06 mg/mEq
W = weight of *Sample* (mg)

Acceptance criteria: 99.0%–100.5%

IMPURITIES

• **RESIDUE ON IGNITION** ⟨281⟩: NMT 0.1%

Delete the following:

•• **HEAVY METALS** ⟨231⟩
Sample solution: 1 g in 25 mL of water
Acceptance criteria: NMT 20 ppm• (Official 1-Jan-2018)

SPECIFIC TESTS

• **OPTICAL ROTATION,** *Specific Rotation* ⟨781S⟩
Sample solution: 100 mg/mL in carbon dioxide-free water. Perform the test immediately after preparation of the *Sample solution*.
Acceptance criteria: +20.5° to +21.5°

ADDITIONAL REQUIREMENTS

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

• **USP REFERENCE STANDARDS** ⟨11⟩
USP Ascorbic Acid RS

Ascorbic Acid Injection

» Ascorbic Acid Injection is a sterile solution, in Water for Injection, of Ascorbic Acid prepared with the aid of Sodium Hydroxide, Sodium Carbonate, or Sodium Bicarbonate. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of ascorbic acid ($C_6H_8O_6$).

Packaging and storage—Preserve in light-resistant, single-dose containers, preferably of Type I or Type II glass.

Change to read:

Labeling—In addition to meeting the requirements for •*Labeling* ⟨7⟩*, Labels and Labeling for Injectable Products,*• (CN 1-May-2016) fused-seal containers of the Injection in concentrations of 250 mg per mL and greater are labeled to indicate that since pressure may develop on long storage, precautions should be taken to wrap the container in a protective covering while it is being opened.

USP Reference standards ⟨11⟩**—**
USP Ascorbic Acid RS
USP Endotoxin RS

Identification—

A: To a volume of Injection, equivalent to 40 mg of ascorbic acid, add 4 mL of 0.1 N hydrochloric acid, then add 4 drops of methylene blue TS, and warm to 40°: the deep blue color becomes appreciably lighter or is completely discharged within 3 minutes.

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that of the *Standard preparation,* obtained as directed in the *Assay*.

C: It responds to the flame test for *Sodium* ⟨191⟩.

Change to read:

•**Bacterial Endotoxins Test** ⟨85⟩• (CN 1-May-2016)**—**It contains not more than 1.2 USP Endotoxin Units per mg of ascorbic acid.

pH ⟨791⟩: between 5.5 and 7.0.

Limit of oxalate—Dilute a volume of Injection, equivalent to 50 mg of ascorbic acid, with water to 5 mL. Add 0.2 mL of acetic acid and 0.5 mL of calcium chloride TS: no turbidity is produced in 1 minute.

Change to read:

Other requirements—It meets the requirements under •*Injections and Implanted Drug Products* ⟨1⟩.• (CN 1-May-2016)

Assay—

Mobile phase—Dissolve 15.6 g of dibasic sodium phosphate and 12.2 g of monobasic potassium phosphate in 2000 mL of water, adjust with phosphoric acid to a pH of 2.5 ± 0.05. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Ascorbic Acid RS in *Mobile phase*, and mix to obtain a solution having a known concentration of about 0.5 mg per mL. [NOTE—Refrigerate and store protected from light until use. The solution is stable for at least 24 hours. Inject within 3 hours after removal from the refrigerator.]

Assay preparation—Dilute the Injection, quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having a concentration of about 0.5 mg per mL. [NOTE—Refrigerate and store protected from light until use. The solution is stable for at least 24 hours. Inject within 3 hours after removal from the refrigerator.]

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 245-nm detector and a 6-mm × 150-mm column that contains packing L39. The flow rate is about 0.6 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the column efficiency is not less than 3500 theoretical plates, the tailing factor is not more than 1.6, and the relative standard deviation for replicate injections is not more than 1.5%.

Procedure—Separately inject equal volumes (about 4 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peak. Calculate the quantity, in mg, of ascorbic acid ($C_6H_8O_6$) in each mL of the Injection taken by the formula:

$$CD(r_U / r_S)$$

in which *C* is the concentration, in mg per mL, of USP Ascorbic Acid RS in the *Standard preparation; D* is the dilution factor; and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Ascorbic Acid Oral Solution

DEFINITION

Ascorbic Acid Oral Solution is a solution of Ascorbic Acid in a hydroxylic organic solvent or an aqueous mixture thereof. It contains NLT 90.0% and NMT 110.0% of the labeled amount of ascorbic acid ($C_6H_8O_6$).

IDENTIFICATION

• **A.**
Sample solution: A volume of Oral Solution equivalent to 40 mg of ascorbic acid
Analysis: To the *Sample solution* add 4 mL of 0.1 N hydrochloric acid, then 4 drops of methylene blue TS, and warm to 40°.