

## 1 Irinotecan Hydrochloride Injection

2 イリノテカン塩酸塩注射液

3

4 Irinotecan Hydrochloride Injection is an aqueous  
5 injection.

6 It contains not less than 95.0% and not more than  
7 105.0% of the labeled amount of irinotecan hydro-  
8 chloride hydrate ( $C_{33}H_{38}N_4O_6 \cdot HCl \cdot 3H_2O$ : 677.18).

9 **Method of preparation** Prepare as directed under Injec-  
10 tions, with Irinotecan Hydrochloride Hydrate.

11 **Description** Irinotecan Hydrochloride Injection is a clear  
12 and pale yellow liquid.

13 It is gradually decomposed by light.

14 **Identification** To a volume of Irinotecan Hydrochloride  
15 Injection, equivalent to 20 mg of Irinotecan Hydrochloride  
16 Hydrate, add water to make 10 mL. To 1 mL of this solution  
17 add water to make 100 mL. Determine the absorption spec-  
18 trum of this solution as directed under Ultraviolet-visible  
19 Spectrophotometry <2.24>: it exhibits maxima between 253  
20 nm and 257 nm, between 354 nm and 358 nm, and between  
21 368 nm and 372 nm.

22 **pH** Being specified separately when the drug is granted  
23 approval based on the Law.

24 **Purity** Related substances—To a volume of Irinotecan  
25 Hydrochloride Injection, equivalent to 40 mg of Irinotecan  
26 Hydrochloride Hydrate, add a mixture of diluted 0.1 mol/L  
27 potassium dihydrogen phosphate TS (1 in 10), methanol  
28 and acetonitrile (6:4:3) and 1 mL of 1 mol/L hydrochloric  
29 acid TS to make 20 mL, and use this solution as the sample  
30 solution. Pipet 1 mL of this solution, add a mixture of di-  
31 luted 0.1 mol/L potassium dihydrogen phosphate TS (1 in  
32 10), methanol and acetonitrile (6:4:3) to make exactly 100  
33 mL, and use this solution as the standard solution. Perform  
34 the test with exactly 25  $\mu$ L each of the sample solution and  
35 standard solution as directed under Liquid Chromatography  
36 <2.01> according to the following conditions. Determine  
37 each peak area by the automatic integration method: the  
38 area of related substance IA, having the relative retention  
39 time of about 0.3 to irinotecan, obtained from the sample  
40 solution is not larger than 1/2 times the peak area of iri-  
41 notecan from the standard solution, the areas of related sub-  
42 stances A and B, having the relative retention time of about  
43 0.8, from the sample solution are not larger than 3/10 times  
44 the peak area of irinotecan from the standard solution, the  
45 area of related substance IB, having the relative retention  
46 time of about 1.3, from the sample solution is not larger than  
47 1/3 times the peak area of irinotecan from the standard so-  
48 lution, the areas of related substances C and D, having the  
49 relative retention time of about 1.6, and related substance

50 IC, having the relative retention time of about 2.2, from the  
51 sample solution are not larger than 1/5 times the peak area  
52 of irinotecan from the standard solution, and the area of the  
53 peak other than irinotecan and the peaks mentioned above  
54 from the sample solution is not larger than 1/10 times the  
55 peak area of irinotecan from the standard solution. Further-  
56 more, the total area of the peaks other than irinotecan from  
57 the sample solution is not larger than 1.5 times the peak area  
58 of irinotecan from the standard solution.

59 *Operating conditions*—

60 Proceed as directed in the operating conditions in the Pu-  
61 rity (2) under Irinotecan Hydrochloride Hydrate.

62 *System suitability*—

63 Test for required detectability: Pipet 1 mL of the standard  
64 solution, add a mixture of diluted 0.1 mol/L potassium  
65 dihydrogen phosphate TS (1 in 10), methanol and  
66 acetonitrile (6:4:3) to make exactly 20 mL. Confirm that the  
67 peak area of irinotecan obtained with 25  $\mu$ L of this solution  
68 is equivalent to 3.5 to 6.5% of that with 25  $\mu$ L of the  
69 standard solution.

70 System performance: When the procedure is run with 25  
71  $\mu$ L of the standard solution under the above operating  
72 conditions, the number of theoretical plates and the  
73 symmetry factor of the peak of irinotecan are not less than  
74 6000 and not more than 2.0, respectively.

75 System repeatability: When the test is repeated 6 times  
76 with 25  $\mu$ L of the standard solution under the above  
77 operating conditions, the relative standard deviation of the  
78 peak area of irinotecan is not more than 2.0%.

79 **Bacterial endotoxins** <4.01> Less than 1.8 EU/mg.

80 **Extractable volume** <6.05> It meets the requirement.

81 **Foreign insoluble matter** <6.06> Perform the test ac-  
82 cording to Method 1: it meets the requirement.

83 **Insoluble particulate matter** <6.07> It meets the re-  
84 quirement.

85 **Sterility** <4.06> Perform the test according to the Mem-  
86 brane filtration method: it meets the requirement.

87 **Assay** Pipet a volume of Irinotecan Hydrochloride Injec-  
88 tion, equivalent to about 20 mg of irinotecan hydrochloride  
89 hydrate ( $C_{33}H_{38}N_4O_6 \cdot HCl \cdot 3H_2O$ ), and add a mixture of  
90 methanol and acetic acid-sodium acetate buffer solution  
91 (pH 4.0) (11:9) to make exactly 50 mL. Pipet 10 mL of this  
92 solution, add the internal standard solution to make exactly  
93 100 mL, and use this solution as the sample solution. Sepa-  
94 rately, weigh accurately about 20 mg of irinotecan hydro-  
95 chloride hydrate for assay (separately determine the water  
96 <2.48> in the same manner as Irinotecan Hydrochloride Hy-  
97 drate), dissolve in a mixture of methanol and acetic acid-

98 sodium acetate buffer solution (pH 4.0) (11:9) to make ex-  
 99 actly 50 mL. Pipet 10 mL of this solution, add the internal  
 100 standard solution to make exactly 100 mL, and use this so-  
 101 lution as the standard solution. Perform the test with 10  $\mu$ L  
 102 each of the sample solution and standard solution as di-  
 103 rected under Liquid Chromatography <2.01> according to  
 104 the following conditions, and calculate the ratios,  $Q_T$  and  $Q_S$ ,  
 105 of the peak area of irinotecan to that of the internal standard.

$$\begin{aligned} 106 & \text{Amount (mg) of irinotecan hydrochloride hydrate} \\ 107 & (\text{C}_{33}\text{H}_{38}\text{N}_4\text{O}_6 \cdot \text{HCl} \cdot 3\text{H}_2\text{O}) \\ 108 & = M_S \times Q_T / Q_S \times 1.087 \end{aligned}$$

109  $M_S$ : Amount (mg) of irinotecan hydrochloride hydrate for  
 110 assay taken, calculated on the anhydrous basis

111 *Internal standard solution*— Dissolve 33.3 mg of propyl  
 112 parahydroxybenzoate in a mixture of methanol and acetic  
 113 acid-sodium acetate buffer solution (pH 4.0) (11:9) to make  
 114 1000 mL.

115 *Operating conditions*—

116 Detector: An ultraviolet absorption photometer  
 117 (wavelength: 254 nm).

118 Column: A stainless steel column 6 mm in inside  
 119 diameter and 15 cm in length, packed with  
 120 octadecylsilanized silica gel for liquid chromatography (5  
 121  $\mu$ m in particle diameter).

122 Column temperature: A constant temperature of about  
 123 40°C.

124 Mobile phase: Dissolve 1.01 g of sodium 1-  
 125 heptanesulfonate in a mixture of methanol and acetic acid-  
 126 sodium acetate buffer solution (pH 4.0) (11:9) to make 1000  
 127 mL.

128 Flow rate: Adjust so that the retention time of irinotecan  
 129 is about 7 minutes.

130 *System Suitability*—

131 System performance: When the procedure is run with 10  
 132  $\mu$ L of the standard solution under the above operating  
 133 conditions, irinotecan and the internal standard are eluted in  
 134 this order with the resolution between these peaks being not  
 135 less than 6.

136 System repeatability: When the test is repeated 6 times  
 137 with 10  $\mu$ L of the standard solution under the above  
 138 operating conditions, the relative standard deviation of the  
 139 ratios of the peak area of irinotecan to that of the internal  
 140 standard is not more than 1.0%.

141 **Containers and storage** Containers—Hermetic contain-  
 142 ers.

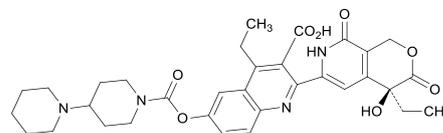
143 Storage—Light-resistant.

144 **Others**

145 Related substances A, B, C and D: refer to them described  
 146 in Irinotecan Hydrochloride Hydrate.

147 Related substances IA:

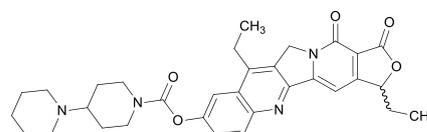
148 6-{{[1,4'-Bipiperidine]-1'-carboxyloxy}-4-ethyl-2-[(4S)-4-  
 149 ethyl-4-hydroxy-3,8-dioxo-3,4,7,8-tetrahydro-1H-pyrano  
 150 [3,4-c]pyridin-6-yl]quinoline-3-carboxylic acid



151

152 Related substances IB:

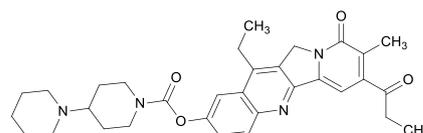
153 3,10-Diethyl-1,13-dioxo-1,3,11,13-tetrahydrofuro  
 154 [3',4':6,7]indolizino[1,2-b]quinolin-8-yl [1,4'-bipiperidine]-  
 155 1'-carboxylate



156

157 Related substances IC:

158 12-Ethyl-8-methyl-9-oxo-7-propionyl-9,11-dihydroin-  
 159 dolizino  
 160 [1,2-b]quinolin-2-yl [1,4'-bipiperidine]-1'-carboxylate



161

162

163 **Add the following to 9.41 Reagents,**  
 164 **Test Solutions:**

165 **Irinotecan hydrochloride hydrate for assay**  
 166  $\text{C}_{33}\text{H}_{38}\text{N}_4\text{O}_6 \cdot \text{HCl} \cdot 3\text{H}_2\text{O}$  [Same as the monograph Irinotecan  
 167 Hydrochloride Hydrate]