

1 Clomipramine Hydrochloride Tablets

2 クロミプラミン塩酸塩錠

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4 Clomipramine Hydrochloride Tablets contain not less
5 than 92.0% and not more than 108.0% of the labeled amount
6 of clomipramine hydrochloride ($C_{19}H_{23}ClN_2.HCl$: 351.31).

7 **Method of preparation** Prepare as directed under Tablets, with
8 Clomipramine Hydrochloride.

9 **Identification** To a portion of powdered Clomipramine Hydro-
10 chloride Tablets, equivalent to 50 mg of Clomipramine Hydro-
11 chloride, add a suitable amount of 0.1 mol/L hydrochloric acid TS,
12 shake, and add 0.1 mol/L hydrochloric acid TS to make 250 mL.
13 Centrifuge this solution, to 10 mL of the supernatant liquid add
14 0.1 mol/L hydrochloric acid TS to make 100 mL. Determine the
15 absorption spectrum of this solution as directed under Ultraviolet-
16 visible Spectrophotometry <2.24>: it exhibits a maximum between
17 250 nm and 254 nm.

18 **Uniformity of dosage unit** <6.02> Perform the test according to
19 the following method: it meets the requirement of the Content uni-
20 formity test.

21 To 1 tablet of Clomipramine Hydrochloride Tablets add $V/5$ mL
22 of a mixture of methanol and 0.1 mol/L hydrochloric acid TS (3:1),
23 sonicate to disintegrate the tablet, and shake for 30 minutes. To
24 this solution add $3V/5$ mL of methanol, shake for 15 minute, and
25 add methanol to make exactly V mL so that each mL contains
26 about 0.1 mg of clomipramine hydrochloride ($C_{19}H_{23}ClN_2.HCl$).
27 Centrifuge this solution, and use the supernatant liquid as the sam-
28 ple solution. Then, proceed as directed in the Assay.

29 Amount (mg) of clomipramine hydrochloride ($C_{19}H_{23}ClN_2.HCl$)

$$30 = M_S \times A_T / A_S \times V / 250$$

31 M_S : Amount (mg) of clomipramine hydrochloride for assay
32 taken

33 **Dissolution** <6.10> When the test is performed at 50 revolutions
34 per minute according to the Paddle method, using 900 mL of water
35 as the dissolution medium, the dissolution rates in 45 minutes of
36 10-mg tablet and in 90 minutes of 25-mg tablet are not less than
37 80%.

38 Start the test with 1 tablet of Clomipramine Hydrochloride Tab-
39 lets, withdraw not less than 20 mL of the medium at the specified
40 minute after starting the test, and filter through a membrane filter
41 with a pore size not exceeding 0.45 μm . Discard the first 10 mL
42 of the filtrate, pipet V mL of the subsequent filtrate, add water to
43 make exactly V' mL so that each mL contains about 11 μg of clom-
44 ipramine hydrochloride ($C_{19}H_{23}ClN_2.HCl$), and use this solution
45 as the sample solution. Separately, weigh accurately about 28 mg
46 of clomipramine hydrochloride for assay, previously dried at
47 105°C for 3 hours, and dissolve in water to make exactly 100 mL.
48 Pipet 4 mL of this solution, add water to make exactly 100 mL,

49 and use this solution as the standard solution. Determine the ab-
50 sorbances, A_T and A_S , of the sample solution and standard solution
51 at 252 nm as directed under Ultraviolet-visible Spectrophotometry
52 <2.24>.

53 Dissolution rate (%) with respect to the labeled amount of clomi-
54 pramine hydrochloride ($C_{19}H_{23}ClN_2.HCl$)

$$55 = M_S \times A_T / A_S \times V' / V \times 1 / C \times 36$$

56 M_S : Amount (mg) of clomipramine hydrochloride for assay
57 taken

58 C : Labeled amount (mg) of clomipramine hydrochloride
59 ($C_{19}H_{23}ClN_2.HCl$) in 1 tablet

60 **Assay** Weigh accurately the mass of not less than 20 Clomipra-
61 mine Hydrochloride Tablets, and powder. Weigh accurately a por-
62 tion of the powder, equivalent to about 25 mg of clomipramine
63 hydrochloride ($C_{19}H_{23}ClN_2.HCl$), add 50 mL of a mixture of meth-
64 anol and 0.1 mol/L hydrochloric acid TS (3:1), sonicate, and shake
65 for 30 minutes. To this solution add 150 mL of methanol, shake
66 for 15 minutes, and add methanol to make exactly 250 mL. Cen-
67 trifuge this solution, and use the supernatant liquid as the sample
68 solution. Separately, weigh accurately about 25 mg of clomipra-
69 mine hydrochloride for assay, previously dried at 105°C for 3
70 hours, dissolve in 50 mL of a mixture of methanol and 0.1 mol/L
71 hydrochloric acid TS (3:1), add methanol to make exactly 250 mL,
72 and use this solution as the standard solution. Perform the test with
73 exactly 20 μL each of the sample solution and standard solution
74 as directed under Liquid Chromatography <2.01> according to the
75 following conditions, and determine the peak areas, A_T and A_S , of
76 clomipramine in each solution.

77 Amount (mg) of clomipramine hydrochloride ($C_{19}H_{23}ClN_2.HCl$)

$$78 = M_S \times A_T / A_S$$

79 M_S : Amount (mg) of clomipramine hydrochloride for assay
80 taken

81 *Operating conditions* —

82 Detector: An ultraviolet absorption photometer (wavelength:
83 254 nm).

84 Column: A stainless steel column 4.6 mm in inside diameter
85 and 25 cm in length, packed with octadecylsilanized silica gel for
86 liquid chromatography (10 μm in particle diameter).

87 Column temperature: A constant temperature of about 25°C.

88 Mobile phase: Dissolve 2 g of sodium 1-octanesulfonate in 300
89 mL of water, and add 450 mL of methanol, 250 mL of acetonitrile
90 and 1 mL of 0.5 mol/L sulfuric acid TS.

91 Flow rate: Adjust so that the retention time of clomipramine is
92 about 13 minutes.

93 *System suitability* —

94 System performance: When the procedure is run with 20 μL of
95 the standard solution under the above operating conditions, the
96 number of theoretical plates and the symmetry factor of the peak
97 of clomipramine are not less than 3000 and not more than 1.5,
98 respectively.

99 System repeatability: When the test is repeated 6 times with 20
100 μL of the standard solution under the above operating conditions,
101 the relative standard deviation of the peak area of clomipramine is
102 not more than 1.0%.

103 **Containers and storage** Containers—Tight containers.

104 **Add the following to 9.41 Reagents, Test**
105 **Solutions:**

106 **Clomipramine hydrochloride for assay** $\text{C}_{19}\text{H}_{23}\text{ClN}_2\cdot\text{HCl}$
107 [Same as the monograph Clomipramine Hydrochloride. When
108 dried, it contains not less than 99.0% of clomipramine hydrochlo-
109 ride ($\text{C}_{19}\text{H}_{23}\text{ClN}_2\cdot\text{HCl}$).]
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