Ethyl Loflazepate Tablets

Dissolution <6.10> Perform the test with 1 tablet of Ethyl Loflazepate Tablets at 50 revolutions per minute according to the Paddle method, using 900 mL of water as the dissolution medium. Start the test, 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 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 ($C_{18}H_{14}ClFN_2O_3$) according to the labeled amount, and use this solution as the sample solution. Separately, weigh accurately about 22 mg of Ethyl Loflazepate RS, previously dried at 105ºC 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 of both solutions.

The requirements are met if Ethyl Loflazepate Tablets conform to the dissolution requirements.

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

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 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 25ºC.

Mobile phase: A mixture of water, acetonitrile and ethanol (99.5) (2:1:1).

Flow rate: Adjust the flow rate 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%.

Dissolution Requirements

Labeled amount	Specified minute	Dissolution rate
1 mg	30 minutes	Not less than 80%
2 mg	30 minutes	Not less than 80%

Ethyl Loflazepate RS $C_{18}H_{14}ClFN_2O_3$: 360.77 7-chloro-5-(*2*-fluorophenyl)-2,3-dihydro-2-oxo-1*H*-1,4-benzodiazepine-3- carboxylate. It meets the following reuirements. Purify according to the following method if needed.

Purification method−To 5 g of ethyl loflazepate add 75 mL of ethanol (95), dissolve by warming to 80ºC, shake well with 0.5 g of activated charcoal, and remove the activated charcoal by filtering by suction. Allow the filtrate to stand overnight in a cold place at 5ºC, filter the crystals separated, wash with a small amount of ice-cooled ethanol (95), and dry at 50ºC under reduced pressure overnight.

Description−Ethyl Loflazepate RS occurs as a white, crystalline powder.

Identification Determine the absorption spectrum of a solution of Ethyl Loflazepate RS in acetonitrile (1 in 100000) as directed under Ultraviolet-visible Spectrophotometry *<2.24>*: it exhibits maxima between 227 nm and 231 nm, and between 314 nm and 319 nm.

Absorbance *<2.24>*: $E_{1cm}^{1\%}$ (229 nm): 970 − 1030 (10 mg, acetonitrile, 2000 mL).

Related substances−Dissolve 0.10 g of Ethyl Loflazepate RS in 5 mL of chloroform, and use this solution as the sample solution. Pipet 1 mL of this solution, and add chloroform to make exactly 100 mL. Further, pipet 5 mL of this solution, add chloroform to make exactly 25 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under Thin-layer Chromatography *<2.03>*. Spot 5 μL each of the sample solution and standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of chloroform, heptane and ethanol (95) (5:4:1) to a distance of about 12 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): the number of the spots other than the principal spot obtained with the sample solution is not more than 2, and is not larger and not more intense than that with the standard solution.

Loss on drying *<2.41>*: not more than 0.2% (0.2 g, 105ºC, 3 hours).

Content: not less than 99.0%. Assay−Weigh accurately about 0.5 g of Ethyl Loflazepate RS, previously dried, dissolve in 60 mL of acetic acid for nonaqueous titration, and titrate *<2.50>* with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination in the same manner, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS

= 36.08 mg of $C_{18}H_{14}ClFN_2O_3$