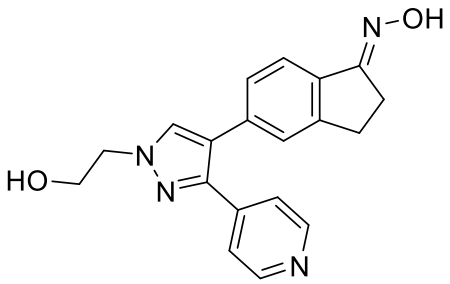
Product data sheet

MedKoo Cat#: 401470 Name: GDC-0879 CAS#: 905281-76-7 Chemical Formula: $C_{19}H_{18}N_4O_2$ Exact Mass: 334.14298 Molecular Weight: 334.37182	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
GDC-0879 is a highly selective, potent, and orally bioavailable RAF small-molecule inhibitor. In GDC-0879 -treated mice, both cell line- and patient-derived BRAF(V600E) tumors exhibited stronger and more sustained pharmacodynamic inhibition (>90% for 8 hours) and improved survival compared with mutant KRAS-expressing tumors.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	49.81	148.98
Ethanol	5.0	14.95

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.99 mL	14.95 mL	29.91 mL
5 mM	0.60 mL	2.99 mL	5.98 mL
10 mM	0.30 mL	1.50 mL	2.99 mL
50 mM	0.06 mL	0.30 mL	0.60 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Sieber J, Wieder N, Clark A, Reitberger M, Matan S, Schoenfelder J, Zhang J, Mandinova A, Bittker JA, Gutierrez J, Aygün O, Udeshi N, Carr S, Mundel P, Jehle AW, Greka A. GDC-0879, a BRAFV600E Inhibitor, Protects Kidney Podocytes from Death. Cell Chem Biol. 2018 Feb 15;25(2):175-184.e4. doi: 10.1016/j.chembiol.2017.11.006. Epub 2017 Dec 14. PMID: 29249695; PMCID: PMC5819995.

In vivo study

1. Sidhom EH, Kim C, Kost-Alimova M, Ting MT, Keller K, Avila-Pacheco J, Watts AJ, Vernon KA, Marshall JL, Reyes-Bricio E, Racette M, Wieder N, Kleiner G, Grinkevich EJ, Chen F, Weins A, Clish CB, Shaw JL, Quinzii CM, Greka A. Targeting a Braf/Mapk pathway rescues podocyte lipid peroxidation in CoQ-deficiency kidney disease. J Clin Invest. 2021 Mar 1;131(5):e141380. doi: 10.1172/JCI141380. PMID: 33444290; PMCID: PMC7919729.

7. Bioactivity
Biological target:

GDC-0879 is a potent and selective B-Raf inhibitor with an IC_{50} of 0.13 nM.

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In vitro activity

In podocytes, GDC-0879 negatively affected thermal stability of endogenous wild type BRAF as assessed by cellular thermal shift assays (Fig. 2A), suggesting GDC-0879 binds BRAF. This experiment suggested that, in addition to BRAF, GDC-0879 could also affect signaling events downstream of BRAF-ARAF in podocytes. GDC-0879 reversed the thapsigargin-mediated reduction in p42/44 phosphorylation (Fig. 2C). CHOP levels remained unaffected, indicating that ER stress persists in podocytes, despite GDC-0879 treatment. GDC-0879 restored both p44/42 and MEK1/2 phosphorylation (Fig. 2D), suggesting that podocytes undergo a paradoxical MEK/ERK activation similar to that observed in some cancer cells. These data indicated that GDC-0879 protects podocytes from thapsigargin-induced death through activation of MEK/ERK signaling.

Reference: Cell Chem Biol. 2018 Feb 15;25(2):175-184.e4. https://pubmed.ncbi.nlm.nih.gov/29249695/

In vivo activity

Four-month-old KDKD (homozygous kidney disease) mice with established proteinuria (specifically albuminuria, the hallmark of a damaged kidney filter) (Supplemental Figure 5D) were treated with either GDC-0879 or vehicle. After a 14-day treatment, GDC-0879–treated animals had significantly reduced albuminuria (Figure 1E). Electron microscopy of glomeruli showed rescue of podocyte foot process effacement (Figure 2A) and a restoration in the number of foot processes (Figure 2B) in GDC-treated versus vehicle-treated animals. Further, loss of foot processes correlated with the magnitude of proteinuria (Figure 2C). To this study's knowledge, these data provide the first in vivo evidence of a Braf/Mapk-targeting compound as a therapeutic strategy for kidney disease.

Reference: J Clin Invest. 2021 Mar 1;131(5):e141380. https://pubmed.ncbi.nlm.nih.gov/33444290/