Fludiazepam Tablets

フルジアゼパム錠

Fludiazepam Tablets contain not less than 93.0% and not more than 107.0% of the labeled amount of fludiazepam ($C_{16}H_{12}ClFN_2O$: 302.73).

Method of preparation Prepare as directed under Tablets, with Fludiazepam.

Identification To a quantity of powdered Fludiazepam Tablets, equivalent to 2 mg of Fludiazepam, add 40 mL of methanol, shake for 20 minutes, and filter. Determine the absorption spectrum of the filtrate as directed under Ultraviolet-visible Spectrophotometry <*2.24*>: it exhibits a maximum between 315 nm and 319 nm. Therefore, to 5 mL of the filtrate add methanol to make 50 mL. Determine the absorption spectrum of this solution as directed under Ultraviolet-visible Spectrophotometry <*2.24*>: it exhibits a maximum between 229 nm and 233 nm.

Uniformity of dosage units <*6.02*> Perform the test according to the following method: it meets the requirement of the Content uniformity test.

To 1 tablet of Fludiazepam Tablets add 2*V*/25 mL of water, disperse the fine particles by sonicating, add 3*V*/25 mL of acetonitrile, and shake for 10 minutes. Add a mixture of acetonitrile and water (3:2) to make exactly *V* mL so that each mL contains about 5 μg of fludiazepam ($C_{16}H_{12}ClFN_2O$), centrifuge, and use the supernatant liquid as the sample solution. Then, proceed as directed in the Assay.

Amount (mg) of fludiazepam ($C_{16}H_{12}ClFN_2O$)
$= M_S \times A_T / A_S \times V / 5000$

M_S: Amount (mg) of fludiazepam for assay taken

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

Start the test with 1 tablet of Fludiazepam Tablets, withdraw not less than 20 mL of the medium at the specified minute after starting the test, and filter through a membrane filter with a pore size not exceeding 0.45 μm. Discard the first 10 mL or more of the filtrate, pipet *V* mL of the subsequent filtrate, add water to make exactly *V*′ mL so that each mL contains about 0.28 μg of fludiazepam ($C_{16}H_{12}ClFN_2O$), and use this solution as the sample solution. Separately, weigh accurately about 28 mg of fludiazepam for assay, previously dried at 60℃ for 3 hours under reduced pressure, and dissolve in methanol to make exactly 100 mL. Pipet 5 mL of this solution, and add water to make exactly 100 mL. Then, pipet 2 mL of this solution, and add water to make exactly 100 mL, and use this solution as the standard solution. Perform the test with exactly 50 μL each of the sample solution and standard solution as directed under Liquid Chromatography <*2.01*> according to the following conditions, and determine the peak areas, A_T and A_S, of fludiazepam in each solution.

Dissolution rate (%) with respect to the labeled amount of fludiazepam ($C_{16}H_{12}ClFN_2O$)
$= M_S \times A_T / A_S \times V'/V \times 1/C \times 9/10$

M_S: Amount (mg) of fludiazepam for assay taken
C: Labeled amount (mg) of fludiazepam ($C_{16}H_{12}ClFN_2O$) in 1 tablet

Operating conditions—
Detector, column temperature and flow rate: Proceed as directed in the operating conditions in the Assay.
Column: A stainless steel column 3.9 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).
Mobile phase: A mixture of water and acetonitrile (1:1).
System suitability—
System performance: When the procedure is run with 50 μL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of fludiazepam are not less than 3000 and not more than 2.0, respectively.
System repeatability: When the test is repeated 6 times with 50 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of fludiazepam is not more than 2.0%.

Assay Weigh accurately the mass of not less than 20 tablets of Fludiazepam Tablets, and powder. Weigh accurately a portion of the powder, equivalent to about 0.25 mg of fludiazepam ($C_{16}H_{12}ClFN_2O$), add 4 mL of water, disperse the fine particles by sonicating, add 6 mL of acetonitrile, and shake for 10 minutes. To this solution add a mixture of acetonitrile and water (3:2) to make exactly 50 mL, centrifuge, and use the supernatant liquid as the sample solution. Separately, weigh accurately about 25 mg of fludiazepam for assay, previously dried at 60℃ for 3 hours under reduced pressure, dissolve in a mixture of acetonitrile and water (3:2) to make exactly 50 mL. Pipet 5 mL of this solution, add a mixture of acetonitrile and water (3:2) to make exactly 50 mL. Then, pipet 5 mL of this solution, add a mixture of acetonitrile and water (3:2) to make exactly 50 mL, and use this solution as the standard solution. Perform the test with exactly 20 μL each of the sample solution and standard so-

lution as directed under Liquid Chromatography <2.01> according to the following conditions, and determine the peak areas, A_T and A_S, of fludiazepam in each solution.

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

M_S: Amount (mg) of fludiazepam for assay taken

Operating conditions—

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

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

Column temperature: A constant temperature of about 25℃.

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

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

System suitability—

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

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

Containers and storage Containers —Tight containers.

Add the following to 9.41 Reagents, Test Solutions:

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

Purity Related substances—Dissolve 25 mg of fludiazepam for assay in 50 mL of a mixture of acetonitrile and water (3:2), and use this solution as the sample solution. Pipet 5 mL of the sample solution, add a mixture of acetonitrile and water (3:2) to make exactly 50 mL. Pipet 2.5 mL of this solution, add a mixture of acetonitrile and water (3:2) to make exactly 50 mL, and use this solution as the standard solution. Perform the test with exactly 20 μL each of the sample solution and standard solution as directed under Liquid Chromatography <2.01> according to the following conditions, and determine each peak area by the automatic integration method: the area of the peak other than fludiazepam obtained from the sample solution is not larger than 2/5 times the peak area of fludiazepam from the standard solution, and the total area of the peaks other than fludiazepam from the sample solution is not larger than the peak area of fludiazepam from the standard solution.

Operating conditions

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

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

System suitability

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

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

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