Gefitinib

RIP2 Tyrosine Kinase Inhibitor

Catalog # tlrl-gef

For research use only

Version # 15K03-MM

PRODUCT INFORMATION

Content:

• 10 mg Gefitinib

Storage and stability:

- Gefitinib is provided as a translucent film and shipped at room temperature. Store at -20 °C. Solid product is stable for 1 year at -20 °C when properly stored.
- Upon resuspension, Gefitinib should be aliquoted and stored at -20 °C. Avoid repeated freeze-thaw cycles. Resuspended product is stable for 3 months at -20 °C when properly stored.

Quality control:

- Purity: ≥98% (UHPLC)
- The absence of bacterial contamination (e.g. lipoproteins and endotoxins) has been confirmed using HEK-Blue™ TLR2 and HEK-Blue™ TLR4 cells.

DESCRIPTION

Gefitinib (also known as Iressa) is a selective inhibitor of epidermal growth factor (EGFR), a growth factor that plays a pivotal role in the control of cell growth, apoptosis, and angiogenesis. EGFR activation stimulates many complex intracellular signaling pathways, primarily the MEK/ERK and PI3K/AKT pathways[1, 2]. Following EGFR activation, Src tyrosine kinases and STAT downstream signaling have also been well documented[2]. Recent studies demonstrated that Gefitinib can inhibit NOD2-induced cytokine release and NF-κB activation by inhibiting RIP2 (receptor-interacting protein 2) tyrosine phosphylation which is critical for activation of NOD2 downsream signaling pathways[3].

1. Okamoto K. *et al*., 2010. Role of survivin in EGFR inhibitor-induced apoptosis in non-small cell lung cancers positive for EGFR mutations. Cancer Res. 70(24):10402-10. **2. Wheeler D. *et al*., 2010.** Understanding resistance to EGFR inhibitors—impact on future treatment strategies. Nat Rev Clin Oncol. 7(9):493-507. **3. Tigno-Aranjuez J. *et al*., 2010.** Inhibition of RIP2's tyrosine kinase activity limits NOD2-driven cytokine responses. Genes Dev. 24(23):2666-77. **4. Pao W. et al., 2005.** Acquired resistance of lung adenocarcinomas to Gefitinib or Erlotinib is associated with a second mutation in the EGFR kinase domain. PLoS Med. 2(3):e73. **5. Helfrich B. et al., 2006.** Antitumor activity of the epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor Gefitinib (ZD1839, Iressa) in non small cell lung cancer cell lines correlates with gene copy number and EGFR mutations but not EGFR protein levels. Clin Cancer Res. 12(23):7117-25.

CHEMICAL PROPERTIES

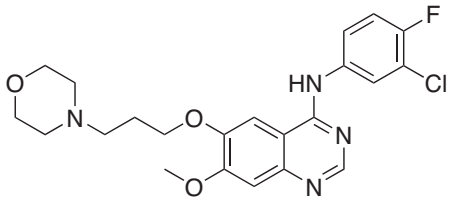
CAS number: 184475-35-2

Formula: $C_{22}H_{24}ClFN_4O_3$

Molecular weight: 446.9

Solubility: 100 mM in DMSO

Structure:



METHODS

Preparation of Gefitinib stock solution (50 mM)

1. Add 450 µl DMSO to 10 mg Gefitinib.
2. Vortex until complete solubilization.
3. Prepare aliquots and store stock solution at -20 °C.

Working concentration: 0.1 - 20 µM for cell culture assays

PROTOCOLS

For reference only; as described in the indicated publications.

Cell Culture Assay[4]

Cells: Non small cell lung cancer (NSCLC) cell lines
Working concentration: 0.1 - 10 µM
Incubation time: 48 h
Method: Cell viability assay

Cell Culture Assay[5]

Cells: NSCLC cell lines
Working concentration: 20 µM
Incubation time: 6 days
Method: MTT cell proliferation assay

Animal Study[5]

Animal model: Athymoc nude mice
Dose: 50-60 mg/mouse daily for 3 - 4 weeks
Administration: Intraperitoneal injection (i.p.)

Other signal transduction inhibitors are available, for more information visit www.invivogen.com/inhibitors

TECHNICAL SUPPORT
InvivoGen USA (Toll-Free): 888-457-5873
InvivoGen USA (International): +1 (858) 457-5873
InvivoGen Europe: +33 (0) 5-62-71-69-39
InvivoGen Hong Kong: +852 3-622-34-80
E-mail: info@invivogen.com

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