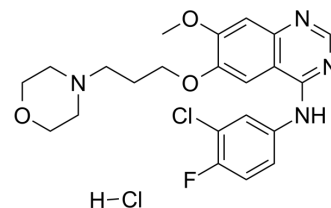


## Gefitinib hydrochloride

<b>Cat. No.:</b>	HY-50895A
<b>CAS No.:</b>	184475-55-6
<b>Molecular Formula:</b>	C <sub>22</sub> H <sub>25</sub> Cl <sub>2</sub> FN <sub>4</sub> O <sub>3</sub>
<b>Molecular Weight:</b>	483.36
<b>Target:</b>	EGFR
<b>Pathway:</b>	JAK/STAT Signaling; Protein Tyrosine Kinase/RTK
<b>Storage:</b>	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



### SOLVENT & SOLUBILITY

#### In Vitro

H<sub>2</sub>O : 6.25 mg/mL (12.93 mM; Need ultrasonic)  
DMSO : 0.227 mg/mL (0.47 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Solvent Concentration	Mass	1 mg	5 mg	10 mg
		1 mM	2.0689 mL	10.3443 mL	20.6885 mL
	5 mM	0.4138 mL	2.0689 mL	4.1377 mL	
	10 mM	0.2069 mL	1.0344 mL	2.0689 mL	

Please refer to the solubility information to select the appropriate solvent.

### BIOLOGICAL ACTIVITY

#### Description

Gefitinib hydrochloride (ZD1839 hydrochloride) is a potent, selective and orally active EGFR tyrosine kinase inhibitor with an IC<sub>50</sub> of 33 nM. Gefitinib hydrochloride selectively inhibits EGF-stimulated tumor cell growth (IC<sub>50</sub> of 54 nM) and that blocks EGF-stimulated EGFR autophosphorylation in tumor cells. Gefitinib hydrochloride also induces autophagy. Gefitinib hydrochloride has antitumour activity<sup>[1][2]</sup>.

#### IC<sub>50</sub> & Target

EGFR

#### In Vitro

Gefitinib (0.01-0.1 mM) results in increased phosphotyrosine load of the receptor, increased signalling to ERK and stimulation of proliferation and anchorage-independent growth, presumably by inducing EGFRVIII dimerisation in long-term exposure of EGFRVIII-expressing cells. On the other hand, gefitinib (1-2 mM) significantly decreases EGFRVIII phosphotyrosine load, EGFRVIII-mediated proliferation and anchorage-independent growth<sup>[1]</sup>. Gefitinib (ZD1839) inhibits the monolayer growth of these EGF-driven untransformed cells with IC<sub>50</sub> of 20 nM<sup>[2]</sup>. Gefitinib leads to an inhibition of CALU-3 and GLC82 cell proliferation, with an IC<sub>50</sub> of 2 μM<sup>[3]</sup>.  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

#### In Vivo

Gefitinib (150 mg/kg, p.o.) in combination with Metformin induces a significant reduction in tumor growth in nude mice

bearing H1299 or CALU-3 GEF-R cells that are grown subcutaneously as tumor xenografts<sup>[3]</sup>. In irradiated rats, Gefitinib treatment augments lung inflammation, including inflammatory cell infiltration and pro-inflammatory cytokine expression, while Gefitinib treatment attenuates fibrotic lung remodeling due to the inhibition of lung fibroblast proliferation<sup>[4]</sup>.

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

## PROTOCOL

### Cell Assay<sup>[3]</sup>

Cancer cells are seeded in 96-well plates and are treated with different doses of Gefitinib (0.01-20  $\mu$ M), Metformin or both for 72 hours. Cell proliferation is measured with the MTT assay. The IC<sub>50</sub> values are determined by interpolation from the dose-response curves. Results represent the median of 3 separate experiments each conducted in quadruplicate. The results of the combined treatment are analyzed according to the method of Chou and Talalay by using the CalcuSyn software program<sup>[3]</sup>.

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

### Animal Administration<sup>[3][4]</sup>

#### Mice<sup>[3]</sup>

Four- to 6-week old female balb/c athymic (nu+/nu+) mice are acclimatized for 1 week before being injected with cancer cells and injected subcutaneously with 10<sup>7</sup> H1299 and CALU-3 GEF-R cells that has been resuspended in 200  $\mu$ L of Matrigel. When established tumors of approximately 75 mm<sup>3</sup> in diameter are detected, mice are left untreated or treated with oral administrations of metformin (200 mg/mL metformin diluted in drinking water and present throughout the experiment), gefitinib (150 mg/kg daily orally by gavage), or both for the indicated time periods. Each treatment group consists of 10 mice. Tumor volume is measured using the formula  $\pi/6 \times \text{larger diameter} \times (\text{smaller diameter})^2$ .

#### Rats<sup>[4]</sup>

The rats are randomly assigned to 1 of 4 experimental groups: 1) the unirradiated rats treated with oral administration of vehicle (0.1% Tween 80) once daily; 2) the unirradiated rats treated with oral administration of gefitinib (50 mg/kg/day) once daily; 3) the irradiated rats treated with oral administration of vehicle once daily; 4) the irradiated rats treated with oral administration of gefitinib once daily. Each experimental group comprised 5-6 rats and all treatments are delivered for 14 days.

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## 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.
- Nat Biomed Eng. 2018 Aug;2(8):578-588.
- Sci Transl Med. 1 Sep 2021.

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## REFERENCES

- [1]. 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.
- [2]. Moasser MM, et al. The tyrosine kinase inhibitor ZD1839 ("Iressa") inhibits HER2-driven signaling and suppresses the growth of HER2-overexpressing tumor cells. Cancer Res. 2001 Oct 1;61(19):7184-8.
- [3]. Morgillo F, et al. Synergistic effects of metformin treatment in combination with gefitinib, a selective EGFR tyrosine kinase inhibitor, in LKB1 wild-type NSCLC cell lines.

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Clin Cancer Res. 2013 Jul 1;19(13):3508-19.

[4]. Miyake K, et al. Epidermal growth factor receptor-tyrosine kinase inhibitor (gefitinib) augments pneumonitis, but attenuates lung fibrosis in response to radiation injury in rats. J Med Invest. 2012;59(1-2):174-85.

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

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**Caution: Product has not been fully validated for medical applications. For research use only.**

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