Minocycline Hydrochloride Granules

ミノサイクリン塩酸塩顆粒

Minocycline Hydrochloride Granules contain not less than 90.0% and not more than 110.0% of the labeled potency of minocycline ($C_{23}H_{27}N_3O_7$: 457.48).

Method of preparation Prepare as directed under Granules, with Minocycline Hydrochloride.

Identification To a quantity of Minocycline Hydrochloride Granules, equivalent to 10 mg (potency) of Minocycline Hydrochloride, add 625 mL of a solution of hydrochloric acid in methanol (19 in 20,000), shake thoroughly, and filter. Determine the absorption spectrum of the filtrate as directed under Ultraviolet-visible Spectrophotometry *<2.24>*: it exhibits maxima between 221 nm and 225 nm, between 261 nm and 265 nm, and between 354 nm and 358 nm.

Purity Related substances — Conduct this procedure within 30 minutes after the preparation of the sample solution. To a quantity of Minocycline Hydrochloride Granules, equivalent to 50 mg (potency) of Minocycline Hydrochloride, add 60 mL of the mobile phase, shake vigorously, add the mobile phase to make 100 mL. Centrifuge this solution, and use the supernatant liquid as the sample solution. Perform the test with 20 μL of the sample solution as directed under Liquid Chromatography *<2.01>* according to the following conditions. Determine each peak area by the automatic integration method, and calculate their amounts by the area percentage method: the amount of the peak of epiminocycline, having the relative retention time of about 0.83 to minocycline, is not more than 4.0%.

Operating conditions—

Detector, column, column temperature, mobile phase and flow rate: Proceed as directed in the operating conditions in the Assay under Minocycline Hydrochloride.

Time span of measurement: About 2.5 times as long as the retention time of minocycline, beginning after the solvent peak.

System suitability—

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

Test for required detectability: To 2 mL of the standard solution obtained in the Assay add the mobile phase to make 100 mL, and use this solution as the solution for system suitability test. Pipet 5 mL of the solution for system suitability test, and add the mobile phase to make exactly 100 mL. Confirm that the peak area of minocycline obtained with 20 μL of this solution is equivalent to 3.5 to 6.5% of that with 20 μL of the solution for system suitability test.

System repeatability: When the test is repeated 6 times with 20 μL of the solution for system suitability test under the above operating conditions, the relative standard deviation of the peak area of minocycline is not more than 2.0%.

Water *<2.48>* Not more than 2.0% (4 g of powdered Minocycline Hydrochloride Granules, volumetric titration, back titration).

Uniformity of dosage units *<6.02>* Perform the test according to the following method: Minocycline Hydrochloride Granules in single-dose packages meet the requirement of the Content uniformity test.

To the total content of 1 package of Minocycline Hydrochloride Granules add water to disintegrate, shake thoroughly, add water to make exactly 100 mL, and filter through a membrane filter with a pore size not exceeding 0.45 μm. Discard the first 10 mL of the filtrate, pipet V mL of the subsequent filtrate, add water to make exactly V' mL so that each mL contains about 20 μg (potency) of minocycline ($C_{23}H_{27}N_3O_7$), and use this solution as the sample solution. Separately, weigh accurately an amount of Minocycline Hydrochloride RS, equivalent to about 20 mg (potency), dissolve in water to make exactly 100 mL. Pipet 5 mL of this solution, add water to make exactly 50 mL, and use this solution as the standard solution. Determine the absorbances, A_T and A_S, of the sample solution and standard solution at 348 nm as directed under Ultraviolet-visible Spectrophotometry *<2.24>*.

$$\text{Amount [mg (potency)] of minocycline } (C_{23}H_{27}N_3O_7) = M_S \times A_T / A_S \times V' / V \times 1/10$$

M_S: Amount [mg (potency)] of Minocycline Hydrochloride RS taken

Dissolution *<6.10>* When the test is performed at 50 revolutions per minute according to the Paddle method, using 900 mL of water as the dissolution medium, the dissolution rates in 15 minutes of Minocycline Hydrochloride Granules is not less than 85%.

Start the test with an accurately weighed amount of Minocycline Hydrochloride Granules, equivalent to about 20 mg (potency) of Minocycline Hydrochloride, withdraw not less than 20 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 not less than 10 mL of the first filtrate, and use the subsequent filtrate as the sample solution. Separately, weigh accurately an amount of Minocycline Hydrochloride RS,

equivalent to about 22 mg (potency), and dissolve in water to make exactly 100 mL. Pipet 5 mL of this solution, add water to make exactly 50 mL, and use this solution as the standard solution. Determine the absorbances, A_T and A_S, of the sample solution and standard solution at 348 nm as directed under Ultraviolet-visible Spectrophotometry *<2.24>*.

Dissolution rate (%) with respect to the labeled amount of minocycline ($C_{23}H_{27}N_3O_7$)

$$= M_S / M_T \times A_T / A_S \times 1 / C \times 90$$

M_S: Amount [mg (potency)] of Minocycline Hydrochloride RS taken

M_T: Amount (g) of Minocycline Hydrochloride Granules taken

C: Labeled amount [mg (potency)] of minocycline ($C_{23}H_{27}N_3O_7$) in 1 g

Assay Weigh accurately an amount of powdered Minocycline Hydrochloride Granules, equivalent to about 50 mg (potency) of Minocycline Hydrochloride, add the mobile phase, shake vigorously, and add the mobile phase to make exactly 100 mL. Centrifuge this solution, and use the supernatant liquid as the sample solution. Separately, weigh accurately an amount of Minocycline Hydrochloride RS, equivalent to about 25 mg (potency), dissolve in the mobile phase to make exactly 50 mL, and use this solution as the standard solution. Then, proceed as directed in the Assay under Minocycline Hydrochloride.

Amount [mg (potency)] of minocycline ($C_{23}H_{27}N_3O_7$)

$$= M_S \times A_T / A_S \times 2$$

M_S: Amount [mg (potency)] of Minocycline Hydrochloride RS taken

Containers and storage Containers—Tight containers.
Storage—Light-resistant.