Gefitinib Tablets

ゲフィチニブ錠

Gefitinib Tablets contain not less than 95.0% and not more than 105.0% of the labeled amount of gefitinib ($C_{22}H_{24}ClFN_4O_3$: 446.90).

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

Identification To a quantity of powdered Gefitinib Tablets, equivalent to 0.25 g of gefitinib ($C_{22}H_{24}ClFN_4O_3$), add 175 mL of a mixture of water, acetonitrile and trifluoroacetic acid (59:40:1), shake, add a mixture of water, acetonitrile and trifluoroacetic acid (59:40:1) to make 500 mL. To 2 mL of this solution add a mixture of water, acetonitrile and trifluoroacetic acid (59:40:1) to make 100 mL, and filter through a membrane filter with a pore size not exceeding 0.45 μm. Determine the absorption spectrum of the filtrate as directed under Ultraviolet-visible Spectrophotometry *<2.24>*: it exhibits maxima between 252 nm and 256 nm, and between 342 nm and 346 nm.

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

To 1 tablet of Gefitinib Tablets add 175 mL of a mixture of water, acetonitrile and trifluoroacetic acid (59:40:1), sonicate until the tablets are completely disintegrated, shake, then add a mixture of water, acetonitrile and trifluoroacetic acid (59:40:1) to make exactly 500 mL. Allow to stand for more than 30 minutes, pipet 2 mL of the supernatant liquid, and add a mixture of water, acetonitrile and trifluoroacetic acid (59:40:1) to make exactly V mL so that each mL contains about 10 μg of gefitinib ($C_{22}H_{24}ClFN_4O_3$). Filter this solution through a membrane filter with a pore size not exceeding 0.45 mm. Discard not less than 3 mL of the first filtrate, and use the subsequent solution as the sample solution. Separately, weigh accurately about 40 mg of Gefitinib RS (separately determine the water *<2.48>* in the same manner as Gefitinib), add 150 mL of a mixture of water, acetonitrile and trifluoroacetic acid (59:40:1), sonicate to dissolve, then add a mixture of water, acetonitrile and trifluoroacetic acid (59:40:1) to make exactly 200 mL. Pipet 5 mL of this solution, add a mixture of water, acetonitrile and trifluoroacetic acid (59:40:1) to make exactly 100 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 344 nm as directed under Ultraviolet-visible Spectrophotometry *<2.24>*.

Amount (mg) of gefitinib ($C_{22}H_{24}ClFN_4O_3$)
$= M_S \times A_T / A_S \times V / 16$

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

Dissolution *<6.10>* When the test is performed at 50 revolutions per minute according to the Paddle method, using 1000 mL of a solution of polysorbate 80 (1 in 20) as the dissolution medium, the dissolution rate in 45 minutes of Gefitinib Tablets is not less than 75%.

Start the test with 1 tablet of Gefitinib Tablets, withdraw not less than 10 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 2 mL of the first filtrate, pipet V mL of the subsequent filtrate, add water to make exactly V' mL so that each mL contains about 25 μg of gefitinib ($C_{22}H_{24}ClFN_4O_3$), and use this solution as the sample solution. Separately, weigh accurately about 25 mg of Gefitinib RS (separately determine the water *<2.48>* in the same manner as Gefitinib), and add 70 mL of the dissolution medium, sonicate to dissolve, then add the dissolution medium to make exactly 100 mL. Pipet 10 mL of this solution, add the dissolution medium to make exactly 100 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 334 nm as directed under Ultraviolet-visible Spectrophotometry *<2.24>*.

Dissolution rate (%) with respect to the labeled amount of gefitinib ($C_{22}H_{24}ClFN_4O_3$)
$= M_S \times A_T / A_S \times V' / V \times 1 / C \times 100$

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

C: Labeled amount (mg) of gefitinib ($C_{22}H_{24}ClFN_4O_3$) in 1 tablet

Assay Weigh accurately the mass of not less than 10 tablets of Gefitinib Tablets, and powder. Weigh accurately a portion of the powder, equivalent to about 35 mg of gefitinib ($C_{22}H_{24}ClFN_4O_3$), add 85 mL of a mixture of a solution of trifluoroacetic acid (1 in 500) and acetonitrile (3:2), sonicate, and add a mixture of a solution of trifluoroacetic acid (1 in 500) and acetonitrile (3:2) to make exactly 100mL. Allow to stand for more than 30 minutes, filter through a membrane filter with a pore size not exceeding 0.45 μm. Discard not less than 3 mL of the first filtrate, and use the subsequent filtrate as the sample solution. Separately, weigh accurately about 35 mg of Gefitinib RS (separately determine the water *<2.48>* in the same manner as Gefitinib), and add 85 mL of a mixture of a solution of trifluoroacetic acid (1 in 500) and acetonitrile (3:2), sonicate to dissolve, then add a mixture of a solution of trifluoroacetic acid (1 in 500) and acetonitrile (3:2) to make exactly 100 mL, and use this solution as the standard solution. Perform the test with 5 μL each of the sample solution and standard solution as directed in the Assay under Gefitinib.

Amount (mg) of gefitinib ($C_{22}H_{24}ClFN_4O_3$)
$= M_S \times A_T / A_S$

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

Containers and storage Containers－Tight containers.