## **Gefitinib Tablets** 1

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4 Gefitinib Tablets contain not less than 95.0% and not more than 105.0% of the labeled amount of gefitinib 5 (C<sub>22</sub>H<sub>24</sub>ClFN<sub>4</sub>O<sub>3</sub>: 446.90). 6

7 Method of preparation Prepare as directed under Tablets, 8 with Gefitinib.

9 Identification To a quantity of powdered Gefitinib Tablets, 10 equivalent to 0.25 g of gefitinib (C<sub>22</sub>H<sub>24</sub>ClFN<sub>4</sub>O<sub>3</sub>), add 175 mL of a mixture of water, acetonitrile and trifluoroacetic acid 11 12 (59:40:1), shake, add a mixture of water, acetonitrile and tri-13 fluoroacetic acid (59:40:1) to make 500 mL. To 2 mL of this 14 solution add a mixture of water, acetonitrile and trifluoroace-15 tic acid (59:40:1) to make 100 mL, and filter through a mem-16 brane filter with a pore size not exceeding 0.45  $\mu$ m. Determine the absorption spectrum of the filtrate as directed under 17 18 Ultraviolet-visible Spectrophotometry <2.24>: it exhibits 19 maxima between 252 nm and 256 nm, and between 342 nm 20 and 346 nm.

Uniformity of dosage units <6.02> Perform the Mass var-21 22 iation test, or the Content uniformity test according to the fol-23 lowing method: it meets the requirement.

To 1 tablet of Gefitinib Tablets add 175 mL of a mixture 24 25 of water, acetonitrile and trifluoroacetic acid (59:40:1), soni-26 cate until the tablets are completely disintegrated, shake, then add a mixture of water, acetonitrile and trifluoroacetic acid 27 28 (59:40:1) to make exactly 500 mL. Allow to stand for more 29 than 30 minutes, pipet 2 mL of the supernatant liquid, and 30 add a mixture of water, acetonitrile and trifluoroacetic acid 31 (59:40:1) to make exactly V mL so that each mL contains 32 about 10  $\mu$ g of gefitinib (C<sub>22</sub>H<sub>24</sub>ClFN<sub>4</sub>O<sub>3</sub>). Filter this solution 33 through a membrane filter with a pore size not exceeding 0.45 34 mm. Discard not less than 3 mL of the first filtrate, and use 35 the subsequent solution as the sample solution. Separately, weigh accurately about 40 mg of Gefitinib RS (separately de-36 37 termine the water  $\langle 2.48 \rangle$  in the same manner as Gefitinib), 38 add 150 mL of a mixture of water, acetonitrile and trifluoro-39 acetic acid (59:40:1), sonicate to dissolve, then add a mixture 40 of water, acetonitrile and trifluoroacetic acid (59:40:1) to 41 make exactly 200 mL. Pipet 5 mL of this solution, add a mix-42 ture of water, acetonitrile and trifluoroacetic acid (59:40:1) to make exactly 100 mL, and use this solution as the standard 43 44 solution. Determine the absorbances,  $A_{\rm T}$  and  $A_{\rm S}$ , of the sam-45 ple solution and standard solution at 344 nm as directed under Ultraviolet-visible Spectrophotometry <2.24>. 46

47 Amount (mg) of gefitinib (
$$C_{22}H_{24}ClFN_4O_3$$
)  
48 =  $M_8 \times A_T / A_8 \times V / 16$ 

49  $M_{\rm S}$ : Amount (mg) of Gefitinib RS taken, calculated on the 50 anhydrous basis

51 **Dissolution** <6.10> When the test is performed at 50 revo-52 lutions per minute according to the Paddle method, using 53 1000 mL of a solution of polysorbate 80 (1 in 20) as the dis-54 solution medium, the dissolution rate in 45 minutes of Ge-55 fitinib Tablets is not less than 75%.

56 Start the test with 1 tablet of Gefitinib Tablets, withdraw 57 not less than 10 mL of the medium at the specified minute 58 after starting the test, and filter through a membrane filter 59 with a pore size not exceeding 0.45  $\mu$ m. Discard not less than 60 2 mL of the first filtrate, pipet V mL of the subsequent filtrate, 61 add water to make exactly V' mL so that each mL contains 62 about 25  $\mu$ g of gefitinib (C<sub>22</sub>H<sub>24</sub>ClFN<sub>4</sub>O<sub>3</sub>), and use this solution as the sample solution. Separately, weigh accurately 63 64 about 25 mg of Gefitinib RS (separately determine the water 65 <2.48> in the same manner as Gefitinib), and add 70 mL of 66 the dissolution medium, sonicate to dissolve, then add the 67 dissolution medium to make exactly 100 mL. Pipet 10 mL of 68 this solution, add the dissolution medium to make exactly 69 100 mL, and use this solution as the standard solution. Deter-70 mine the absorbances, AT and As, of the sample solution and standard solution at 334 nm as directed under Ultraviolet-vis-71 72 ible Spectrophotometry <2.24>.

73 Dissolution rate (%) with respect to the labeled amount of 74 gefitinib (C<sub>22</sub>H<sub>24</sub>ClFN<sub>4</sub>O<sub>3</sub>)

75  $=M_{\rm S} \times A_{\rm T}/A_{\rm S} \times V'/V \times 1/C \times 100$ 

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 $M_{\rm S}$ : Amount (mg) of Gefitinib RS taken, calculated on the anhydrous basis

78 C: Labeled amount (mg) of gefitinib (C22H24ClFN4O3) in 1 tablet

80 Assay Weigh accurately the mass of not less than 10 tablets of Gefitinib Tablets, and powder. Weigh accurately a portion 81 82 of the powder, equivalent to about 35 mg of gefitinib 83 (C22H24ClFN4O3), add 85 mL of a mixture of a solution of 84 trifluoroacetic acid (1 in 500) and acetonitrile (3:2), sonicate, 85 and add a mixture of a solution of trifluoroacetic acid (1 in 86 500) and acetonitrile (3:2) to make exactly 100mL. Allow to 87 stand for more than 30 minutes, filter through a membrane 88 filter with a pore size not exceeding 0.45  $\mu$ m. Discard not less 89 than 3 mL of the first filtrate, and use the subsequent filtrate 90 as the sample solution. Separately, weigh accurately about 35 91 mg of Gefitinib RS (separately determine the water <2.48> in 92 the same manner as Gefitinib), and add 85 mL of a mixture 93 of a solution of trifluoroacetic acid (1 in 500) and acetonitrile 94 (3:2), sonicate to dissolve, then add a mixture of a solution of 95 trifluoroacetic acid (1 in 500) and acetonitrile (3:2) to make 96 exactly 100 mL, and use this solution as the standard solution. 97 Perform the test with 5  $\mu$ L each of the sample solution and 98 standard solution as directed in the Assay under Gefitinib.

- 99 Amount (mg) of gefitinib ( $C_{22}H_{24}ClFN_4O_3$ ) 100  $=M_S \times A_T \swarrow A_S$
- 101 *M*<sub>S</sub>: Amount (mg) of Gefitinib RS taken, calculated on the102 anhydrous basis
- 103 Containers and storage Containers Tight containers.

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