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产品名称：4-(3-氯-4-氟苯基氨基)-7-甲氧基-6-[3-(4-吗啉基)丙氧基]喹唑啉盐酸盐

产品别名：盐酸吉非替尼；Gefitinib hydrochloride；ZD-1839 hydrochloride

生物活性：

Description	Gefitinib hydrochloride is an inhibitor that specifically binds and inhibits the EGFR tyrosine kinase, with the IC50 value of 2-37 nM in NR6wtEGFR cells.
IC_{50} & 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[1]. Gefitinib (ZD1839) inhibits the monolayer growth of these EGF-driven untransformed cells with IC50 of 20 nM[2]. Gefitinib leads to an inhibition of CALU-3 and GLC82 cell proliferation, with an IC50 of 2 μM[3].
In Vivo	Gefitinib (150 mg/kg, p.o.) in conbination 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[3]. In irradiated rats, Gefitinib treatment augmentes 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[4].
Solvent&Solubility	***In Vitro:*** **H_2O : 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 / Mass / Concentration	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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

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. 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.

实验参考：

Cell Assay	Cancer cells are seeded in 96-well plates and are treated with different doses of Gefitinib (0.01-20 μM), Metformin or both for 72 hours. Cell proliferation is measured with the MTT assay. The IC50 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[3].
Animal Administration	Mice[3] 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 10^7 H1299 and CALU-3 GEF-R cells that has been resuspended in 200 μL of Matrigel. When established tumors of approximately 75 mm^3 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 π/6×larger diameter×(smaller diameter)^2. Rats[4] 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.
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. 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.