Silodosin Orally Disintegrating Tablets

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Silodosin Orally Disintegrating Tablets contain not less than 95.0% and not more than 105.0% of the labeled amount of silodosin ($C_{25}H_{32}F_3N_3O_4$: 495.53).

Method of preparation Prepare as directed under Tablets, with Silodosin.

Identification Conduct this procedure using light-resistant vessels. To 1 tablet of Silodosin Orally Disintegrating Tablets add 15 mL of a mixture of methanol and a solution of sodium chloride (1 in 200) (7:3) per 1 mg of Silodosin, and sonicate until the tablet is completely disintegrated while occasional shaking. Add a mixture of methanol and a solution of sodium chloride (1 in 200) (7:3) so that each mL contains about 40 μg of Silodosin, and filter through a membrane filter with a pore size not exceeding 0.45 μm. Discard the first 3 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, dissolve 20 mg of Silodosin RS in a mixture of methanol and a solution of sodium chloride (1 in 200) (7:3) to make 50 mL. To 5 mL of this solution add a mixture of methanol and a solution of sodium chloride (1 in 200) (7:3) to make 50 mL, and use this solution as the standard solution. Perform the test with 10 μL each of the sample solution and standard solution as directed under Liquid Chromatography <*2.01*> according to the following conditions: the retention times of the principal peaks in the chromatograms obtained from the sample solution and standard solution are the same, and both absorption spectra of these peaks exhibit similar intensities of absorption at the same wavelengths.

Operating conditions—

Column, column temperature, mobile phase, and flow rate: Proceed as directed in the operating conditions in the Assay under Silodosin.

Detector: A photodiode array detector (wavelength: 270 nm, spectrum range of measurement: 200 – 370 nm).

System suitability—

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

Purity Related substances—Conduct this procedure using light-resistant vessels. To a number of Silodosin Orally Disintegrating Tablets, equivalent to 20 mg of Silodosin, add 60 mL of a mixture of methanol and a solution of sodium chloride (1 in 200) (7:3), sonicate until the tablet is completely disintegrated while occasional shaking, and add a mixture of methanol and a solution of sodium chloride (1 in 200) (7:3) to make 100 mL. Centrifuge this solution, and filter the supernatant liquid through a membrane filter with a pore size not exceeding 0.45 μm. Discard the first 3 mL of the filtrate, and use the subsequent filtrate as the sample solution. Pipet 1 mL of the sample solution, add a mixture of methanol and a solution of sodium chloride (1 in 200) (7:3) to make exactly 100 mL, and use this solution as the standard solution. Perform the test with exactly 25 μL each of the sample solution and standard solution as directed under Liquid Chromatography <*2.01*> according to the following conditions, and determine each peak area by the automatic integration method: the peak area of the related substance A, having a relative retention time of about 1.3 to silodosin, obtained from the sample solution is not lager than the peak area of silodosin from the standard solution, the area of the peak other than silodosin and the peak mentioned above from the sample solution is not larger than 1/4 times the peak area of silodosin from the standard solution. Furthermore, the total area of the peaks other than silodosin from the sample solution is not larger than 2 times the peak area of silodosin from the standard solution. For the peak area of the related substance A, multiply the relative response factor 0.6.

Operating conditions—

Detector, column, column temperature, and mobile phases A and B: Proceed as directed in the Purity (2) under Silodosin.

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

Time after injection of sample (min)	Mobile phase A (vol%)	Mobile phase B (vol%)
0 － 15	75	25
15 － 47	75 → 35	25 → 65
47 － 53	35	65

Flow rate: Adjust so that the retention time of silodosin is about 13 minutes.

Time span of measurement: About 3.5 times as long as the retention time of silodosin, beginning after the solvent peak.

System suitability—

Test for required detectability: Pipet 1 mL of the standard solution, and add a mixture of methanol and a solution of sodium chloride (1 in 200) (7:3) to make exactly 20 mL. Confirm that the peak area of silodosin obtained with 25 μL of this solution is equivalent to 3.5 to 6.5% of that with 25 μL of the standard solution.

System performance: Thinly spread out an amount of silodosin in a petri dish, exposure to a 4000 lx light for not less than 24 hours using a D_{65} fluorescent lamp, and dissolve 4 mg of this sample in 20 mL of a mixture of methanol and a solution of sodium chloride (1 in 200) (7:3).

When the procedure is run with 25 μL of this solution under the above operating conditions, the resolution between the peaks of silodosin and the related substance A is not less than 6.

System repeatability: When the test is repeated 6 times with 25 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of silodosin is not more than 2.0%.

Uniformity of dosage units <*6.02*> Perform the test according to the following method: it meets the requirement of the Content uniformity test.

Conduct this procedure using light-resistant vessels. To 1 tablet of Silodosin Orally Disintegrating Tablets add 3*V*/5 mL of a mixture of methanol and a solution of sodium chloride (1 in 200) (7:3), sonicate until the tablet is completely disintegrated while occasional shaking. Add a mixture of methanol and a solution of sodium chloride (1 in 200) (7:3) to make exactly *V* mL so that each mL contains about 40 μg of Silodosin, and filter through a membrane filter with a pore size not exceeding 0.45 μm. Discard the first 3 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, weigh accurately about 20 mg of Silodosin RS (separately determine the water <*2.48*> in the same manner as Silodosin), and dissolve in a mixture of methanol and a solution of sodium chloride (1 in 200) (7:3) to make exactly 50 mL. Pipet 5 mL of this solution, add a mixture of methanol and a solution of sodium chloride (1 in 200) (7:3) to make exactly 50 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 following conditions, and determine the peak areas, A_T and A_S, of silodosin in each solution.

Amount (mg) of silodosin ($C_{25}H_{32}F_3N_3O_4$)
$= M_S \times A_T / A_S \times V / 500$

M_S: Amount (mg) of Silodosin RS taken, calculated on the anhydrous basis

Operating conditions—
Proceed as directed in the operating conditions in the Assay under Silodosin.
System suitability—
Proceed as directed in the system suitability in the Assay.

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

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 dissolution test as the dissolution medium, the dissolution rate in 15 minutes of Silodosin Orally Disintegrating Tablets is not less than 80%.

Start the test with 1 tablet of Silodosin Orally Disintegrating Tablets, withdraw not less than 9 mL of the medium at the specified minute after starting the test, and filter through a membrane filter with a pore size not exceeding 0.45 μm. Discard the first 5 mL or more of the filtrate, pipet *V* mL of the subsequent filtrate, add 0.2 mol/L hydrochloric acid TS to make exactly *V'* mL so that each mL contains about 1.1 μg of silodosin ($C_{25}H_{32}F_3N_3O_4$), and use this solution as the sample solution. Separately, weigh accurately about 22 mg of Silodosin RS (separately determine the water <*2.48*> in the same manner as Silodosin), and dissolve in 0.1 mol/L hydrochloric acid TS to make exactly 100 mL. Pipet 5 mL of this solution, add 0.1 mol/L hydrochloric acid TS to make exactly 50 mL. Pipet 5 mL of this solution, add 0.1 mol/L hydrochloric acid TS to make exactly 100 mL, and use this solution as the standard solution. Perform the test with exactly 100 μL each of the sample solution and standard solution as directed under Liquid Chromatography <*2.01*> according to the following conditions, and determine the peak areas, A_T and A_S, of silodosin in each solution.

Dissolution rate (%) with respect to the labeled amount of silodosin ($C_{25}H_{32}F_3N_3O_4$)
$= M_S \times A_T / A_S \times V' / V \times 1 / C \times 9 / 2$

M_S: Amount (mg) of Silodosin RS taken, calculated on the anhydrous basis
C: Labeled amount (mg) of silodosin ($C_{25}H_{32}F_3N_3O_4$) in 1 tablet

Operating conditions—
Proceed as directed in the Assay under Silodosin.
System suitability—
System performance: When the procedure is run with 100 μL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of silodosin are not less than 3000 and not more than 1.6, respectively.
System repeatability: When the test is repeated 6 times with 100 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of silodosin is not more than 2.0%.

Assay Conduct this procedure using light-resistant vessels. To 20 tablets of Silodosin Orally Disintegrating Tablets add 3*V*/5 mL of a mixture of methanol and a solution of sodium chloride (1 in 200) (7:3), and sonicate until the tablet is completely disintegrated while occasional shaking. Add a mixture of methanol and a solution of sodium chloride (1 in 200) (7:3) to make exactly *V* mL so that each mL

contains about 40 μg of Silodosin. Pipet 5 mL of this solution, add a mixture of methanol and a solution of sodium chloride (1 in 200) (7:3) to make exactly 20 mL, and filter through a membrane filter with a pore size not exceeding 0.45 μm. Discard the first 3 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, weigh accurately about 20 mg of Silodosin RS (separately determine the water <2.48> in the same manner as Silodosin), and dissolve in a mixture of methanol and a solution of sodium chloride (1 in 200) (7:3) to make exactly 50 mL. Pipet 5 mL of this solution, add a mixture of methanol and a solution of sodium chloride (1 in 200) (7:3) to make exactly 50 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 following conditions, and determine the peak areas, A_T and A_S, of silodosin in each solution.

Amount (mg) of silodosin ($C_{25}H_{32}F_3N_3O_4$)
$= M_S \times A_T / A_S \times V / 2500$

M_S: Amount (mg) of Silodosin RS taken, calculated on the anhydrous basis

Operating conditions—

Proceed as directed in the operating conditions in the Assay under Silodosin.

System suitability—

System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of silodosin are not less than 3000 and not more than 1.6, respectively.

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 silodosin is not more than 1.0%.

Containers and storage Containers—Tight containers.

Storage—Light-resistant.

Others

Related substance A: Refer to it described in Silodosin.