

Clomipramine Hydrochloride Capsules

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click www.uspnf.com/rb-clomipramine-hcl-caps-20240628.

DEFINITION
Clomipramine Hydrochloride Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of clomipramine hydrochloride ($C_{19}H_{23}ClN_2 \cdot HCl$).

IDENTIFICATION

- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.
- **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY
Change to read:

- **PROCEDURE**
Solution A: Add 2.5 mL of [acetic acid](#) to 1 L of [water](#). Adjust with ▲[ammonia water, stronger](#)▲ (RB 1-Jul-2024) to a pH of 7.5.
Solution B: [Acetonitrile, methanol](#), and ▲[tetrahydrofuran, stabilizer-free](#)▲ (RB 1-Jul-2024) (80:15:5)
Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0.0	65	35
2.0	65	35
5.0	50	50
11.0	20	80
14.0	20	80
14.1	65	35
18.0	65	35

Diluent: *Solution A* and [acetonitrile](#) (50:50)
System suitability solution: 0.2 mg/mL of [USP Clomipramine Hydrochloride RS](#) and 0.005 mg/mL of [USP Clomipramine Related Compound A RS](#) in *Diluent*
Standard solution: 0.2 mg/mL of [USP Clomipramine Hydrochloride RS](#) in *Diluent*
Sample solution: Nominally 0.2 mg/mL of clomipramine hydrochloride from Capsules in *Diluent* prepared as follows. Transfer a sufficient portion of the contents of Capsules (NLT 20) to a suitable volumetric flask. Add 60% of the final flask volume of *Diluent*. Shake by mechanical means for about 30 min. Dilute with *Diluent* to volume. Centrifuge to obtain a clear supernatant and use the clear supernatant.
[NOTE—The use of a centrifuge speed of 3000 rpm for 10 min may be suitable.]
Chromatographic system

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

Mode: LC

Detector: UV 254 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 2.1-mm × 10-cm; 1.7-μm packing [L1](#)

Column temperature: 30°

Flow rate: 0.3 mL/min

Injection volume: 2 μL

System suitability

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

[NOTE—See [Table 2](#) for relative retention times.]

Suitability requirements

Resolution: NLT 2.0 between clomipramine and clomipramine related compound A, *System suitability solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of clomipramine hydrochloride ($C_{19}H_{23}ClN_2 \cdot HCl$) in the portion of Capsules taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

C_U = nominal concentration of clomipramine hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• [DISSOLUTION \(711\)](#).

Test 1

Medium: ▲0.1 N [hydrochloric acid](#)▲ (RB 1-Jul-2024) ; 500 mL

Apparatus 2: 50 rpm. With suitable sinkers, if needed.

Time: 30 min

Standard solution: [USP Clomipramine Hydrochloride RS](#) in *Medium*

Sample solution: Pass the solution under test through a suitable filter and use the filtrate. Dilute with *Medium*, if necessary, to a concentration that is similar to the *Standard solution*.

Instrumental conditions

(See [Ultraviolet-Visible Spectroscopy \(857\)](#).)

Mode: UV

Analytical wavelength: 252 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of clomipramine hydrochloride ($C_{19}H_{23}ClN_2 \cdot HCl$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times D \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

D = dilution factor for the *Sample solution*

V = volume of *Medium*, 500 mL