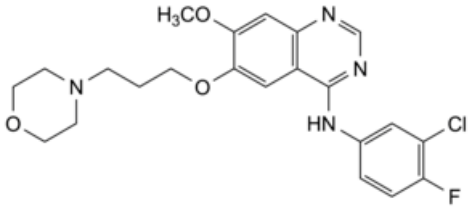
Edition: BP 2025 (Ph. Eur. 11.6 update)

Gefitinib

General Notices

(Ph. Eur. monograph 2866)



$C_{22}H_{24}ClFN_4O_3$ 446.9 *184475-35-2*

Action and use

Cytotoxic.

Ph Eur

DEFINITION

N-(3-Chloro-4-fluorophenyl)-7-methoxy-6-[3-(morpholin-4-yl)propoxy]quinazolin-4-amine.

Content

98.0 per cent to 102.0 per cent (anhydrous substance).

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Practically insoluble in water, slightly soluble in anhydrous ethanol, practically insoluble in heptane.

IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

Comparison *gefitinib CRS*.

TESTS

Related substances

Liquid chromatography (2.2.29).

Solvent mixture acetonitrile R, 0.2 per cent *V/V* solution of trifluoroacetic acid R (40:60 *V/V*).

Test solution Dissolve 35.0 mg of the substance to be examined in 85 mL of the solvent mixture, with the aid of ultrasound, and dilute to 100.0 mL with the solvent mixture.

Reference solution (a) Dissolve 35.0 mg of gefitinib CRS in 85 mL of the solvent mixture, with the aid of ultrasound, and dilute to 100.0 mL with the solvent mixture.

Reference solution (b) Dilute 1.0 mL of the test solution to 100.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 10.0 mL with the solvent mixture.

Reference solution (c) Dissolve the contents of a vial of gefitinib for system suitability CRS (containing impurity B) in 1.0 mL of the solvent mixture with the aid of ultrasound.

Column:

— *size*: *l* = 0.10 m, *Ø* = 3 mm;

— *stationary phase*: base-deactivated end-capped octadecylsilyl silica gel for chromatography R (3 µm);

— *temperature*: 60 °C.

Mobile phase acetonitrile R, 9.68 g/L solution of ammonium acetate R (38:62 *V/V*).

Flow rate 0.9 mL/min.

Detection Spectrophotometer at 247 nm.

Injection 5 µL of the test solution and reference solutions (b) and (c).

Run time 5 times the retention time of gefitinib.

Identification of impurities Use the chromatogram supplied with gefitinib for system suitability CRS and the chromatogram obtained with reference solution (c) to identify the peak due to impurity B.

Relative retention With reference to gefitinib (retention time = about 5.5 min): impurity B = about 1.3.

System suitability Reference solution (c):

— resolution: minimum 3.0 between the peaks due to gefitinib and impurity B.

Calculation of percentage contents:

— for each impurity, use the concentration of gefitinib in reference solution (b).

Limits:

— *impurity B*: maximum 0.2 per cent;

— *unspecified impurities*: for each impurity, maximum 0.10 per cent;

— *total*: maximum 0.4 per cent;

— *reporting threshold*: 0.05 per cent.

Water (2.5.32)

Maximum 0.5 per cent, determined on 0.100 g by direct sample introduction.

Sulfated ash (2.4.14)

Maximum 0.2 per cent, determined on 1.0 g in a platinum crucible.

ASSAY

Liquid chromatography (2.2.29) as described in the test for related substances with the following modification.

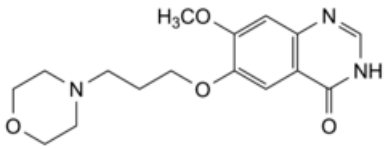
Injection Test solution and reference solution (a).

Calculate the percentage content of $C_{22}H_{24}ClFN_4O_3$ taking into account the assigned content of *gefitinib CRS*.

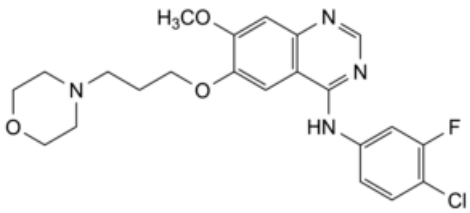
IMPURITIES

Specified impurities *B*.

Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical use (2034). It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use) *A*.



A. 7-methoxy-6-[3-(morpholin-4-yl)propoxy]quinazolin-4(3*H*)-one,



B. *N*-(4-chloro-3-fluorophenyl)-7-methoxy-6-[3-(morpholin-4-yl)propoxy]quinazolin-4-amine.