

1 Lornoxicam Tablets

2 ロルノキシカム錠

3

4 Lornoxicam Tablets contain not less than 95.0% and
5 not more than 105.0% of the labeled amount of lornox-
6 icam ($C_{13}H_{10}ClN_3O_4S_2$; 371.82).

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

9 **Identification** Take an amount of powdered Lornoxicam
10 Tablets, equivalent to 4 mg of Lornoxicam, add 70 mL of a
11 solution of hydrochloric acid in methanol (9 in 10,000), son-
12 icate, and add a solution of hydrochloric acid in methanol (9
13 in 10,000) to make 100 mL. Centrifuge this solution, to 5 mL
14 of the supernatant liquid add a solution of hydrochloric acid
15 in methanol (9 in 10,000) to make 20 mL. Determine the ab-
16 sorption spectrum of this solution as directed under Ultravi-
17 olet-visible Spectrophotometry <2.24>: it exhibits maximum
18 between 359 nm and 363 nm.

19 **Purity** Related substances—Take a quantity of Lornoxicam
20 Tablets, equivalent to 4 mg of Lornoxicam, add exactly 20
21 mL of the mobile phase, and sonicate. Centrifuge this solu-
22 tion, and use the supernatant liquid as the sample solution.
23 Separately, weigh accurately about 40 mg of Lornoxicam RS,
24 previously dried at 105°C for 4 hours, dissolve in acetonitrile
25 to make exactly 200 mL. Pipet 1 mL of this solution, add the
26 mobile phase to make exactly 100 mL, and use this solution
27 as the standard solution. Perform the test with exactly 10 μ L
28 each of the sample solution and standard solution as directed
29 under Liquid Chromatography <2.01> according to the fol-
30 lowing conditions. Determine each peak area by the auto-
31 matic integration method, and calculate the amounts of the
32 related substances by the following equation: the amount of
33 related substance B having the relative retention time of
34 about 0.13 to lornoxicam is not more than 2.0%, the amount
35 of related substance TA having the relative retention time of
36 about 0.15 is not more than 1.2%, the amount of related sub-
37 stance TB having the relative retention time of about 0.21 is
38 not more than 2.0%, the amount of related substance TC hav-
39 ing the relative retention time of about 0.25 is not more than
40 3.0%, the amount of related substance TD having the relative
41 retention time of about 0.36 is not more than 2.0%, and the
42 amount of the related substances other than the peak of lor-
43 noxicam, the related substances A having the relative reten-
44 tion time of about 0.4 to lornoxicam and the peaks mentioned
45 above is not more than 2.0%. Furthermore, the total amount
46 of the related substances is not more than 5.0%. For the peak
47 areas of the related substances TA and TC, multiply their cor-
48 rection factors 0.6 and 1.5, respectively.

49 Amount (%) of related substance (%)

$$50 = M_S \times A_T / A_S \times 1 / 40$$

51 M_S : Amount (mg) of Lornoxicam RS taken

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

54 A_S : Peak area of lornoxicam obtained from the standard
55 solution

56 *Operating conditions—*

57 Detector: An ultraviolet absorption photometer (wave-
58 length: 280 nm).

59 Column: A stainless steel column 4 mm in inside diameter
60 and 15 cm in length, packed with octadecylsilanized silica gel
61 for liquid chromatography (5 μ m in particle diameter).

62 Column temperature: A constant temperature of about
63 50°C.

64 Mobile phase: Dissolve 4.2 g of tetra-*n*-butylammonium
65 bromide, 4.6 g of disodium hydrogen phosphate dodecahy-
66 drate and 4.4 g of potassium dihydrate phosphate in 1300 mL
67 of water, and add 700 mL of acetonitrile for liquid chroma-
68 tography.

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

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

74 *System suitability—*

75 System performance: When the procedure is run with 10
76 μ L of the standard solution under the above operating condi-
77 tions, the number of theoretical plates and symmetry factor
78 of the peak of lornoxicam are not less than 10,000 and not
79 more than 1.5, respectively..

80 System repeatability: When the test is repeated 6 times
81 with 10 μ L of the standard solution under the above operating
82 conditions, the relative standard deviation of the peak area of
83 lornoxicam is not more than 2.0%.

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

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

91 To 1 tablet of Lornoxicam Tablets add V/10 mL of water,
92 and sonicate. Add 3V/5 mL of a mixture of acetonitrile and
93 methanol (1:1), sonicate, then add a mixture of acetonitrile
94 and methanol (1:1) to make exactly V mL so that each mL
95 contains about 80 μ g of lornoxicam ($C_{13}H_{10}ClN_3O_4S_2$), and
96 centrifugate. Pipet 10 mL of the supernatant liquid, add ex-
97 actly 1 mL of the internal standard solution, then add the mo-
98 bile phase to make 20 mL, and use this solution as the sample

99 solution. Separately, weigh accurately about 40 mg of Lor-
 100 noxicam RS, previously dried 105°C for 4 hours, dissolve in
 101 a mixture of acetonitrile and methanol (1:1) to make exactly
 102 200 mL. Pipet 20 mL of this solution, add 5 mL of water, and
 103 add a mixture of acetonitrile and methanol (1:1) to make ex-
 104 actly 50 mL. Pipet 10 mL of this solution, add exactly 1 mL
 105 of the internal standard solution, then add the mobile phase
 106 to make 20 mL, and use this solution as the standard solution.
 107 Perform the test with 10 μ L each of the sample solution and
 108 standard solution as directed under Liquid Chromatography
 109 <2.01> according to the following conditions. and calculate
 110 the ratios, Q_T and Q_S , of the peak area of lornoxicam to that
 111 of the internal standard.

$$\begin{aligned} &\text{Amount (mg) of lornoxicam (C}_{13}\text{H}_{10}\text{ClFN}_3\text{O}_4\text{S}_2\text{)} \\ &= M_S \times Q_T / Q_S \times V / 500 \end{aligned}$$

114 M_S : Amount (mg) of Lornoxicam RS taken

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

117 *Operating conditions*—

118 Proceed as directed in the operating conditions in the As-
 119 say.

120 *System suitability*—

121 System performance: When the procedure is run with 10
 122 μ L of the standard solution under the above operating condi-
 123 tions, lornoxicam and the internal standard are eluted in this
 124 order with the resolution being not less than 6.

125 System repeatability: When the test is repeated 6 times
 126 with 10 μ L of the standard solution under the above operating
 127 conditions, the relative standard deviation of the ratio of the
 128 peak area of lornoxicam to that of the internal standard is not
 129 more than 1.5%.

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

134 Prepare the sample solution within 1 hour. Start the test
 135 with 1 tablet of Lornoxicam Tablets, withdraw not less than
 136 20 mL of the medium at the specified minute after starting
 137 the test, and filter through a membrane filter with a pore size
 138 not exceeding 0.45 μ m. Discard not less than 10 mL of the
 139 first filtrate, pipet V mL of the subsequent filtrate, add the
 140 mobile phase to make exactly V' mL so that each mL contains
 141 about 1.1 μ g of lornoxicam (C₁₃H₁₀ClFN₃O₄S₂), and use this
 142 solution as the sample solution. Separately, weigh accurately
 143 about 40 mg of lornoxicam for assay, previously dried 105°C
 144 for 4 hours, dissolve in acetonitrile to make exactly 200 mL.
 145 Pipet 2 mL of this solution, add the mobile phase to make
 146 exactly 100 mL. Pipet 5 mL of this solution, add the mobile
 147 phase to make exactly 20 mL, and use this solution as the
 148 standard solution. Perform the test with exactly 100 μ L each

149 of the sample solution and standard solution as directed under
 150 Liquid Chromatography <2.01> according to the following
 151 conditions. and determine the peak areas, A_T and A_S , of lor-
 152 noxicam in each solution.

153 Dissolution rate (%) with respect to the labeled amount of
 154 lornoxicam (C₁₃H₁₀ClFN₃O₄S₂)

$$= M_S \times A_T / A_S \times V' / V \times 1 / C \times 9 / 4$$

156 M_S : Amount (mg) of lornoxicam for assay taken

157 C : Labeled amount (mg) of lornoxicam (C₁₃H₁₀ClFN₃O₄S₂)
 158 in 1 tablet

159 *Operating conditions*—

160 Proceed as directed in the operating conditions in the As-
 161 say.

162 *System suitability*—

163 System performance: When the procedure is run with 100
 164 μ L of the standard solution under the above operating condi-
 165 tions, the theoretical plates and the symmetry factor of the
 166 peak area of lornoxicam are not less than 1500 and not more
 167 than 2.0, respectively.

168 System repeatability: When the test is repeated 6 times
 169 with 100 μ L of the standard solution under the above operat-
 170 ing conditions, the relative standard deviation of the peak
 171 area of lornoxicam is not more than 1.5%.

172 **Assay** To 15 tablets of Lornoxicam Tablets, add $V/10$ mL
 173 of water, and sonicate. Add $7V/10$ of a mixture of acetonitrile
 174 and methanol (1:1), sonicate, then add a mixture of acetoni-
 175 trile and methanol (1:1) to make exactly V mL so that each
 176 mL contains about 120 μ g of lornoxicam (C₁₃H₁₀ClFN₃O₄S₂),
 177 and centrifuge. Pipet 5 mL of the supernatant liquid, add ex-
 178 actly 1 mL of the internal standard solution, then add the mo-
 179 bile phase to make 20 mL, and use this solution as the sample
 180 solution. Separately, weigh accurately about 60 mg of Lor-
 181 noxicam RS, previously dried at 105°C or 4 hours, and dis-
 182 solve in a mixture of acetonitrile and methanol (1:1) to make
 183 exactly 200 mL. Pipet 20 mL of this solution, add 5 mL of
 184 water, and add a mixture of acetonitrile and methanol (1:1)
 185 to make exactly 50 mL. Pipet 5 mL of this solution, add ex-
 186 actly 1 mL of the internal standard solution, then add the mo-
 187 bile phase to make 20 mL, and use this solution as the stand-
 188 ard solution. Perform the test with 10 μ L each of the sample
 189 solution and standard solution as directed under Liquid chro-
 190 matography <2.01> according to the following conditions,
 191 and calculate the ratios, Q_T and Q_S , of the peak area of lor-
 192 noxicam to that of the internal standard.

$$\begin{aligned} &\text{Amount (mg) of lornoxicam (C}_{13}\text{H}_{10}\text{ClFN}_3\text{O}_4\text{S}_2\text{) in 1 tablet} \\ &= M_S \times Q_T / Q_S \times V / 7500 \end{aligned}$$

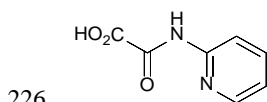
195 M_S : Amount (mg) of Lornoxicam RS taken

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

198 *Operating conditions—*199 Detector: An ultraviolet absorption photometer (wave-
200 length: 295 nm).201 Column: A stainless steel column 4 mm in inside diameter 236
202 and 15 cm in length, packed with octadecylsilanized silica gel
203 for liquid chromatography (5 μ m in particle diameter).204 Column temperature: A constant temperature of about 237
205 50°C. 238206 Mobile phase: A mixture of methanol, a solution of sodium 239
207 lauryl sulfate (1 in 90) and phosphoric acid (550:450:1). 240208 Flow rate: Adjust so that the retention time of lornoxicam
209 is about 4 minutes.210 *System suitability—*211 System performance: When the procedure is run with 10
212 μ L of the standard solution under the above operating condi-
213 tions, lornoxicam and the internal standard are eluted in this
214 order with the resolution being not less than 6.215 System repeatability: When the test is repeated 6 times
216 with 10 μ L of the standard solution under the above operating
217 conditions, the relative standard deviation of the ratio of the
218 peak area of lornoxicam to that of the internal standard is not
219 more than 1.5%.220 **Containers and storage** Containers—Tight containers.221 **Others**222 Related substances A and B: Refer to them described in Lor-
223 noxicam.

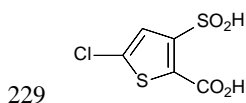
224 Related substance TA:

225 (Pyridin-2-yl)oxamic acid



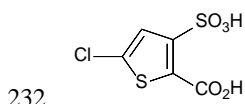
227 Related substance TB:

228 5-Chloro-3-sulfinothiophene-2-carboxylic acid

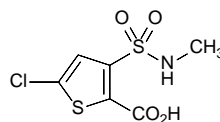


230 Related substance TC:

231 5-Chloro-3-sulfothiophene-2-carboxylic acid



233 Related substance TD:

234 5-Chloro-3-(N-methylsulfamoyl)thiophene-2-carboxylic
235 acid237 **Add the following to 9.01 Reference**
238 **Standards (1):**

239 Lornoxicam RS