

Product Data Sheet

Product Name: Icotinib Hydrochloride

Cat. No.: GC16244

Chemical Properties

Cas. No. 1204313-51-8

Chemical Name N-(3-ethynylphenyl)-7,8,10,11,13,14-hexahydro-[1,4,7,10]tetraoxacyclododecino[2,3-g]quinazolin-4-amine hydrochloride

SMILES Cl[H].[H]C1=C2C(N=C([H])N=C2N([H])C3=C([H])C([H])=C([H])C(C#C[H])=C3[H])=C([H])C4=C1OC([H])([H])C([H])([H])OC([H])([H])C([H])([H])OC([H])([H])C([H])([H])O4

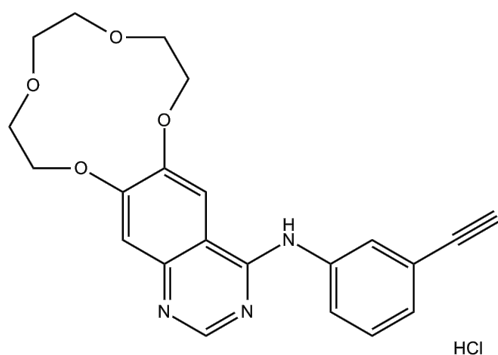
Formula $C_{22}H_{22}ClN_3O_4$ M.Wt 427.88

Solubility Soluble in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

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

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- Kinase experiment:** In the in vitro kinase assays, 2.4 ng/ μ L EGFR protein is mixed with 32 ng/ μ L Crk in 25 μ L kinase reaction buffer containing 1 μ M cold ATP and 1 μ Ci³²P- γ -ATP. The mix is incubated with Icotinib at 0, 0.5, 2.5, 12.5 or 62.5 nM on ice for 10 min followed by incubation at 30°C for 20 min. After quenching with SDS sample buffer at 100°C for 4 min, the protein mix is resolved by electrophoresis in a 10% SDS-PAGE gel. The dried gel is then exposed to detect radioactivity. Quantification is performed by software[1].
- Cell experiment:** Cells (1000/well) are seeded into 96-well plates in RPMI-1640 medium containing 10% FBS and grown in a 5% CO₂ incubator at 37°C. After 24 h, cells are treated with Icotinib at 0, 0.78, 1.56, 3.125, 6.25, 12.5 or 25 μ M for 96 h. Cell proliferation is calculated by subtracting the mean absorbance value on day 0 from the mean absorbance value on day 4[1].
- Animal experiment:** Mice: The effect of three doses of Icotinib (30, 60, and 120 mg/kg/dose p.o. qd) on antitumor activity and survival is determined in mice bearing A431, A549, H460 and HCT8 tumor xenografts. Taxol (30 mg/kg/dose i.p. once a week) is employed in these experiments as a positive control group[1].

References:

[1]. Tan F, et al. Icotinib (BPI-2009H), a novel EGFR tyrosine kinase inhibitor, displays potent efficacy in preclinical studies. Lung Cancer. 2012 May;76(2):177-82.

Background

Icotinib Hydrochloride is a potent and highly selective inhibitor of epidermal growth factor receptor tyrosine kinases (EGFR-TKI) with IC₅₀ value of 5 nM.

EGFR is an oncogenic driver which is expressed on the cell surface of normal cells and cancer cells [1], and patients with somatic mutations, particularly an exon 19 deletion or exon 21 L858R mutation, within the tyrosine kinase domain have activating mutations that lead to unchecked cell proliferation.

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[2] Overexpression of EGFR caused inappropriate activation of the anti-apoptotic Ras signaling pathway, found in many different types of cancer.[3]

Icotinib is a quinazoline derivative that binds reversibly to the ATP binding site of the EGFR protein, preventing completion of the signal transduction cascade.[4] Icotinib inhibited the intracellular phosphorylation of tyrosine kinase(TK) associated with the epidermal growth factor receptor (EGFR). [5]

Icotinib is indicated for the treatment for EGFR mutation-positive, advanced or metastatic non-small cell lung cancer (NSCLC) as a second-line or third-line treatment, for patients who have failed at least one prior treatment with platinum-based chemotherapy.[6]

References:

- 1.A Douglas Laird, and Julie M Cherrington. *Small molecule tyrosine kinase inhibitors: clinical development of anticancer agents*. 2003, 12(1): 51-64.
- 2.Raymond E, Faivre S, Armand JP: *Epidermal growth factor receptor tyrosine kinase as a target for anticancer therapy*. *Drugs*. 2000;60 Suppl 1:15-23.
- 3.Sordella, R. "Gefitinib-Sensitizing EGFR Mutations in Lung Cancer Activate Anti-Apoptotic Pathways". *Science*, 2004, 305 (5687): 1163-1167.
- 4.Bulgaru AM. et al. Erlotinib (Tarceva): a promising drug targeting epidermal growth factor receptor tyrosine kinase. *Expert Rev Anticancer Ther*. 2003 Jun;3(3):269-79.
- 5.Dudek AZ. et al. Skin rash and bronchoalveolar histology correlates with clinical benefit in patients treated with gefitinib as a therapy for previously treated advanced or metastatic non-small cell lung cancer. *Lung Cancer*. 2006, 51(1):89-96.
- 6.C Delbaldo, S Faivre, E Raymond. Les inhibiteurs des récepteurs de l'Epidermal Growth Factor (EGF) Epidermal growth factor inhibitors. *La Revue de Médecine Interne*. 2003,24(6): 372–383.

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