产品名称：GDC-0879
产品别名：GDC-0879

生物活性：

Description	GDC-0879 is a potent and selective B-Raf inhibitor with an IC_{50} of 0.13 nM.
IC_{50} & Target	B-Raf
	0.13 nM (IC_{50})
In Vitro	GDC-0879 also inhibits pERK with an IC_{50} of 63 nM[1]. GDC-0879 represents a novel potent and selective B-Raf inhibitor that is being evaluated as a potential antitumor agent. GDC-0879 exhibits potent inhibition of Raf/MEK/ERK signaling pathway in V600E B-Raf mutant cell lines with low cellular pMEK1 inhibition IC_{50} estimates of 59 and 29 nM in A375 melanoma and Colo205 colorectal carcinoma cells, respectively[2].
In Vivo	The pharmacokinetic parameters of GDC-0879 after oral administration of 15, 25, 50, 100, and 200 mg/kg in MCT in mice are estimated as follows: k_a=8.20 h^{-1}, k_e=0.59 h^{-1}, and apparent volume of distribution=6.19 L/kg[2].

Solvent&Solubility

In Vitro:

DMSO : 50 mg/mL (**149.53 mM**; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.9907 mL	14.9535 mL	29.9070 mL
	5 mM	0.5981 mL	2.9907 mL	5.9814 mL
	10 mM	0.2991 mL	1.4953 mL	2.9907 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 (7.48 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (7.48 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 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% corn oil

Solubility: ≥ 2.5 mg/mL (7.48 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (7.48 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]. Hansen JD, et al. Potent and selective pyrazole-based inhibitors of B-Raf kinase. Bioorg Med Chem Lett. 2008 Aug 15;18(16):4692-5. [2]. Wong H, et al. Pharmacodynamics of 2-[4-[(1E)-1-(hydroxyimino)-2,3-dihydro-1H-inden-5-yl]-3-(pyridine-4-yl)-1H-pyrazol-1-yl]ethan-1-ol (GDC-0879), a potent and selective B-Raf kinase inhibitor: understanding relationships between systemic concentrations, phosphorylated mitogen-activated protein kinase kinase 1 inhibition, and efficacy. J Pharmacol Exp Ther. 2009 Apr;329(1):360-7.

实验参考：

Cell Assay	GDC-0879 in vitro IC_{50} estimates for pMEK inhibition are determined using A375 and Colo205 cells. In brief, A375 or Colo205 cells are incubated with a range of GDC-0879 concentrations (from 0.5 nM to 6.75 μM) for 25 min. Cells are lysed, and the lysates are subjected to centrifugation at 16,100g for 30 min, and the level of total protein is determined. Enzyme-linked immunosorbent assay kits are used to determine pMEK1 and total MEK1 protein levels in a 96-well format. Samples are analyzed in duplicate at 20 μg of protein per well. The optical densities obtained at 450 nm are converted to units per milliliter (for pMEK1) or nanograms per milliliter (for total MEK1) using a standard curve determined with recombinant pMEK1 or MEK1. The pMEK1/total MEK1 ratios are then calculated as units per nanogram. The IC_{50} estimates for pMEK1 inhibition are estimated by nonlinear regression using GraphPad Prism version 4.02[2].
Animal Administration	Mice[2]. Female athymic nu/nu mice (weighing 25-28 g) are administered oral doses of 15, 25, 50, 100, and 200 mg/kgGDC-0879. Blood samples (~1 mL) are collected at 0.5, 1, 2, 4, 8, and 24 h after dose via cardiac puncture (terminal collection) into tubes containing K_2EDTA anticoagulant. Immediately upon collection, the blood is mixed with K2EDTA and stored on ice. Within 30 min, blood samples are centrifuged at approximately 1000 to 1500g for 5 min at 4°C, and plasma is harvested. The plasma samples are stored at -80°C until analysis[2].
References	[1]. Hansen JD, et al. Potent and selective pyrazole-based inhibitors of B-Raf kinase. Bioorg Med Chem Lett. 2008 Aug 15;18(16):4692-5. [2]. Wong H, et al. Pharmacodynamics of 2-[4-[(1E)-1-(hydroxyimino)-2,3-dihydro-1H-inden-5-yl]-3-(pyridine-4-yl)-1H-pyrazol-1-yl]ethan-1-ol (GDC-0879), a potent and selective B-Raf kinase inhibitor: understanding relationships between systemic concentrations, phosphorylated mitogen-activated protein kinase kinase 1 inhibition, and efficacy. J Pharmacol Exp Ther. 2009 Apr;329(1):360-7.