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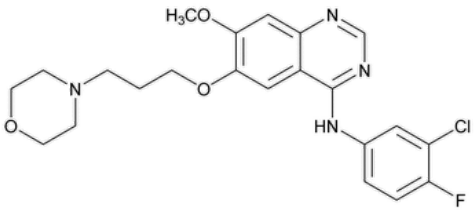
Add the following:

▲Gefitinib



$C_{22}H_{24}ClFN_4O_3$ 446.91

4-Quinazolinamine, *N*-(3-chloro-4-fluorophenyl)-7-methoxy-6-[3-(4-morpholinyl)propoxy]-;
N-(3-Chloro-4-fluorophenyl)-7-methoxy-6-[3-(4-morpholinyl)propoxy]-4-quinazolinamine;
(3-Chloro-4-fluorophenyl)[7-methoxy-6-[3-(morpholin-4-yl)propoxy]quinazolin-4-yl]amine CAS RN®: 184475-35-2; UNII: S65743JHBS.

DEFINITION

Gefitinib contains NLT 98.0% and NMT 102.0% of gefitinib ($C_{22}H_{24}ClFN_4O_3$), calculated on the anhydrous basis.

IDENTIFICATION

• **A.** **Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 197D

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Solution A: 9.7 g/L of ammonium acetate in water

Solution B: 0.2% trifluoroacetic acid in water

Mobile phase: Acetonitrile and *Solution A* (38:62)

Diluent: Acetonitrile and *Solution B* (40:60)

System suitability solution: 0.35 mg/mL of USP Gefitinib RS and 0.25 mg/mL of USP Dichloroaniline RS in *Diluent*. Sonicate to dissolve.

Standard solution: 0.35 mg/mL of USP Gefitinib RS in *Diluent*. Sonicate to dissolve.

Sample solution: 0.35 mg/mL of Gefitinib in *Diluent*. Sonicate to dissolve.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 247 nm

Column: 3.0-mm × 10-cm; 3-µm packing L1

Column temperature: 60°

Flow rate: 0.9 mL/min

Injection volume: 5 µL

Run time: NLT 5 times the retention time of gefitinib

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 5.0 between dichloroaniline and gefitinib, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of gefitinib ($C_{22}H_{24}ClFN_4O_3$) in the portion of Gefitinib taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of gefitinib from the *Sample solution*

r_S = peak response of gefitinib from the *Standard solution*

C_S = concentration of USP Gefitinib RS in the *Standard solution* (mg/mL)

C_U = concentration of Gefitinib in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.2%
- **Organic Impurities**

Solution A, Solution B, Mobile phase, Diluent, System suitability solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution A: 0.7 µg/mL of USP Gefitinib RS in *Diluent*

Standard solution B: 0.7 µg/mL each of USP Gefitinib Related Compound A RS and USP Gefitinib Related Compound B RS in *Diluent*

Sensitivity solution: 0.18 µg/mL of USP Gefitinib RS from *Standard solution A* in *Diluent*

System suitability

Samples: *System suitability solution*, *Standard solution A*, *Standard solution B*, and *Sensitivity solution*

[Note—The relative retention times in *Table 1* are provided as information that could aid in peak assignment.]

Table 1

Name	Relative Retention Time
Gefitinib related compound A	0.13
Dichloroaniline	0.7
Gefitinib	1.0
Gefitinib related compound B	1.26

Suitability requirements

Resolution: NLT 5.0 between dichloroaniline and gefitinib, *System suitability solution*

Relative standard deviation: NMT 5.0% for gefitinib, *Standard solution A*; NMT 5.0% for gefitinib related compound A and gefitinib related compound B, *Standard solution B*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution A*, *Standard solution B*, and *Sample solution*

Calculate the percentage of gefitinib related compound A and gefitinib related compound B in the portion of Gefitinib taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of gefitinib related compound A or gefitinib related compound B from the *Sample solution*

r_S = peak response of gefitinib related compound A or gefitinib related compound B from *Standard solution B*

C_S = concentration of USP Gefitinib Related Compound A RS or USP Gefitinib Related Compound B RS in *Standard solution B* (mg/mL)

C_U = concentration of Gefitinib in the *Sample solution* (mg/mL)

Calculate the percentage of any unspecified impurity in the portion of Gefitinib taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of any unspecified impurity from the *Sample solution*

r_S = peak response of gefitinib from *Standard solution A*

C_S = concentration of USP Gefitinib RS in *Standard solution A* (mg/mL)

C_U = concentration of Gefitinib in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Acceptance Criteria, NMT (%)
Gefitinib related compound A	0.1
Gefitinib related compound B	0.2
Any unspecified impurity	0.10
Total impurities	0.4

SPECIFIC TESTS

• **Water Determination** ⟨921⟩, *Method I, Method Ia*: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers and protect from light. Store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Dichloroaniline RS

3,4-Dichloroaniline.

$C_6H_5Cl_2N$ 162.01

USP Gefitinib RS

USP Gefitinib Related Compound A RS

7-Methoxy-6-(3-morpholinopropoxy)quinazolin-4(3*H*)-one.

$C_{16}H_{21}N_3O_4$ 319.36

USP Gefitinib Related Compound B RS

N-(4-Chloro-3-fluorophenyl)-7-methoxy-6-(3-morpholinopropoxy)quinazolin-4-amine.

$C_{22}H_{24}ClFN_4O_3$ 446.91▲ (USP 1-Aug-2024)

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
GEFITINIB	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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