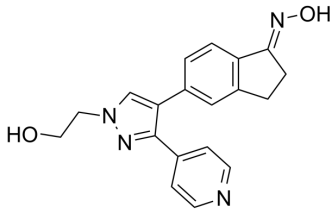
GDC-0879

Cat. No.:	HY-50864
CAS No.:	905281-76-7
Molecular Formula:	$C_{19}H_{18}N_4O_2$
Molecular Weight:	334.37
Target:	Raf
Pathway:	MAPK/ERK Pathway
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 1 year -20°C 6 months



SOLVENT & SOLUBILITY

In Vitro

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

Preparing Stock Solutions	Mass / Solvent / 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

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

In Vivo

1. Add each solvent one by one: 0.5% CMC-Na >> 0.5% Tween-80
   Solubility: 3.23 mg/mL (9.66 mM); Clear solution; Need ultrasonic and warming and heat to 60°C
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (7.48 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.48 mM); Clear solution

BIOLOGICAL ACTIVITY

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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice[2] Female athymic nu/nu mice (weighing 25-28 g) are administered oral doses of 15, 25, 50, 100, and 200 mg/kg GDC-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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- ACS Comb Sci. 2019 Dec 9;21(12):805-816.
- Oncotarget. 2017 Nov 22;8(65):109135-109150.
- Harvard Medical School LINCS LIBRARY

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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.

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

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA