Ethyl Loflazepate Tablets

ロフラゼプ酸エチル錠

Ethyl Loflazepate Tablets contain not less than 93.0% and not more than 107.0% of the labeled amount of ethyl loflazepate ($C_{18}H_{14}ClFN_2O_3$: 360.77).

Method of preparation Prepare as directed under Tablets, with Ethyl Loflazepate.

Identification To a quantity of powdered Ethyl Loflazepate Tablets, equivalent to 1 mg of Ethyl Loflazepate, add 10 mL of acetonitrile, shake for 15 minutes, and centrifuge. To 1 mL of the supernatant liquid add acetonitrile to make 10 mL. Determine the absorption spectrum of this solution as directed under Ultraviolet-visible Spectrophotometry *<2.24>*: it exhibits a maximum between 227 nm and 231 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 Ethyl Loflazepate Tablets add exactly 0.5 mL of water, sonicate to disintegrate the tablet, add exactly 10 mL of the internal standard solution, shake for 20 minutes, and centrifuge. Pipet V mL of the supernatant liquid, add water so that each mL contains 48 μL of water, add the internal standard solution to make exactly V' mL so that each mL contains about 95 μg of ethyl loflazepate ($C_{18}H_{14}ClFN_2O_3$), and use this solution as the sample solution. Then, proceed as directed in the Assay.

Amount (mg) of ethyl loflazepate ($C_{18}H_{14}ClFN_2O_3$) in 1 tablet $= M_S \times Q_T / Q_S \times V' / V \times 1 / 10$

M_S: Amount (mg) of Ethyl Loflazepate RS taken

Internal standard solution—A solution of methyl parahydroxybenzoate in acetonitrile for liquid chromatography (1 in 3000).

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 30 minutes of Ethyl Loflazepate Tablets is not less than 80%.

Start the test with 1 tablet of Ethyl Loflazepate 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 1.1 μg of ethyl loflazepate ($C_{18}H_{14}ClFN_2O_3$), and use this solution as the sample solution. Separately, weigh accurately about 22 mg of Ethyl Loflazepate RS, previously dried at 105℃ for 3 hours, and dissolve in ethanol (95) to make exactly 100 mL. Pipet 1 mL of this solution, add water to make exactly 200 mL, and use this solution as the standard solution. Perform the test with exactly 10 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 ethyl loflazepate in each solution.

Dissolution rate (%) with respect to the labeled amount of ethyl loflazepate ($C_{18}H_{14}ClFN_2O_3$)
$= M_S \times A_T / A_S \times V' / V \times 1 / C \times 9 / 2$

M_S: Amount (mg) of Ethyl Loflazepate RS taken
C: Labeled amount (mg) of ethyl loflazepate ($C_{18}H_{14}ClFN_2O_3$) in 1 tablet

Operating conditions—
Detector: An ultraviolet absorption photometer (wavelength: 230 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 water, acetonitrile and ethanol (99.5) (2:1:1).
Flow rate: Adjust so that the retention time of ethyl loflazepate is about 7 minutes.
System suitability—
System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of ethyl loflazepate are not less than 1500 and not more than 1.5, respectively.
System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of ethyl loflazepate is not more than 3.0%.

Assay Weigh accurately the mass of not less than 20 tablets of Ethyl Loflazepate Tablets, and powder. Weigh accurately a portion of the powder, equivalent to about 1 mg of ethyl loflazepate ($C_{18}H_{14}ClFN_2O_3$), add 0.5 mL of water, and sonicate. Add exactly 10 mL of the internal standard, shake, centrifuge, and use the supernatant liquid as the sample solution. Separately, weigh accurately about 10 mg of Ethyl Loflazepate RS, previously dried at 105℃ for 3 hours, and add the internal standard solution to make exactly 100 mL. Pipet 10 μL of this solution, add 0.5 mL of

water, and use this solution as the standard solution. Perform the test with exactly 10 mL each of the sample solution and standard solution as directed under Liquid Chromatography <2.01> according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak area of ethyl loflazepate to that of the internal standard.

Amount (mg) of ethyl loflazepate ($C_{18}H_{14}ClFN_2O_3$)
$= M_S \times Q_T / Q_S \times 1/10$

M_S: Amount (mg) of Ethyl Loflazepate RS taken

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 229 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 25 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 water, acetonitrile for liquid chromatography and ethanol (95) (2:1:1).

Flow rate: Adjust so that the retention time of ethyl loflazepate is about 13 minutes.

System suitability—

System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, the internal standard and ethyl loflazepate are eluted in this order with the resolution between these peaks being not less than 6.

System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratio of the peak area of ethyl loflazepate to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Well-closed containers.

Add the following to 9.01 Reference Standards (1):

Ethyl Loflazepate RS