Ceritinib dihydrochloride

Cat. No.: HY-15656A

CAS No.: 1380575-43-8

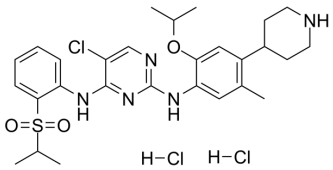
Molecular Formula: $C_{28}H_{38}Cl_3N_5O_3S$

Molecular Weight: 631.06

Target: Anaplastic lymphoma kinase (ALK); Insulin Receptor; IGF-1R

Pathway: Protein Tyrosine Kinase/RTK

Storage: 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

DMSO : 100 mg/mL (158.46 mM; Need ultrasonic)
H_2O : 10 mg/mL (15.85 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.5846 mL	7.9232 mL	15.8464 mL
5 mM	0.3169 mL	1.5846 mL	3.1693 mL
10 mM	0.1585 mL	0.7923 mL	1.5846 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 33.33 mg/mL (52.82 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.5 mg/mL (3.96 mM); Clear solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (3.96 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (3.96 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Ceritinib dihydrochloride (LDK378 dihydrochloride) is a selective, orally bioavailable and ATP-competitive ALK tyrosine kinase inhibitor with an IC_{50} of 200 pM. Ceritinib dihydrochloride (LDK378 dihydrochloride) also inhibits IGF-1R, InsR, and STK22D with IC_{50} values of 8, 7, and 23 nM, respectively. Ceritinib dihydrochloride (LDK378 dihydrochloride) shows great antitumor potency[1][2].

IC_{50} & Target

IC50: 0.2 nM (ALK), 8 nM (IGF-1R), 7 nM (InsR), 23 nM (STK22D)[1]

In Vitro	Ceritinib (LDK378) shows great anti-proliferative activity in Ba/F3-NPM-ALK and Karpas290 cells with IC_{50} of 26.0 nM and 22.8 nM, compared with IC_{50} of 319.5 nM and 2477 nM in Ba/F3-Tel-InsR and Ba/F3-WT cells[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Ceritinib (LDK378) is designed to reduce the possibility of forming reactive metabolites and shows undetectable levels of glutathione (GSH) adducts (<1%) in liver microsomes. Ceritinib (LDK378) has relatively good metabolic stability, with moderate CYP3A4 (Midazolam substrate) inhibition and hERG inhibition. Ceritinib (LDK378) exhibits low plasma clearance in animals (mouse, rat, dog and monkey) compared to liver blood flow, with the oral bioavailability of above 55% in mouse, rat, dog and monkey. Ceritinib (LDK378) induces a dose-dependent growth inhibition and tumor regression in the Karpas299 and H2228 rat xenograft models, with no body-weight loss. Ceritinib (LDK378) shows no impact on insulin levels or plasma glucose utilization in the mouse upon chronic dosing up to 100 mg/kg[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Science. 2017 Dec 1;358(6367):eaan4368.
- Cell Discov. 2021 May 11;7(1):33.
- Nat Cancer. 2022 Oct;3(10):1211-1227.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Cell Rep Med. 2023 Jan 10;100911.

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REFERENCES

[1]. Marsilje TH, et al. Synthesis, structure-activity relationships, and in vivo efficacy of the novel potent and selective anaplastic lymphoma kinase (ALK) inhibitor 5-chloro-N2-(2-isopropoxy-5-methyl-4-(piperidin-4-yl)phenyl)-N4-(2-(isopropylsulfonyl)phenyl

[2]. Rothschild SI. Ceritinib-a second-generation ALK inhibitor overcoming resistance in ALK-rearranged non-small celllung cancer. Transl Lung Cancer Res. 2014 Dec;3(6):379-81.

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