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Quinidine Gluconate Injection

DEFINITION

Quinidine Gluconate Injection is a sterile solution of Quinidine Gluconate in Water for Injection. Each mL contains amounts of quinidine gluconate and dihydroquinidine gluconate totaling to NLT 76 mg and NMT 84 mg of quinidine gluconate ($C_{20}H_{24}N_2O_2 \cdot C_6H_{12}O_7$).

IDENTIFICATION

- **A.**

Sample solution: 1-in-150 solution of Injection in dilute sulfuric acid (1 in 350)

Acceptance criteria: The *Sample solution* exhibits a vivid blue fluorescence. On the addition of a few drops of hydrochloric acid, the fluorescence disappears.

- **B.**

Sample solution: 1-in-4 solution of Injection

Acceptance criteria: The *Sample solution* is dextrorotatory.

- **C.** The R_F value of the principal spot of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in *Organic Impurities*.

ASSAY

- **Procedure**

Solution A: Add 35.0 mL of methanesulfonic acid to 20.0 mL of glacial acetic acid, and dilute with water to 500 mL.

Solution B: Dissolve 10.0 mL of diethylamine in water to prepare a 100-mL solution.

Mobile phase: Acetonitrile, *Solution A*, *Solution B*, and water (100:20:20:860). Adjust with *Solution B* to a pH of 2.6.

System suitability solution: 0.2 mg/mL each of quinidine gluconate and dihydroquinidine hydrochloride prepared as follows. Dissolve a suitable quantity of each quinidine gluconate and dihydroquinidine hydrochloride in about 10% of the total volume of methanol, and dilute with *Mobile phase* to volume.

Standard solution: 0.26 mg/mL of USP Quinidine Gluconate RS in *Mobile phase*

Sample stock solution: Transfer a volume of Injection, equivalent to 400 mg of quinidine gluconate, to a 50-mL volumetric flask, and dilute with methanol to volume.

Sample solution: Transfer 3 mL of the *Standard stock solution* to a 100-mL volumetric flask, and dilute with *Mobile phase* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 235 nm

Column: 3.9-mm × 30-cm column; packing L1

Injection volume: 50 µL

System suitability

Sample: *System suitability solution*

[Note—The relative retention times for quinidine and dihydroquinidine are 1 and 1.5, respectively.]

Suitability requirements

Resolution: NLT 2.5 between quinidine and dihydroquinidine

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the quantity in mg/mL of the sum of quinidine gluconate and dihydroquinidine gluconate in the portion of Injection taken:

$$\text{Result} = (r_{B,U} + r_{D,U})/(r_{B,S} + r_{D,S}) \times (C_S/V) \times F$$

$r_{B,U}$ = peak response of quinidine from the *Sample solution*

$r_{D,U}$ = peak response of dihydroquinidine from the *Sample solution*

$r_{B,S}$ = peak response of quinidine from the *Standard solution*

$r_{D,S}$ = peak response of dihydroquinidine from the *Standard solution*

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

V = volume of the Injection taken (mL)

F = dilution factor, 5000/3

Acceptance criteria: Each mL contains amounts of quinidine gluconate and dihydroquinidine gluconate totaling to NLT 76 mg and NMT 84 mg of quinidine gluconate ($C_{20}H_{24}N_2O_2 \cdot C_6H_{12}O_7$).

IMPURITIES

• **Organic Impurities**

Standard solution A: 6 mg/mL of USP Quinidine Gluconate RS in diluted alcohol

Standard solution B: 0.06 mg/mL of USP Quinidine Gluconate RS in diluted alcohol from the *Standard solution A*

Standard solution C: 0.04 mg/mL of USP Quininone RS (corresponding to 0.06 mg of the gluconate) and 0.08 mg/mL of cinchonine (corresponding to 0.12 mg of the gluconate) in diluted alcohol

Sample solution: Mix, equivalent to 80 mg of quinidine gluconate from a volume of Injection, with 25 mL of water. Add 2 drops of 2 N sulfuric acid, and extract with 50 mL of ether, discarding the ether extract. To the aqueous solution add 2 mL of 1 N sodium hydroxide, extract with 50 mL of ether, wash the extract with 25 mL of water, and discard the aqueous solutions. Evaporate the ether extract just to dryness, and dissolve the residue in 10 mL of alcohol.

Chromatographic system

(See *Chromatography ⟨621⟩, Thin-Layer Chromatography*.)

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 10 µL

Developing solvent system: Chloroform, acetone, and diethylamine (5:4:1)

Analysis

Samples: *Standard solution A, Standard solution B, Standard solution C*, and *Sample solution*

Proceed as directed in the chapter. The solvent chamber is used without previous equilibration. When the solvent front has moved about 15 cm, remove the plate from the chamber, mark the solvent front, and allow the solvent to evaporate. Spray with glacial acetic acid. Locate the spots on the plate by examination under long-wavelength UV light. Then spray the plate with potassium iodoplatinate TS.

Acceptance criteria: Any spot produced by the *Sample solution* at the R_F value of a spot produced by *Standard solution C* is not greater in size or intensity than that corresponding spot. Apart from these spots and from the spots appearing at the R_F value of quinidine gluconate and dihydroquinidine gluconate (the two spots most evident from *Standard solution A*), any additional fluorescent spot is not greater in size or intensity than the principal spot of *Standard solution B*. After the treatment with potassium iodoplatinate TS, any spot produced by the *Sample solution* is not greater in size or intensity than a corresponding spot from *Standard solution C*.

SPECIFIC TESTS

• **Bacterial Endotoxins Test ⟨85⟩:** NMT 0.6 USP Endotoxin Unit/mg of quinidine gluconate

• **Other Requirements:** Meets the requirements in *Injections and Implanted Drug Products ⟨1⟩*

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in single-dose or in multiple-dose containers, preferably of Type I glass.

• **USP Reference Standards ⟨11⟩**

USP Quinidine Gluconate RS

USP Quininone RS

Cinchonan-9-one, 6'-methoxy-, (8alpha)-.
$C_{20}H_{22}N_2O_2$ 322.40

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

Topic/Question	Contact	Expert Committee
QUINIDINE GLUCONATE INJECTION	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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