

1 **Solifenacin Succinate Orally Disintegrating**
2 **Tablets**

3 ソリフェナシンコハク 酸塩 口腔内崩壊錠

4
5 Solifenacin Succinate Orally Disintegrating Tablets
6 contain not less than 95.0% and not more than 105.0%
7 of the labeled amount of solifenacin succinate
8 ($C_{23}H_{26}N_2O_2 \cdot C_4H_6O_4$; 480.55).

9 **Method of preparation** Prepare as directed under Tablets,
10 with Solifenacin Succinate.

11 **Identification** To a quantity of Solifenacin Succinate
12 Orally Disintegrating Tablets, equivalent to 20 mg of solifen-
13 acin succinate ($C_{23}H_{26}N_2O_2 \cdot C_4H_6O_4$), add 40 mL of a mixture
14 of water and methanol (1:1), shake for 30 minutes using a
15 shaker, and filter through a membrane filter with a pore size
16 not exceeding $0.45 \mu\text{m}$. Discard the first 2 mL of the filtrate,
17 and use the subsequent filtrate as the sample solution. Deter-
18 mine the absorption spectrum of the sample solution as di-
19 rected under Ultraviolet-visible Spectrophotometry <2.24>: it
20 exhibits maxima between 257 nm and 261 nm, and between
21 263 nm and 267 nm.

22 **Purity** Related substances—To 10 tablets of Solifenacin
23 Succinate Orally Disintegrating Tablets add about 3V/5 mL
24 of a mixture of water and acetonitrile (7:3), shake for 30
25 minutes using a shaker, and add a mixture of water and ace-
26 tonitrile (7:3) to make exactly V mL so that each mL contains
27 about 0.5 mg of solifenacin succinate ($C_{23}H_{26}N_2O_2 \cdot C_4H_6O_4$).
28 Filter this solution through a membrane filter with a pore size
29 not exceeding $0.45 \mu\text{m}$. Discard the first 2 mL of the filtrate,
30 and use the subsequent filtrate as the sample solution. Sepa-
31 rately, weigh accurately about 50 mg of Solifenacin Succin-
32 ate RS and dissolve in a mixture of water and acetonitrile
33 (7:3) to make exactly 100 mL. Pipet 1 mL of this solution,
34 add a mixture of water and acetonitrile (7:3) to make exactly
35 100 mL, and use this solution as the standard solution. Per-
36 form the test with exactly $10 \mu\text{L}$ each of the sample solution
37 and standard solution as directed under Liquid Chromatog-
38 raphy <2.01> according to the conditions described below.
39 Determine each peak area by the automatic integration
40 method. Calculate the amount of each related substance and
41 the total amount of related substances by the following equa-
42 tion: the amount of the related substance TA, having the re-
43 lative retention time of about 0.5 to solifenacin, is not more
44 than 0.2%, the amount of the related substance TB, having
45 the relative retention time of about 0.8, is not more than 0.5%,
46 the amount of each related substance other than the sub-
47 stances mentioned above is not more than 0.2%, and the total
48 amount of related substances is not more than 0.7%.

49 Amount (%) of each related substance
50 $= M_S \times A_T / A_S \times 1 / 50$

51 Total amount (%) of related substances
52 $= M_S \times \Sigma A_T / A_S \times 1 / 50$

53 M_S : Amount (mg) of Solifenacin Succinate RS taken

54 A_S : Peak area of solifenacin from the standard solution

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

57 ΣA_T : Total peak area of related substances from the sample
58 solution

59 *Operating conditions*—

60 Detector, column, column temperature and mobile phase:
61 Proceed as directed in the operating conditions in the Assay
62 under Solifenacin Succinate.

63 Flow rate: Adjust so that the retention time of solifenacin
64 is about 15 minutes.

65 Time span of measurement: About 2 times as long as the
66 retention time of solifenacin, beginning after the solvent and
67 succinic acid peaks.

68 *System suitability*—

69 System performance: Proceed as directed in the system
70 suitability in the Assay.

71 Test for required detectability: To exactly 2.5 mL of the
72 standard solution add a mixture of water and acetonitrile (7:3)
73 to make exactly 50 mL. Confirm that the peak area of sol-
74 ifenacin obtained with $10 \mu\text{L}$ of this solution is equivalent to
75 2.5 to 7.5% of that with $10 \mu\text{L}$ of the standard solution.

76 System repeatability: When the test is repeated 6 times
77 with $10 \mu\text{L}$ of the standard solution under the above operating
78 conditions, the relative standard deviation of the peak area of
79 solifenacin is not more than 2.5%.

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

83 To 1 tablet of Solifenacin Succinate Orally Disintegrating
84 Tablets add exactly V mL of a mixture of water and acetonit-
85 rile (7:3) so that each mL contains about 0.5 mg of solifen-
86 acin succinate ($C_{23}H_{26}N_2O_2 \cdot C_4H_6O_4$), shake for 30 minutes
87 using a shaker. Filter this solution through a membrane filter
88 with a pore size not exceeding $0.45 \mu\text{m}$. Discard the first 2
89 mL of the filtrate, and use the subsequent filtrate as the sam-
90 ple solution. Separately, weigh accurately about 50 mg of
91 Solifenacin Succinate RS, and dissolve in a mixture of water
92 and acetonitrile (7:3) to make exactly 100 mL, and use this
93 solution as the standard solution. Perform the test with ex-
94 actly $10 \mu\text{L}$ each of the sample solution and standard solution
95 as directed under Liquid Chromatography <2.01> according
96 to the conditions described below. Determine the peak areas,
97 A_T and A_S , of solifenacin in each solution.

98 Amount (mg) of solifenacin succinate ($C_{23}H_{26}N_2O_2 \cdot C_4H_6O_4$)
 99 $=M_S \times A_T/A_S \times V \times 1/100$

100 M_S : Amount (mg) of Solifenacin Succinate RS taken

101 *Operating conditions*—

102 Detector, column, column temperature and mobile phase:
 103 Proceed as directed in the operating conditions in the Assay
 104 under Solifenacin Succinate.

105 Flow rate: Adjust so that the retention time of solifenacin
 106 is about 15 minutes.

107 *System suitability*—

108 Proceed as directed in the system suitability in the Assay.

109 **Dissolution** <6.10> When the test is performed at 50 revo-
 110 lutions per minute according to the Paddle method, using 900
 111 mL of 2nd fluid for disintegration test as the dissolution me-
 112 dium, the Q value in 30 minutes of Solifenacin Succinate
 113 Orally Disintegrating Tablets is 80%.

114 Start the test with 1 tablet of Solifenacin Succinate Orally
 115 Disintegrating Tablets, withdraw not less than 5 mL of the
 116 medium using an instrument equipped with a filter laminated
 117 with polyethylene fiber at the specified minute after starting
 118 the test, and, if necessary, filter through a membrane filter
 119 with a pore size not exceeding $0.45 \mu\text{m}$. Pipet 3.5 mL of the
 120 medium, add exactly 1.5 mL of acetonitrile, shake thor-
 121 oughly, and use this solution as the sample solution. Sepa-
 122 rately, weigh accurately about 28 mg of Solifenacin Succinate
 123 RS, and dissolve in a mixture of water and acetonitrile
 124 (7:3) to make exactly 100 mL. Pipet V mL of this solution
 125 containing solifenacin succinate ($C_{23}H_{26}N_2O_2 \cdot C_4H_6O_4$)
 126 equivalent to $7/25$ of the labeled amount, and add the disso-
 127 lution medium to make exactly 250 mL. Pipet 3.5 mL of the
 128 solution, add exactly 1.5 mL of acetonitrile, shake thoroughly,
 129 and use this solution as the standard solution. Perform the test
 130 with exactly $50 \mu\text{L}$ each of the sample solution and standard
 131 solution as directed under Liquid Chromatography <2.01> ac-
 132 cording to the conditions described below. Determine the
 133 peak areas, A_T and A_S , of solifenacin in each solution.

134 Dissolution rate (%) with respect to the labeled amount of
 135 solifenacin succinate ($C_{23}H_{26}N_2O_2 \cdot C_4H_6O_4$)

136 $=M_S \times A_T/A_S \times V \times 1/C \times 18/5$

137 M_S : Amount (mg) of Solifenacin Succinate RS taken

138 C : Labeled amount (%) of solifenacin succinate
 139 ($C_{23}H_{26}N_2O_2 \cdot C_4H_6O_4$) in 1 tablet

140 *Operating conditions*—

141 Detector, column and column temperature: Proceed as di-
 142 rected in the operating conditions in the Assay under Solifen-
 143 acin Succinate.

144 Mobile phase: Dissolve 8.7 g of dipotassium hydrogen
 145 phosphate in water to make 1000 mL, and adjust to pH 6.0

146 with phosphoric acid. To 650 mL of this solution add 350 mL
 147 of acetonitrile for liquid chromatography.

148 Flow rate: Adjust so that the retention time of solifenacin
 149 is about 9 minutes.

150 *System suitability*—

151 System performance: To 10 mg of Solifenacin Succinate
 152 RS, add 1 mL of hydrogen peroxide (30) and 5 mL of sodium
 153 hydroxide solution (43 in 10000), and then add 15 mL of a
 154 mixture of water and acetonitrile (7:3). Stir this solution for
 155 10 minutes, and use as the related substance TB solution.
 156 Separately, weigh 5 mg of Solifenacin Succinate RS, add 0.1
 157 mol/L hydrochloric acid TS to make 10 mL. To 1 mL of this
 158 solution, add 1 mL of the related substance TB solution, and
 159 add a mixture of water and acetonitrile (7:3) to make 100 mL.
 160 When the procedure is run with $50 \mu\text{L}$ of this solution under
 161 the above operating conditions, the related substance TB and
 162 solifenacin are eluted in this order with the resolution be-
 163 tween these peaks being not less than 3.

164 System repeatability: When the test is repeated 6 times
 165 with $50 \mu\text{L}$ of the standard solution under the above operating
 166 conditions, the relative standard deviation of the peak area of
 167 solifenacin is not more than 2.0%.

168 **Disintegration** Being specified separately when the drug is
 169 granted approval based on the Law.

170 **Assay** To 20 tablets of Solifenacin Succinate Orally Disin-
 171 tegrating Tablets add about $3V/5$ mL of a mixture of water
 172 and acetonitrile (7:3), shake for 30 minutes using a shaker,
 173 and add a mixture of water and acetonitrile (7:3) to make ex-
 174 actly V mL so that each mL contains about 0.5 mg of solifen-
 175 acin succinate ($C_{23}H_{26}N_2O_2 \cdot C_4H_6O_4$). Filter this solution
 176 through a membrane filter with a pore size not exceeding 0.45
 177 μm . Discard the first 2 mL of the filtrate, and use the subse-
 178 quent filtrate as the sample solution. Separately, weigh accu-
 179 rately about 50 mg of Solifenacin Succinate RS, and dissolve
 180 in a mixture of water and acetonitrile (7:3) to make exactly
 181 100 mL, and use this solution as the standard solution. Per-
 182 form the test with exactly $10 \mu\text{L}$ each of the sample solution
 183 and standard solution as directed under Liquid Chromatog-
 184 raphy <2.01> according to the conditions described below.
 185 Determine the peak areas, A_T and A_S , of solifenacin in each
 186 solution.

187 Amount (mg) of solifenacin succinate ($C_{23}H_{26}N_2O_2 \cdot C_4H_6O_4$)
 188 in 1 tablet

189 $=M_S \times A_T/A_S \times V \times 1/2000$

190 M_S : Amount (mg) of Solifenacin Succinate RS taken

191 *Operating conditions*—

192 Detector, column, column temperature and mobile phase:
 193 Proceed as directed in the operating conditions in the Assay
 194 under Solifenacin Succinate.

195 Flow rate: Adjust so that the retention time of solifenacin
196 is about 15 minutes.

197 *System suitability*—

198 System performance: To 10 mg of Solifenacin Succinate
199 RS, add 1 mL of hydrogen peroxide (30) and 5 mL of sodium
200 hydroxide solution (43 in 10000), and then add 15 mL of a
201 mixture of water and acetonitrile (7:3). Stir this solution for
202 10 minutes, and use as the related substance TB solution.
203 Separately, weigh 5 mg of Solifenacin Succinate RS, add 0.1
204 mol/L hydrochloric acid TS to make 10 mL. To 1 mL of this
205 solution, add 1 mL of the related substance TB solution, and
206 add a mixture of water and acetonitrile (7:3) to make 100 mL.
207 When the procedure is run with 10 μ L of this solution under
208 the above operating conditions, the related substance TB and
209 solifenacin are eluted in this order with the resolution be-
210 tween these peaks being not less than 3.

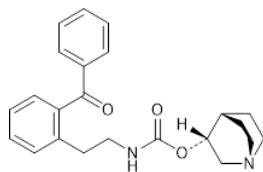
211 System repeatability: When the test is repeated 6 times
212 with 10 μ L of the standard solution under the above operating
213 conditions, the relative standard deviation of the peak area of
214 solifenacin is not more than 1.0%.

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

216 **Others**

217 Related substance TA:

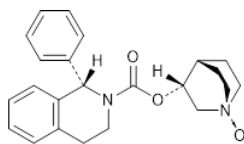
218 (3*R*)-1-Azabicyclo[2.2.2]octan-3-yl[2-(2-
219 benzoylphenyl)ethyl]carbamate



220

221 Related substance TB:

222 (3*R*)-3-[[*(1S)*-1-Phenyl-3,4-dihydroisoquinoline-2(*1H*)-
223 carbonyl]oxy]-1-azabicyclo[2.2.2]octane 1-oxide



224

225 **Add the following to 9.01 Reference**

226 **Standards (1):**

227 Solifenacin Succinate RS

228