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Carboprost Tromethamine Injection

DEFINITION

Carboprost Tromethamine Injection is a sterile solution of Carboprost Tromethamine in aqueous solution, which may also contain Benzyl Alcohol, Sodium Chloride, and Tromethamine. It contains NLT 90.0% and NMT 110.0% of the labeled amount of carboprost ($C_{21}H_{36}O_5$).

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K

Sample: Extract the equivalent of 2.5 mg of carboprost tromethamine from a volume of Injection, with 1.5–2 times its volume of chloroform. Discard the chloroform layer, and acidify the aqueous layer with 3–5 drops of hydrochloric acid. Extract the acidified solution with an equivalent volume of chloroform. Filter the chloroform layer through a pledget of cotton, and concentrate it to a volume of less than 1 mL. Combine the resulting solution with 150–180 mg of potassium bromide. Dry the potassium bromide mixture in a vacuum overnight, and prepare a pellet from the dried mixture.

Acceptance criteria: Meets the requirements

ASSAY

Change to read:

• **Procedure**

Buffer: Dissolve 10.5 g of citric acid in 75 mL of water. Adjust with 5 N sodium hydroxide to a pH of 4.0, and dilute with water to 100 mL.

Mobile phase: Methylene chloride, 1,3-butanediol, and water (992:7: 0.5)

Internal standard solution: 3 mg/mL of guaifenesin in *Mobile phase*

System suitability solution: Transfer 5 mg of USP Carboprost Tromethamine RS to a stoppered, 50-mL centrifuge tube. Add 20.0 mL of methylene chloride and 2 mL of *Buffer*. Shake the stoppered tube for 10 min, and centrifuge. Remove and discard the top (aqueous) layer, and transfer a 4.0-mL aliquot of the lower (methylene chloride) layer to a suitable vial. Evaporate with the aid of a stream of nitrogen to dryness. Add 100 µL of a freshly prepared solution of α-bromo-2'-acetonaphthone in acetonitrile (1 in 50). Swirl to wash down the sides of the vial. Add 50 µL of a freshly prepared solution of diisopropylethylamine in acetonitrile (1 in 100), swirl again, and place the vial in a suitable heating device maintained at 30°–35° for NLT 15 min. Evaporate the acetonitrile from the vial with the aid of a stream of nitrogen, add 2.0 mL of *Internal standard solution*, mix, and pass the resulting solution through a filter of fine pore size. Protect the filtrate from light prior to injection to prevent degradation of the naphthacyl ester of carboprost.

Standard stock solution: ▲▲ (USP 1-Aug-2022) 332 µg/mL of USP Carboprost Tromethamine RS and 9 mg/mL of benzyl alcohol ▲in water▲ (USP 1-Aug-2022)

Standard solution: 266 µg/mL of USP Carboprost Tromethamine RS, prepared as follows. Transfer 2.0 mL of *Standard stock solution* into a stoppered centrifuge tube. Add 20.0 mL of methylene chloride and 1.0 mL of *Buffer*, shake the stoppered tube for 10 min, and centrifuge. Remove and discard the top (aqueous) layer, transfer an 8.0-mL aliquot of the lower (methylene chloride) layer to a suitable vial, and evaporate the solution with the aid of a stream of nitrogen. [Note—The residue does not evaporate to dryness because of the presence of benzyl alcohol.] Add 100 µL of a freshly prepared solution of α-bromo-2'-acetonaphthone in acetonitrile (1 in 50), and swirl to wash down the sides of the vial. Add 50 µL of a freshly prepared solution of diisopropylethylamine in acetonitrile (1 in 100). Swirl again, and place the vial in a suitable heating device maintained at 30°–35° for NLT 15 min. Evaporate the acetonitrile from the vial with the aid of a stream of nitrogen, add 1.0 mL of *Internal standard solution*, mix, and pass the resulting solution through a filter of fine pore size. Protect the filtrate from light prior to injection to prevent degradation of the naphthacyl ester of carboprost.

Sample solution: Nominally 200 µg/mL of carboprost, prepared as follows. ▲Transfer▲ (USP 1-Aug-2022) a volume of Injection, equivalent to 500 µg of carboprost, to a stoppered, 50-mL centrifuge tube. Add 20.0 mL of methylene chloride and 1.0 mL of *Buffer*, shake the stoppered tube for 10 min, and centrifuge. Remove and discard the top (aqueous) layer, transfer an 8.0-mL aliquot of the lower (methylene chloride) layer to a suitable vial, and evaporate the solution with the aid of a stream of nitrogen. [Note—The residue does not evaporate to dryness because of the presence of benzyl alcohol.] Add 100 µL of a freshly prepared solution of α-bromo-2'-acetonaphthone in acetonitrile (1 in 50), and swirl to wash down the sides of the vial. Add 50 µL of a freshly prepared solution of diisopropylethylamine in acetonitrile (1 in 100). Swirl again, and place the vial in a suitable heating device maintained at 30°–35° for NLT 15 min. Evaporate the acetonitrile from the vial with the aid of a stream of nitrogen, add 1.0 mL of *Internal standard solution*, mix, and pass the resulting solution through a filter of fine pore size. Protect the filtrate from light prior to injection to prevent degradation of the naphthacyl ester of carboprost.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; 10-µm packing L3

Flow rate: 1.8 mL/min

Injection volume: 10 µL

System suitability

Sample: *System suitability solution*

[NOTE—The relative retention times for guaifenesin and 2-naphthacyl ester of carboprost are 0.6 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 4.0 between guaifenesin and 2-naphthacyl ester of carboprost

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of carboprost ($C_{21}H_{36}O_5$) 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 = peak response ratio of the 2-naphthacyl ester of carboprost to the internal standard of the *Sample solution*

R_S = peak response ratio of the 2-naphthacyl ester of carboprost to the internal standard of the *Standard solution*

C_S = concentration of USP Carboprost Tromethamine RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of carboprost in the *Sample solution* (µg/mL)

M_{r1} = molecular weight of carboprost, 368.51

M_{r2} = molecular weight of carboprost tromethamine, 489.64

Acceptance criteria: 90.0%–110.0%

SPECIFIC TESTS

Change to read:

- **BACTERIAL ENDOTOXINS TEST ⟨85⟩:** ▲Meets the requirements▲ (USP 1-Aug-2022)
- **pH ⟨791⟩:** 7.0–8.0
- **OTHER REQUIREMENTS:** Meets the requirements in *Injections and Implanted Drug Products ⟨1⟩*

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in single-dose or multiple-dose containers, preferably of Type I glass, and store in a refrigerator.
- **USP REFERENCE STANDARDS ⟨11⟩**
  USP Carboprost Tromethamine RS

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

Topic/Question	Contact	Expert Committee
CARBOPROST TROMETHAMINE 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

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