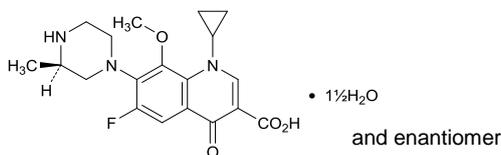


# 1 Gatifloxacin Hydrate

2 ガチフロキサシン水和物



3  
4 C<sub>19</sub>H<sub>22</sub>FN<sub>3</sub>O<sub>4</sub>·1½H<sub>2</sub>O: 402.42

5 1-Cyclopropyl-6-fluoro-8-methoxy-7-[(3*RS*)-3-methylpiperazin-1-  
6 yl]-4-oxo-1,4-dihydroquinoline-3-carboxylic acid sesquihydrate

7 [180200-66-2]

8

9 Gatifloxacin Hydrate contains not less than 98.5%  
10 and not more than 101.5% of gatifloxacin  
11 (C<sub>19</sub>H<sub>22</sub>FN<sub>3</sub>O<sub>4</sub>: 375.39), calculated on the anhydrous  
12 basis.

13 **Description** Gatifloxacin Hydrate occurs as white to pale  
14 yellow, crystals or crystalline powder.

15 It is slightly soluble in methanol and in ethanol (99.5),  
16 and very slightly soluble in water.

17 It dissolves in sodium hydroxide TS.

18 It is gradually colored to pale yellow by light.

19 A solution of Gatifloxacin Hydrate in dilute sodium hy-  
20 droxide TS (1 in 100) shows no optical rotation.

21 **Identification** (1) Determine the absorption spectrum  
22 of a solution of Gatifloxacin Hydrate in dilute sodium hy-  
23 droxide TS (1 in 100,000) as directed under Ultraviolet-vis-  
24 ible Spectrophotometry <2.24>, and compare the spectrum  
25 with the Reference Spectrum or the spectrum of a solution  
26 of Gatifloxacin RS prepared in the same manner as the sam-  
27 ple solution: both spectra exhibit similar intensities of ab-  
28 sorption at the same wavelengths.

29 (2) Determine the infrared absorption spectrum of Gat-  
30 ifloxacin Hydrate as directed in the potassium bromide disk  
31 method under Infrared Spectrophotometry <2.25>, and  
32 compare the spectrum with the Reference Spectrum or the  
33 spectrum of Gatifloxacin RS: both spectra exhibit similar  
34 intensities of absorption at the same wave numbers.

35 **Purity** (1) Clarity and color of solution—Dissolve 1.0  
36 g of Gatifloxacin Hydrate in 10 mL of sodium hydroxide  
37 TS: the solution is clear. Perform the test with the solution  
38 as directed under Methods for Color Matching <2.65>: the  
39 solution has no more color than diluted Matching Fluid O  
40 (1 in 5).

41 (2) Heavy metals <1.07>—Proceed with 1.0 g of Gat-  
42 ifloxacin Hydrate according to Method 4, and perform the  
43 test. Prepare the control solution with 2.0 mL of Standard  
44 Lead Solution (not more than 20 ppm).

45 (3) Related substances—Dissolve 20 mg of Gatifloxa-  
46 cin Hydrate in 50 mL of the dissolving solution, and use  
47 this solution as the sample solution. Pipet 1 mL of the sam-  
48 ple solution, and add the dissolving solution to make ex-  
49 actly 100 mL. Pipet 2 mL of this solution, add the dissolv-  
50 ing solution to make exactly 20 mL, and use this solution  
51 as the standard solution. Perform the test with exactly 20  
52 μL each of the sample solution and standard solution as di-  
53 rected under Liquid Chromatography <2.01> according to  
54 the following conditions. Determine each peak area by the  
55 automatic integration method: the peak area of the related  
56 substance A, having the relative retention time of about 1.2  
57 to gatifloxacin, obtained from the sample solution is not  
58 larger than 2 times the peak area of gatifloxacin from the  
59 standard solution, and the area of the peak other than gat-  
60 ifloxacin and the peak mentioned above from the sample  
61 solution is not larger than the peak area of gatifloxacin from  
62 the standard solution. Furthermore, the total area of the  
63 peaks other than gatifloxacin from the sample solution is  
64 not larger than 3 times the peak area of gatifloxacin from  
65 the standard solution.

66 Dissolving solution: A mixture of diluted phosphoric  
67 acid (1 in 1000) and acetonitrile (4:1).

68 **Operating conditions**—

69 Detector: An ultraviolet absorption photometer  
70 (wavelength: 325 nm).

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

75 Column temperature: A constant temperature of about  
76 35°C.

77 Mobile phase A: A mixture of diluted triethylamine (1 in  
78 100), adjusted to pH 4.3 with phosphoric acid, and  
79 acetonitrile (22:3).

80 Mobile phase B: A mixture of diluted triethylamine (1 in  
81 100), adjusted to pH 4.3 with phosphoric acid, and  
82 acetonitrile (1:1).

83 Flowing of mobile phase: Control the gradient by mixing  
84 the mobile phases A and B as directed in the following table.  
85

Time after injection of sample (min)	Mobile phase A (vol%)	Mobile phase B (vol%)
0 — 15	100	0
15 — 30	100 → 0	0 → 100
30 — 40	0	100

86  
87 Flow rate: 1.0 mL per minute (the retention time of  
88 gatifloxacin is about 16 minutes).

89 Time span of measurement: About 2.5 times as long as  
90 the retention time of gatifloxacin, beginning after the  
91 solvent peak.

92 *System suitability*—

93 Test for required detectability: Pipet 5 mL of the  
94 standard solution, and add the dissolving solution to make  
95 exactly 10 mL. Confirm that the peak area of gatifloxacin  
96 obtained with 20  $\mu\text{L}$  of this solution is equivalent to 40 to  
97 60% of that with 20  $\mu\text{L}$  of the standard solution.

98 System performance: Dissolve 20 mg of methyl 4-  
99 aminobenzoate in 50 mL of the dissolving solution. To 5  
100 mL of this solution add 1 mL of the sample solution and the  
101 dissolving solution to make 100 mL. When the procedure  
102 is run with 20  $\mu\text{L}$  of this solution under the above operating  
103 conditions, gatifloxacin and methyl 4-aminobenzoate are  
104 eluted in this order with the resolution between these peaks  
105 being not less than 4.

106 System repeatability: When the test is repeated 6 times  
107 with 20  $\mu\text{L}$  of the standard solution under the above  
108 operating conditions, the relative standard deviation of the  
109 peak area of gatifloxacin is not more than 3.0%.

110 **Water** <2.48> 6.0 – 9.0% (0.1 g, volumetric titration, di-  
111 rect titration).

112 **Residue on ignition** <2.44> Not more than 0.1% (1 g).

113 **Assay** Weigh accurately about 50 mg of Gatifloxacin Hy-  
114 drate, and dissolve in the dissolving solution to make ex-  
115 actly 100 mL. Pipet 2 mL of this solution, add exactly 2 mL  
116 of the internal standard solution, add the dissolving solution  
117 to make 25 mL, and use this solutions as the sample solu-  
118 tion. Separately, weigh accurately about 50 mg of Gatiflox-  
119 acin RS (separately determine the water <2.48> in the same  
120 manner as Gatifloxacin Hydrate), and dissolve in the dis-  
121 solving solution to make exactly 100 mL. Pipet 2 mL of  
122 this solution, add exactly 2 mL of the internal standard so-  
123 lution, add the dissolving solution to make 25 mL, and use  
124 this solutions as the standard solution. Perform the test with  
125 20  $\mu\text{L}$  each of the sample solution and standard solution as  
126 directed under Liquid Chromatography <2.01> according to  
127 the following conditions, and calculate the ratios,  $Q_T$  and  
128  $Q_S$ , of the peak area of gatifloxacin to that of the internal  
129 standard.

$$130 \quad \text{Amount (mg) of gatifloxacin (C}_{19}\text{H}_{22}\text{FN}_3\text{O}_4) \\ 131 \quad = M_S \times Q_T / Q_S$$

132  $M_S$ : Amount (mg) of Gatifloxacin RS taken, calculated  
133 on the anhydrous basis

134 *Internal standard solution*— A solution of methyl 4-amino-  
135 benzoate in the dissolving solution (1 in 4000).

136 Dissolving solution: A mixture of diluted phosphoric  
137 acid (1 in 1000) and acetonitrile (4:1).

138 *Operating conditions*—

139 Detector: An ultraviolet absorption photometer  
140 (wavelength: 280 nm).

141 Column: A stainless steel column 4 mm in inside  
142 diameter and 12.5 cm in length, packed with  
143 octadecylsilanized silica gel for liquid chromatography (5  
144  $\mu\text{m}$  in particle diameter).

145 Column temperature: A constant temperature of about  
146 40°C.

147 Mobile phase: To 10 mL of triethylamine add water to  
148 make 1000 mL, and adjust to pH 4.5 with phosphoric acid.  
149 To 870 mL of this solution add 130 mL of acetonitrile.

150 Flow rate: Adjust so that the retention time of  
151 gatifloxacin is about 5 minutes.

152 *System suitability*—

153 System performance: When the procedure is run with 20  
154  $\mu\text{L}$  of the standard solution under the above operating  
155 conditions, gatifloxacin and the internal standard are eluted  
156 in this order with the resolution between these peaks being  
157 not less than 4.

158 System repeatability: When the test is repeated 6 times  
159 with 20  $\mu\text{L}$  of the standard solution under the above  
160 operating conditions, the relative standard deviation of the  
161 ratio of the peak area of gatifloxacin to that of the internal  
162 standard is not more than 1.0%.

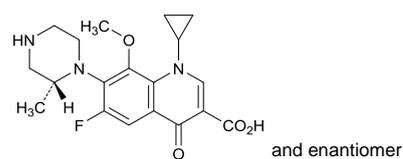
163 **Containers and storage** Containers— Tight containers.

164 Storage— Light-resistant.

165 **Others**

166 Related substance A: 1-Cyclopropyl-6-fluoro-8-methoxy-  
167 7-[(2*RS*)-2-methylpiperazin-1-yl]-4-oxo-1,4-dihydroquin-  
168 oline-3-carboxylic acid

169



170

171 **Add the following to 9.01 Reference**  
172 **Standards (1):**

173 **Gatifloxacin RS**

174 **Add the following to 9.41 Reagents,**  
175 **Test Solutions:**

176 **Methyl 4-aminobenzoate**  $\text{H}_2\text{NC}_6\text{H}_4\text{COOCH}_3$  Pale  
177 yellow, crystals or crystalline powder.

178 *Melting point* <2.60>: 111 – 114°C

179