# Gefitinib dihydrochloride

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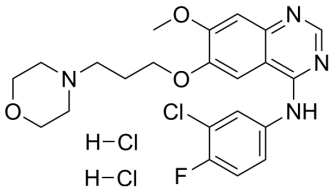
| **Cat. No.:** | HY-50895B |
| **CAS No.:** | 184475-56-7 |
| **Molecular Formula:** | $C_{22}H_{26}Cl_3FN_4O_3$ |
| **Molecular Weight:** | 519.82 |
| **Target:** | EGFR; Autophagy; Apoptosis |
| **Pathway:** | JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Autophagy; Apoptosis |
| **Storage:** | Please store the product under the recommended conditions in the Certificate of Analysis. |




## BIOLOGICAL ACTIVITY

**Description**

Gefitinib (ZD 1839) dihydrochloride is a potent, selective and orally active EGFR tyrosine kinase inhibitor with an $IC_{50}$ of 33 nM. Gefitinib dihydrochloride selectively inhibits EGF-stimulated tumor cell growth ($IC_{50}$ of 54 nM) and blocks EGF-stimulated EGFR autophosphorylation in tumor cells. Gefitinib dihydrochloride also induces autophagy and cell apoptosis, which can be used for cancer related research, such as Lung cancer and breast cancer [1][2][5].

**$IC_{50}$ & Target**

IC50: 37 nM (Tyr1173 site, in NR6wtEGFR cells), 37 nM (Tyr992 site, in NR6wtEGFR cells)[1].

**In Vitro**

Gefitinib dihydrochloride (0.01–0.1 μM, 72 h) results in increased phosphotyrosine load of the receptor, increased signalling to ERK and stimulation of proliferation and anchorage-independent growth[2].
Gefitinib dihydrochloride (1-2 μM, 72 h) significantly decreases EGFRvIII phosphotyrosine load, EGFRvIII-mediated proliferation and anchorage-independent growth[2].
Gefitinib dihydrochloride (0.62 μM, 24-72 h) inhibits IL-13-induced M2-like polarization of RAW 264.7 cells through the STAT6-dependent signaling pathway[3].
Gefitinib dihydrochloride (0.62 μM, 72 h) inhibits M2-like macrophage-promoted invasion and migration[3].
Gefitinib dihydrochloride (0-10 μM, 72 h) induces apoptosis (induction of BIM protein) in NSCLC Cell Lines (H3255 and HCC827 cells)[4].
Gefitinib dihydrochloride (100 nM, 24 h) suppresses macropinocytosis and increases the cellular uptake of extracellular vesicles( EVs) in HCC827 and A549 cells[6].
Gefitinib dihydrochloride (1.5-60 μM, 48 h) increases inhibition of proliferation in $H358^R$ and $A549^R$ cells (Cisplatin-resistant wtEGFR NSCLC cell lines)[7].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[2]

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| Cell Line: | NR6wtEGFR, NR6W and NR6M |
| Concentration: | 1, 10, 100 μM |
| Incubation Time: | 5 h |
| Result: | Inhibited EGFR tyrosine phosphorylations. |

Cell Migration Assay [3]

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| Cell Line: | LLCs cell |

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| Concentration: | 0.62 μM |
| Incubation Time: | 72 h |
| Result: | Abrogated M2-like macrophage promoted invasion and migration of LLCs. |

**In Vivo**

Gefitinib dihydrochloride (Oral administration, 75 mg/kg/d, 21 days) inhibits the M2-like polarization of macrophages in LLC mice metastasis model[3].
Gefitinib dihydrochloride (Oral administration, 75 mg/kg for the initial week, daily for 5 consecutive days per week) eliminates phosphorylation of HER2 and HER3 and signaling through MAPK and Akt in lobular hyperplasias and carcinomas, increases MAPK activity and cytokine production in splenocytes and lymph nodes[5].
Gefitinib dihydrochloride (Oral gavage, 150 mg/kg, daily) enhances the anti-tumor effect of Cisplatin in $H358^R$ xenograft[7].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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| Animal Model: | LLC mice metastasis model[3] |
| Dosage: | 75 mg/kg/d, for 21 days. |
| Administration: | Oral administration |
| Result: | Reduced the number of lung metastasis nodules, down-regulated the expression of M2 marker genes and the percentages $CD206^+$ and $CD68^+$ macrophages in tumor tissues. |

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| Animal Model: | BALB-NeuT transgenic mouse model[5] |
| Dosage: | 75 mg/kg for the initial week, and increased by 15 mg/kg every other week, daily for 5 consecutive days per week, followed by 2 days without treatment and repeated for 8–9 weeks. |
| Administration: | Oral administration |
| Result: | Reduced tumor multiplicity from 9.6 to 0.58 (83%), and reduced the number and size of lobules and lobular nodules in treated mice. |

## CUSTOMER VALIDATION

- Cancer Cell. 2018 Jun 11;33(6):1061-1077.e6.
- Cell Res. 2021 Jun;31(6):631-648.
- Cell Res. 2020 Oct;30(10):833-853.
- Signal Transduct Target Ther. 2019 Dec 13;4:60.
- Nat Biomed Eng. 2018 Aug;2(8):578-588.

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## REFERENCES

[1]. Wakeling AE, et al. ZD1839: an orally active inhibitor of epidermal growth factor signaling with potential for cancer therapy. Cancer Res. 2002 Oct 15;62(20):5749-54.

[2]. Pedersen MW, et al. Differential response to gefitinib of cells expressing normal EGFR and the mutant EGFRvIII. Br J Cancer. 2005 Oct 17;93(8):915-23.

[3]. Muhammad Tariq, et al. Gefitinib inhibits M2-like polarization of tumor-associated macrophages in Lewis lung cancer by targeting the STAT6 signaling pathway. Acta Pharmacol Sin. 2017 Nov;38(11):1501-1511.

[4]. Mark S Cragg, et al. Gefitinib-induced killing of NSCLC cell lines expressing mutant EGFR requires BIM and can be enhanced by BH3 mimetics. PLoS Med. 2007 Oct;4(10):1681-89; discussion 1690.

[5]. Marie P Piechocki, et al. Gefitinib prevents cancer progression in mice expressing the activated rat HER2/neu. Int J Cancer. 2008 Apr 15;122(8):1722-9.

[6]. Tomoya Takenaka, et al. Effects of gefitinib treatment on cellular uptake of extracellular vesicles in EGFR-mutant non-small cell lung cancer cells. Int J Pharm. 2019 Dec 15;572:118762.

[7]. Amin Li, et al. Gefitinib sensitization of cisplatin-resistant wild-type EGFR non-small cell lung cancer cells. J Cancer Res Clin Oncol. 2020 Jul;146(7):1737-1749.



Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA