产品名称：LDK378 (dihydrochloride)
产品别名：Ceritinib dihydrochloride；色瑞替尼二盐酸盐

生物活性：

Description	Ceritinib dihydrochloride (LDK378 dihydrochloride) is a selective, orally bioavailable and ATP-competitive ALK tyrosine kinase inhibitor with an IC50 of 200 pM. Ceritinib dihydrochloride (LDK378 dihydrochloride) also inhibits IGF-1R, InsR, and STK22D with IC50 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 IC50 of 26.0 nM and 22.8 nM, compared with IC50 of 319.5 nM and 2477 nM in Ba/F3-Tel-InsR and Ba/F3-WT cells[1].
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].

Solvent&Solubility

In Vitro:

H_2O : ≥ 170 mg/mL (269.39 mM)

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

* "≥" means soluble, but saturation unknown.

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

*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。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: 2.5 mg/mL (3.96 mM); Clear solution; Need ultrasonic

此方案可获得 2.5 mg/mL (3.96 mM)的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；

	向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (3.96 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (3.96 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (3.96 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (3.96 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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)pyrimidine-2, 4-diamine (LDK378) currently in phase 1 and phase 2 clinical trials. J Med Chem. 2013, Jun 6. [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.