

1 Fludiazepam Tablets

2 フルジアゼパム錠

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4 Fludiazepam Tablets contain not less than 93.0%
5 and not more than 107.0% of the labeled amount of
6 fludiazepam (C₁₆H₁₂ClFN₂O: 302.73).

7 **Method of preparation** Prepare as directed under Tab-
8 lets, with Fludiazepam.

9 **Identification** To a quantity of powdered Fludiazepam
10 Tablets, equivalent to 2 mg of Fludiazepam, add 40 mL of
11 methanol, shake for 20 minutes, and filter. Determine the
12 absorption spectrum of the filtrate as directed under Ultra-
13 violet-visible Spectrophotometry <2.24>: it exhibits a max-
14 imum between 315 nm and 319 nm. Therefore, to 5 mL of
15 the filtrate add methanol to make 50 mL. Determine the ab-
16 sorption spectrum of this solution as directed under Ultra-
17 violet-visible Spectrophotometry <2.24>: it exhibits a max-
18 imum between 229 nm and 233 nm.

19 **Uniformity of dosage units** <6.02> Perform the test ac-
20 cording to the following method: it meets the requirement
21 of the Content uniformity test.

22 To 1 tablet of Fludiazepam Tablets add 2V/25 mL of wa-
23 ter, disperse the fine particles by sonicating, add 3V/25 mL
24 of acetonitrile, and shake for 10 minutes. Add a mixture of
25 acetonitrile and water (3:2) to make exactly V mL so that
26 each mL contains about 5 μg of fludiazepam
27 (C₁₆H₁₂ClFN₂O), centrifuge, and use the supernatant liquid
28 as the sample solution. Then, proceed as directed in the As-
29 say.

30 Amount (mg) of fludiazepam (C₁₆H₁₂ClFN₂O)
31 $= M_S \times A_T / A_S \times V / 5000$

32 M_S : Amount (mg) of fludiazepam for assay taken

33 **Dissolution** <6.10> When the test is performed at 50 rev-
34 olutions per minute according to the Paddle method, using
35 900 mL of water as the dissolution medium, the dissolution
36 rate in 15 minutes of Fludiazepam Tablets is not less than
37 80%.

38 Start the test with 1 tablet of Fludiazepam Tablets, with-
39 draw not less than 20 mL of the medium at the specified
40 minute after starting the test, and filter through a membrane
41 filter with a pore size not exceeding 0.45 μm. Discard the
42 first 10 mL or more of the filtrate, pipet V mL of the subse-
43 quent filtrate, add water to make exactly V' mL so that each
44 mL contains about 0.28 μg of fludiazepam (C₁₆H₁₂ClFN₂O),
45 and use this solution as the sample solution. Separately,
46 weigh accurately about 28 mg of fludiazepam for assay,
47 previously dried at 60°C for 3 hours under reduced pressure,
48 and dissolve in methanol to make exactly 100 mL. Pipet 5

49 mL of this solution, and add water to make exactly 100 mL.
50 Then, pipet 2 mL of this solution, and add water to make
51 exactly 100 mL, and use this solution as the standard solu-
52 tion. Perform the test with exactly 50 μL each of the sample
53 solution and standard solution as directed under Liquid
54 Chromatography <2.01> according to the following condi-
55 tions, and determine the peak areas, A_T and A_S, of fludiazep-
56 am in each solution.

57 Dissolution rate (%) with respect to the labeled amount of
58 fludiazepam (C₁₆H₁₂ClFN₂O)

59 $= M_S \times A_T / A_S \times V' / V \times 1 / C \times 9 / 10$

60 M_S : Amount (mg) of fludiazepam for assay taken

61 C : Labeled amount (mg) of fludiazepam (C₁₆H₁₂ClFN₂O)
62 in 1 tablet

63 *Operating conditions*—

64 Detector, column temperature and flow rate: Proceed as
65 directed in the operating conditions in the Assay.

66 Column: A stainless steel column 3.9 mm in inside
67 diameter and 15 cm in length, packed with
68 octadecylsilanized silica gel for liquid chromatography (5
69 μm in particle diameter).

70 Mobile phase: A mixture of water and acetonitrile (1:1).

71 *System suitability*—

72 System performance: When the procedure is run with 50
73 μL of the standard solution under the above operating
74 conditions, the number of theoretical plates and the
75 symmetry factor of the peak of fludiazepam are not less than
76 3000 and not more than 2.0, respectively.

77 System repeatability: When the test is repeated 6 times
78 with 50 μL of the standard solution under the above
79 operating conditions, the relative standard deviation of the
80 peak area of fludiazepam is not more than 2.0%.

81 **Assay** Weigh accurately the mass of not less than 20 tab-
82 lets of Fludiazepam Tablets, and powder. Weigh accurately
83 a portion of the powder, equivalent to about 0.25 mg of
84 fludiazepam (C₁₆H₁₂ClFN₂O), add 4 mL of water, disperse
85 the fine particles by sonicating, add 6 mL of acetonitrile,
86 and shake for 10 minutes. To this solution add a mixture of
87 acetonitrile and water (3:2) to make exactly 50 mL, centri-
88 fuge, and use the supernatant liquid as the sample solution.
89 Separately, weigh accurately about 25 mg of fludiazepam
90 for assay, previously dried at 60°C for 3 hours under re-
91 duced pressure, dissolve in a mixture of acetonitrile and wa-
92 ter (3:2) to make exactly 50 mL. Pipet 5 mL of this solution,
93 add a mixture of acetonitrile and water (3:2) to make exactly
94 50 mL. Then, pipet 5 mL of this solution, add a mixture of
95 acetonitrile and water (3:2) to make exactly 50 mL, and use
96 this solution as the standard solution. Perform the test with
97 exactly 20 μL each of the sample solution and standard so-

98 lution as directed under Liquid Chromatography <2.01> ac-
99 cording to the following conditions, and determine the peak
100 areas, A_T and A_S , of fludiazepam in each solution.

101 Amount (mg) of fludiazepam ($C_{16}H_{12}ClFN_2O$)
102 $= M_S \times A_T / A_S \times 1 / 100$

103 M_S : Amount (mg) of fludiazepam for assay taken

104 *Operating conditions—*

105 Detector: An ultraviolet absorption photometer
106 (wavelength: 232 nm).

107 Column: A stainless steel column 4.6 mm in inside
108 diameter and 15 cm in length, packed with
109 octadecylsilanized silica gel for liquid chromatography (5
110 μm in particle diameter).

111 Column temperature: A constant temperature of about
112 25°C .

113 Mobile phase: A mixture of methanol and water (3:2).

114 Flow rate: Adjust so that the retention time of
115 fludiazepam is about 10 minutes.

116 *System suitability—*

117 System performance: When the procedure is run with 20
118 μL of the standard solution under the above operating
119 conditions, the number of theoretical plates and the
120 symmetry factor of the peak of fludiazepam are not less than
121 6000 and not more than 2.0, respectively.

122 System repeatability: When the test is repeated 6 times
123 with 20 μL of the standard solution under the above
124 operating conditions, the relative standard deviation of the
125 peak area of fludiazepam is not more than 1.0%.

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

127 **Add the following to 9.41 Reagents,**

128 **Test Solutions:**

129 **Fludiazepam for assay** $C_{16}H_{12}ClFN_2O$ [Same as the
130 monograph Fludiazepam. It meets the following additional
131 requirements.]

132 *Purity* Related substances—Dissolve 25 mg of fludiaz-
133 epam for assay in 50 mL of a mixture of acetonitrile and
134 water (3:2), and use this solution as the sample solution. Pi-
135 pet 5 mL of the sample solution, add a mixture of acetoni-
136 trile and water (3:2) to make exactly 50 mL. Pipet 2.5 mL
137 of this solution, add a mixture of acetonitrile and water (3:2)
138 to make exactly 50 mL, and use this solution as the standard
139 solution. Perform the test with exactly 20 μL each of the
140 sample solution and standard solution as directed under Liq-
141 uid Chromatography <2.01> according to the following con-
142 ditions, and determine each peak area by the automatic in-
143 tegration method: the area of the peak other than fludiaz-
144 epam obtained from the sample solution is not larger than 2/5
145 times the peak area of fludiazepam from the standard solu-
146 tion, and the total area of the peaks other than fludiazepam

147 from the sample solution is not larger than the peak area of
148 fludiazepam from the standard solution.

149 *Operating conditions*

150 Detector, column, column temperature, mobile phase and
151 flow rate: Proceed as directed in the operating conditions in
152 the Assay under Fludiazepam Tablets.

153 Time span of measurement: About 4 times as long as the
154 retention time of fludiazepam, beginning after the solvent
155 peak.

156 *System suitability*

157 Test for required detectability: Pipet 1 mL of the standard
158 solution, and add a mixture of acetonitrile and water (3:2)
159 to make exactly 10 mL. Confirm that the peak area of
160 fludiazepam obtained with 20 μL of this solution is
161 equivalent to 7 to 13% of that with 20 μL of the standard
162 solution.

163 *System performance:* When the procedure is run with 20
164 μL of the standard solution under the above operating
165 conditions, the number of theoretical plates and the
166 symmetry factor of the peak of fludiazepam are not less than
167 6000 and not more than 2.0, respectively.

168 *System repeatability:* When the test is repeated 6 times
169 with 20 μL of the standard solution under the above
170 operating conditions, the relative standard deviation of the
171 peak area of fludiazepam is not more than 2.0%.

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