Lornoxicam Tablets

ロルノキシカム錠

Lornoxicam Tablets contain not less than 95.0% and not more than 105.0% of the labeled amount of lornoxicam ($C_{13}H_{10}ClN_3O_4S_2$: 371.82).

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

Identification Take an amount of powdered Lornoxicam Tablets, equivalent to 4 mg of Lornoxicam, add 70 mL of a solution of hydrochloric acid in methanol (9 in 10,000), sonicate, and add a solution of hydrochloric acid in methanol (9 in 10,000) to make 100 mL. Centrifuge this solution, to 5 mL of the supernatant liquid add a solution of hydrochloric acid in methanol (9 in 10,000) to make 20 mL. Determine the absorption spectrum of this solution as directed under Ultraviolet-visible Spectrophotometry *<2.24>*: it exhibits maximum between 359 nm and 363 nm.

Purity Related substances—Take a quantity of Lornoxicam Tablets, equivalent to 4 mg of Lornoxicam, add exactly 20 mL of the mobile phase, and sonicate. Centrifuge this solution, and use the supernatant liquid as the sample solution. Separately, weigh accurately about 40 mg of Lornoxicam RS, previously dried at 105℃ for 4 hours, dissolve in acetonitrile to make exactly 200 mL. Pipet 1 mL of this solution, add the mobile phase to make exactly 100 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. Determine each peak area by the automatic integration method, and calculate the amounts of the related substances by the following equation: the amount of related substance B having the relative retention time of about 0.13 to lornoxicam is not more than 2.0%, the amount of related substance TA having the relative retention time of about 0.15 is not more than 1.2%, the amount of related substance TB having the relative retention time of about 0.21 is not more than 2.0%, the amount of related substance TC having the relative retention time of about 0.25 is not more than 3.0%, the amount of related substance TD having the relative retention time of about 0.36 is not more than 2.0%, and the amount of the related substances other than the peak of lornoxicam, the related substances A having the relative retention time of about 0.4 to lornoxicam and the peaks mentioned above is not more than 2.0%. Furthermore, the total amount of the related substances is not more than 5.0%. For the peak areas of the related substances TA and TC, multiply their correction factors 0.6 and 1.5, respectively.

$$\text{Amount (\%) of related substance (\%)} = M_S \times A_T / A_S \times 1/40$$

M_S: Amount (mg) of Lornoxicam RS taken

A_T: Peak area of each related substance obtained from the sample solution

A_S: Peak area of lornoxicam obtained from the standard solution

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 280 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 50℃.

Mobile phase: Dissolve 4.2 g of tetra-*n*-butylammonium bromide, 4.6 g of disodium hydrogen phosphate dodecahydrate and 4.4 g of potassium dihydrate phosphate in 1300 mL of water, and add 700 mL of acetonitrile for liquid chromatography.

Flow rate: Adjust so that the retention time of lornoxicam is about 20 minutes.

Time span of measurement: About 1.5 times as long as the retention time of lornoxicam, beginning after the solvent peak.

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 symmetry factor of the peak of lornoxicam are not less than 10,000 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 lornoxicam is not more than 2.0%.

Loss on drying *<2.41>* Not more than 2.0% (in vacuum, phosphorus (V) oxide, 24 hours). Take a number of Lornoxicam Tablets, equivalent to 24 mg of Lornoxicam, powder immediately, and perform the test.

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 Lornoxicam Tablets add *V*/10 mL of water, and sonicate. Add 3*V*/5 mL of a mixture of acetonitrile and methanol (1:1), sonicate, then add a mixture of acetonitrile and methanol (1:1) to make exactly *V* mL so that each mL contains about 80 μg of lornoxicam ($C_{13}H_{10}ClN_3O_4S_2$), and centrifugate. Pipet 10 mL of the supernatant liquid, add exactly 1 mL of the internal standard solution, then add the mobile phase to make 20 mL, and use this solution as the sample

solution. Separately, weigh accurately about 40 mg of Lornoxicam RS, previously dried 105℃ for 4 hours, dissolve in a mixture of acetonitrile and methanol (1:1) to make exactly 200 mL. Pipet 20 mL of this solution, add 5 mL of water, and add a mixture of acetonitrile and methanol (1:1) to make exactly 50 mL. Pipet 10 mL of this solution, add exactly 1 mL of the internal standard solution, then add the mobile phase to make 20 mL, and use this solution as the standard solution. Perform the test with 10 μL 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 lornoxicam to that of the internal standard.

Amount (mg) of lornoxicam ($C_{13}H_{10}ClN_3O_4S_2$)
$= M_S \times Q_T / Q_S \times V / 500$

M_S: Amount (mg) of Lornoxicam RS taken

Internal standard solution—A solution of diphenylamine in the mobile phase (1 in 4000).

Operating conditions—

Proceed as directed in the operating conditions in the Assay.

System suitability—

System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, lornoxicam and the internal standard are eluted in this order with the resolution 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 lornoxicam to that of the internal standard is not more than 1.5%.

Dissolution *<6.10>* When the test is performed at 75 revolutions per minute according to the Paddle method, using 900 mL of water as the dissolution medium, the dissolution rate in 10 minutes of Lornoxicam Tablets is not less than 80%.

Prepare the sample solution within 1 hour. Start the test with 1 tablet of Lornoxicam 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 not less than 10 mL of the first filtrate, pipet V mL of the subsequent filtrate, add the mobile phase to make exactly V' mL so that each mL contains about 1.1 μg of lornoxicam ($C_{13}H_{10}ClFN_3O_4S_2$), and use this solution as the sample solution. Separately, weigh accurately about 40 mg of lornoxicam for assay, previously dried 105℃ for 4 hours, dissolve in acetonitrile to make exactly 200 mL. Pipet 2 mL of this solution, add the mobile phase to make exactly 100 mL. Pipet 5 mL of this solution, add the mobile phase to make exactly 20 mL, and use this solution as the standard solution. Perform the test with exactly 100 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 lornoxicam in each solution.

Dissolution rate (%) with respect to the labeled amount of lornoxicam ($C_{13}H_{10}ClFN_3O_4S_2$)
$= M_S \times A_T / A_S \times V' / V \times 1 / C \times 9 / 4$

M_S: Amount (mg) of lornoxicam for assay taken

C: Labeled amount (mg) of lornoxicam ($C_{13}H_{10}ClFN_3O_4S_2$) in 1 tablet

Operating conditions—

Proceed as directed in the operating conditions in the Assay.

System suitability—

System performance: When the procedure is run with 100 μL of the standard solution under the above operating conditions, the theoretical plates and the symmetry factor of the peak area of lornoxicam are not less than 1500 and not more than 2.0, respectively.

System repeatability: When the test is repeated 6 times with 100 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of lornoxicam is not more than 1.5%.

Assay To 15 tablets of Lornoxicam Tablets, add V/10 mL of water, and sonicate. Add 7V/10 of a mixture of acetonitrile and methanol (1:1), sonicate, then add a mixture of acetonitrile and methanol (1:1) to make exactly V mL so that each mL contains about 120 μg of lornoxicam ($C_{13}H_{10}ClFN_3O_4S_2$), and centrifuge. Pipet 5 mL of the supernatant liquid, add exactly 1 mL of the internal standard solution, then add the mobile phase to make 20 mL, and use this solution as the sample solution. Separately, weigh accurately about 60 mg of Lornoxicam RS, previously dried at 105℃ or 4 hours, and dissolve in a mixture of acetonitrile and methanol (1:1) to make exactly 200 mL. Pipet 20 mL of this solution, add 5 mL of water, and add a mixture of acetonitrile and methanol (1:1) to make exactly 50 mL. Pipet 5 mL of this solution, add exactly 1 mL of the internal standard solution, then add the mobile phase to make 20 mL, and use this solution as the standard solution. Perform the test with 10 μL 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 lornoxicam to that of the internal standard.

Amount (mg) of lornoxicam ($C_{13}H_{10}ClFN_3O_4S_2$) in 1 tablet
$= M_S \times Q_T / Q_S \times V / 7500$

M_S: Amount (mg) of Lornoxicam RS taken

Internal standard solution—A solution of diphenylamine in the mobile phase (1 in 5000).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 295 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 50°C.

Mobile phase: A mixture of methanol, a solution of sodium lauryl sulfate (1 in 90) and phosphoric acid (550:450:1).

Flow rate: Adjust so that the retention time of lornoxicam is about 4 minutes.

System suitability—

System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, lornoxicam and the internal standard are eluted in this order with the resolution 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 lornoxicam to that of the internal standard is not more than 1.5%.

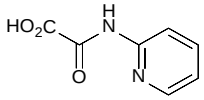
Containers and storage Containers—Tight containers.

Others

Related substances A and B: Refer to them described in Lornoxicam.

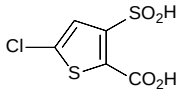
Related substance TA:

(Pyridin-2-yl)oxamic acid



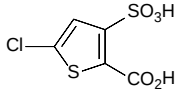
Related substance TB:

5-Chloro-3-sulfinothiophene-2-carboxylic acid



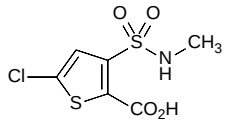
Related substance TC:

5-Chloro-3-sulfothiophene-2-carboxylic acid



Related substance TD:

5-Chloro-3-(*N*-methylsulfamoyl)thiophene-2-carboxylic acid



Add the following to 9.01 Reference Standards (1):

Lornoxicam RS