Solifenacin Succinate Orally Disintegrating Tablets

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Solifenacin Succinate Orally Disintegrating Tablets contain not less than 95.0% and not more than 105.0% of the labeled amount of solifenacin succinate ($C_{23}H_{26}N_2O_2.C_4H_6O_4$: 480.55).

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

Identification To a quantity of Solifenacin Succinate Orally Disintegrating Tablets, equivalent to 20 mg of solifenacin succinate ($C_{23}H_{26}N_2O_2.C_4H_6O_4$), add 40 mL of a mixture of water and methanol (1:1), shake for 30 minutes using a shaker, and filter through a membrane filter with a pore size not exceeding 0.45 μm. Discard the first 2 mL of the filtrate, and use the subsequent filtrate as the sample solution. Determine the absorption spectrum of the sample solution as directed under Ultraviolet-visible Spectrophotometry *<2.24>*: it exhibits maxima between 257 nm and 261 nm, and between 263 nm and 267 nm.

Purity Related substances—To 10 tablets of Solifenacin Succinate Orally Disintegrating Tablets add about 3*V*/5 mL of a mixture of water and acetonitrile (7:3), shake for 30 minutes using a shaker, and add a mixture of water and acetonitrile (7:3) to make exactly *V* mL so that each mL contains about 0.5 mg of solifenacin succinate ($C_{23}H_{26}N_2O_2.C_4H_6O_4$). Filter this solution through a membrane filter with a pore size not exceeding 0.45 μm. Discard the first 2 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, weigh accurately about 50 mg of Solifenacin Succinate RS and dissolve in a mixture of water and acetonitrile (7:3) to make exactly 100 mL. Pipet 1 mL of this solution, add a mixture of water and acetonitrile (7:3) 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 conditions described below. Determine each peak area by the automatic integration method. Calculate the amount of each related substance and the total amount of related substances by the following equation: the amount of the related substance TA, having the relative retention time of about 0.5 to solifenacin, is not more than 0.2%, the amount of the related substance TB, having the relative retention time of about 0.8, is not more than 0.5%, the amount of each related substance other than the substances mentioned above is not more than 0.2%, and the total amount of related substances is not more than 0.7%.

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

$$\text{Total amount (\%) of related substances} = M_S \times \Sigma A_T / A_S \times 1/50$$

M_S: Amount (mg) of Solifenacin Succinate RS taken
A_S: Peak area of solifenacin from the standard solution
A_T: Peak area of each related substance from the sample solution
ΣA_T: Total peak area of related substances from the sample solution

Operating conditions—
Detector, column, column temperature and mobile phase: Proceed as directed in the operating conditions in the Assay under Solifenacin Succinate.
Flow rate: Adjust so that the retention time of solifenacin is about 15 minutes.
Time span of measurement: About 2 times as long as the retention time of solifenacin, beginning after the solvent and succinic acid peaks.
System suitability—
System performance: Proceed as directed in the system suitability in the Assay.
Test for required detectability: To exactly 2.5 mL of the standard solution add a mixture of water and acetonitrile (7:3) to make exactly 50 mL. Confirm that the peak area of solifenacin obtained with 10 μL of this solution is equivalent to 2.5 to 7.5% of that with 10 μL of the standard solution.
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 solifenacin is not more than 2.5%.

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 Solifenacin Succinate Orally Disintegrating Tablets add exactly *V* mL of a mixture of water and acetonitrile (7:3) so that each mL contains about 0.5 mg of solifenacin succinate ($C_{23}H_{26}N_2O_2.C_4H_6O_4$), shake for 30 minutes using a shaker. Filter this solution through a membrane filter with a pore size not exceeding 0.45 μm. Discard the first 2 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, weigh accurately about 50 mg of Solifenacin Succinate RS, and dissolve in a mixture of water and acetonitrile (7:3) 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 conditions described below. Determine the peak areas, A_T and A_S, of solifenacin in each solution.

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

M_S: Amount (mg) of Solifenacin Succinate RS taken

Operating conditions—

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

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

System suitability—

Proceed as directed in the system suitability in the Assay.

Dissolution *<6.10>* When the test is performed at 50 revolutions per minute according to the Paddle method, using 900 mL of 2nd fluid for disintegration test as the dissolution medium, the *Q* value in 30 minutes of Solifenacin Succinate Orally Disintegrating Tablets is 80%.

Start the test with 1 tablet of Solifenacin Succinate Orally Disintegrating Tablets, withdraw not less than 5 mL of the medium using an instrument equipped with a filter laminated with polyethylene fiber at the specified minute after starting the test, and, if necessary, filter through a membrane filter with a pore size not exceeding 0.45 μm. Pipet 3.5 mL of the medium, add exactly 1.5 mL of acetonitrile, shake thoroughly, and use this solution as the sample solution. Separately, weigh accurately about 28 mg of Solifenacin Succinate RS, and dissolve in a mixture of water and acetonitrile (7:3) to make exactly 100 mL. Pipet *V* mL of this solution containing solifenacin succinate ($C_{23}H_{26}N_2O_2.C_4H_6O_4$) equivalent to 7/25 of the labeled amount, and add the dissolution medium to make exactly 250 mL. Pipet 3.5 mL of the solution, add exactly 1.5 mL of acetonitrile, shake thoroughly, and use this solution as the standard solution. Perform the test with exactly 50 μL each of the sample solution and standard solution as directed under Liquid Chromatography *<2.01>* according to the conditions described below. Determine the peak areas, A_T and A_S, of solifenacin in each solution.

Dissolution rate (%) with respect to the labeled amount of solifenacin succinate ($C_{23}H_{26}N_2O_2.C_4H_6O_4$)
$= M_S \times A_T / A_S \times V \times 1/C \times 18/5$

M_S: Amount (mg) of Solifenacin Succinate RS taken

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

Operating conditions—

Detector, column and column temperature: Proceed as directed in the operating conditions in the Assay under Solifenacin Succinate.

Mobile phase: Dissolve 8.7 g of dipotassium hydrogen phosphate in water to make 1000 mL, and adjust to pH 6.0 with phosphoric acid. To 650 mL of this solution add 350 mL of acetonitrile for liquid chromatography.

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

System suitability—

System performance: To 10 mg of Solifenacin Succinate RS, add 1 mL of hydrogen peroxide (30) and 5 mL of sodium hydroxide solution (43 in 10000), and then add 15 mL of a mixture of water and acetonitrile (7:3). Stir this solution for 10 minutes, and use as the related substance TB solution. Separately, weigh 5 mg of Solifenacin Succinate RS, add 0.1 mol/L hydrochloric acid TS to make 10 mL. To 1 mL of this solution, add 1 mL of the related substance TB solution, and add a mixture of water and acetonitrile (7:3) to make 100 mL. When the procedure is run with 50 μL of this solution under the above operating conditions, the related substance TB and solifenacin are eluted in this order with the resolution between these peaks being not less than 3.

System repeatability: When the test is repeated 6 times with 50 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of solifenacin is not more than 2.0%.

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

Assay To 20 tablets of Solifenacin Succinate Orally Disintegrating Tablets add about 3*V*/5 mL of a mixture of water and acetonitrile (7:3), shake for 30 minutes using a shaker, and add a mixture of water and acetonitrile (7:3) to make exactly *V* mL so that each mL contains about 0.5 mg of solifenacin succinate ($C_{23}H_{26}N_2O_2.C_4H_6O_4$). Filter this solution through a membrane filter with a pore size not exceeding 0.45 μm. Discard the first 2 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, weigh accurately about 50 mg of Solifenacin Succinate RS, and dissolve in a mixture of water and acetonitrile (7:3) 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 conditions described below. Determine the peak areas, A_T and A_S, of solifenacin in each solution.

Amount (mg) of solifenacin succinate ($C_{23}H_{26}N_2O_2.C_4H_6O_4$) in 1 tablet
$= M_S \times A_T / A_S \times V \times 1/2000$

M_S: Amount (mg) of Solifenacin Succinate RS taken

Operating conditions—

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

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

System suitability—

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

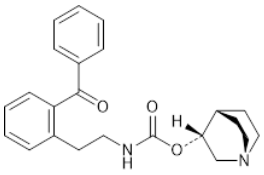
System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of solifenacin is not more than 1.0%.

Containers and storage Containers—Tight containers.

Others

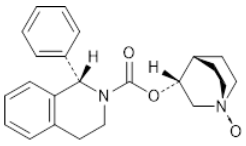
Related substance TA:

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



Related substance TB:

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



Add the following to 9.01 Reference Standards (1):

Solifenacin Succinate RS