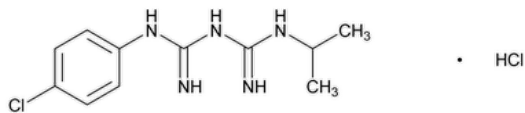


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Proguanil Hydrochloride



$C_{11}H_{16}ClN_5 \cdot HCl$ 290.19
Biguanide, 1-(4-chlorophenyl)-5-isopropyl, hydrochloride;
1-(p-Chlorophenyl)-5-isopropylbiguanide hydrochloride CAS RN®: 637-32-1; UNII: R71Y86M0WT.

DEFINITION
Proguanil Hydrochloride contains NLT 98.5% and NMT 101.0% of proguanil hydrochloride ($C_{11}H_{16}ClN_5 \cdot HCl$), calculated on the dried basis.

IDENTIFICATION
Change to read:

- **A.** [▲SPECTROSCOPIC IDENTIFICATION TESTS \(197\), Infrared Spectroscopy: 197K▲](#) (CN 1-MAY-2020)
- **B.** [IDENTIFICATION TESTS—GENERAL, Chloride\(191\)](#): Meets the requirements

ASSAY

- **PROCEDURE**
Solution A: 0.65 g/L of 1-pentanesulfonic acid sodium salt and 7.0 g/L of sodium perchlorate in water. Adjust with 1% trifluoroacetic acid to a pH of 3.0.
Solution B: 0.65 g/L of 1-pentanesulfonic acid sodium salt and 7.0 g/L of sodium perchlorate in a mixture of methanol, acetonitrile, and water (400:400:200). Add 4 mL of 1% trifluoroacetic acid to 1 L of this solution.
Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	75	25
20	40	60
25	75	25
35	75	25

Diluent: Acetonitrile, methanol, and water (200:200:600)
Standard solution: 0.2 mg/mL of [USP Proguanil Hydrochloride RS](#) in Diluent
Sample solution: 0.2 mg/mL of Proguanil Hydrochloride in Diluent
Chromatographic system
(See [Chromatography \(621\), System Suitability.](#))
Mode: LC
Detector: UV 235 nm
Column: 4.6-mm × 7.5-cm; 3.5-μm packing L7
Column temperature: 40°
Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of proguanil hydrochloride ($C_{11}H_{16}ClN_5 \cdot HCl$) in the portion of Proguanil Hydrochloride taken:

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

r_U = peak response of proguanil from the *Sample solution*

r_S = peak response of proguanil from the *Standard solution*

C_S = concentration of [USP Proguanil Hydrochloride RS](#) in the *Standard solution* (mg/mL)

C_U = concentration of Proguanil Hydrochloride in the *Sample solution* (mg/mL)

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

IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#): NMT 0.1%

• **LIMIT OF CHLOROANILINE**

Solution A: 3.45 g/L solution of sodium nitrite

Solution B: 50 g/L solution of ammonium sulfamate

Solution C: 1 mg/mL of naphthylethylenediamine dihydrochloride in water. Prepare immediately before use.

Standard solution: 1.25 mg/L solution of chloroaniline

Sample solution: Dissolve 100 mg in 1 mL of 2 N hydrochloric acid, and dilute with water to 20 mL.

Analysis: Cool the *Sample solution* to 5°. Add 1 mL of *Solution A*, and allow to stand at 5° for 5 min. Add 2 mL of *Solution B*, and allow to stand for 10 min. Add 2 mL of *Solution C*, dilute with water to 50 mL, and allow to stand for 30 min.

Acceptance criteria: Any red color produced is not more intense than that of a standard prepared at the same time and in the same manner, using 20 mL of *Standard solution* (250 ppm).

• **ORGANIC IMPURITIES, PROCEDURE 1**

[NOTE—On the basis of the synthetic route, perform either *Procedure 1* or *Procedure 2*. *Procedure 2* is recommended when proguanil related compound A, proguanil related compound E, proguanil related compound F, and proguanil related compound G (see [Table 3](#)) may be present.]

Mobile phase: Dissolve 3.78 g of sodium hexanesulfonate in a mixture of 1200 mL of methanol, 800 mL of water, and 10 mL of glacial acetic acid.

Identification solution: 0.5 µg/mL of [USP Proguanil Related Compound C RS](#) in *Mobile phase*

System suitability stock solution: 0.5 µg/mL of [USP Proguanil Related Compound D RS](#) in *Mobile phase*

System suitability solution: Dilute 1 mL of the *Standard stock solution* with *Mobile phase* to 200 mL. To 1 mL of the resulting solution, add 1 mL of *System suitability stock solution*.

Standard stock solution: 0.1 mg/mL of [USP Proguanil Hydrochloride RS](#) in *Mobile phase*

Standard solution: 0.2 µg/mL of [USP Proguanil Hydrochloride RS](#) from the *Standard stock solution* in *Mobile phase*

Sample solution: 0.1 mg/mL of Proguanil Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 230 and 254 nm

Column: 4.6-mm × 12.5-cm; 5-µm packing L1, or 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: At least 5 times the retention time of the proguanil peak at both wavelengths

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements