

Product Specification Sheet

Product Name: GDC-0879

Catalog Number: C4087

Technical information:

Chemical Formula: $C_{19}H_{18}N_4O_2$

CAS #: 905281-76-7

Molecular Weight: 334.37

Purity: > 98%

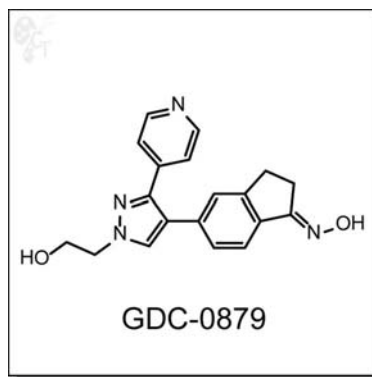
Appearance: White solid

Solubility: Soluble in DMSO up to 100 mM

Chemical Name: (E)-5-(1-(2-hydroxyethyl)-3-(pyridin-4-yl)-1H-pyrazol-4-yl)-2,3-dihydroinden-1-one oxime

Storage: Store solid powder at 4°C desiccated; Store DMSO solution at -20°C.

Shelf Life: In the unopened package, powder is stable for 1 year and DMSO solution is stable for 6 months under proper storage condition.



- Handling:**
- To make 10 mM stock solution, add 0.299mL of DMSO for each mg of GDC-0879
 - For DMSO solution, briefly spin the vial at 500 rpm in a 50 mL conical tube to ensure maximum sample recovery.

Biological Activity: GDC0879 is highly selective, orally-bioavailable, oxime-containing pyrazole type inhibitor of B-Raf (V600E) kinase with a potency of 0.13 nM. [1] In a screening of a panel of kinases at 1 uM activity only RAF kinases were shown to have >90% inhibition, with only one additional kinase (casein kinase 1-delta) at >50% inhibition. [2] GDC0879 effectively reduces pERK levels at 63 nM and cellular viability of B-Raf mutant MALME3M cells at 0.75 uM. [2]

In A375 melanoma and Colo205 colorectal carcinoma cell lines, GDC0879 exhibits dose-dependent pMEK1 inhibition of 59 and 29 nM, respectively. No evidence of apoptotic activation pathways in vitro was observed, suggesting that GDC0879's antitumor activity is based primarily on its effect on cell proliferation. [1] Pathway modulation in A375 tumors was shown to be significant (13% and 28% activity remaining at 1 and 4 hours, respectively) by measuring MEK1 phosphorylation of Ser217/221. Reduced levels of pMEK1 were still evident at 8h post dose (59%), but returned to baseline at 12h. Similar studies in SK23 tumors did not display such a strong PD effect.

- Reference:**
1. Wong 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. Pharm. Exp. Ther. 2009, 329(1), 360-367 Pubmed ID: 19147858
 2. Hoeflich et al., Antitumor efficacy of the novel RAF inhibitor GDC-0879 is predicted by BRAFV600E mutational status and sustained extracellular signal-regulated kinase/mitogen-activated protein kinase pathway suppression. Cancer Res. 2009, 69(7), 3042-3051 Pubmed ID: 19276360

To reorder: <http://www.cellagentech.com/GDC-0879/>
For Technical Support: technical@cellagentech.com

Chemicals are sold for research use only, not for clinical or diagnostic use.