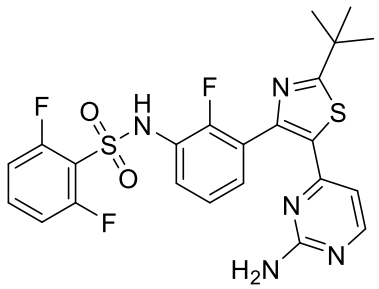
Product data sheet

MedKoo Cat#: 205479 Name: Dabrafenib CAS#: 1195765-45-7 (free base) Chemical Formula: $C_{23}H_{20}F_3N_5O_2S_2$ Exact Mass: 519.10105 Molecular Weight: 519.56	
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:
Dabrafenib, also known as GSK2118436 , is an orally bioavailable inhibitor of B-raf (BRAF) protein with potential antineoplastic activity. Dabrafenib selectively binds to and inhibits the activity of B-raf, which may inhibit the proliferation of tumor cells which contain a mutated BRAF gene. B-raf belongs to the the raf/mil family of serine/threonine protein kinases and plays a role in regulating the MAP kinase/ERKs signaling pathway, which may be constitutively activated due to BRAF gene mutations. On May 29, 2013, FDA approved this drug.

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	100	192.47

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.92 mL	9.62 mL	19.25 mL
5 mM	0.38 mL	1.92 mL	3.85 mL
10 mM	0.19 mL	0.96 mL	1.92 mL
50 mM	0.04 mL	0.19 mL	0.38 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. Lee S, Ku SK, Bae JS. Anti-inflammatory effects of dabrafenib on polyphosphate-mediated vascular disruption. Chem Biol Interact. 2016 Aug 25;256:266-73. doi: 10.1016/j.cbi.2016.07.024. Epub 2016 Jul 25. PMID: 27458080.

2. Jung B, Kang H, Lee W, Noh HJ, Kim YS, Han MS, Baek MC, Kim J, Bae JS. Anti-septic effects of dabrafenib on HMGB1-mediated inflammatory responses. BMB Rep. 2016 Apr;49(4):214-9. doi: 10.5483/bmbrep.2016.49.4.220. PMID: 26592934; PMCID: PMC4915240.

In vivo study

1. Lee S, Ku SK, Bae JS. Anti-inflammatory effects of dabrafenib on polyphosphate-mediated vascular disruption. Chem Biol Interact. 2016 Aug 25;256:266-73. doi: 10.1016/j.cbi.2016.07.024. Epub 2016 Jul 25. PMID: 27458080.

2. Posobiec LM, Vidal JD, Hughes-Earle A, Laffan SB, Hart T. Early Vaginal Opening in Juvenile Female Rats Given BRAF-Inhibitor Dabrafenib Is Not Associated with Early Physiologic Sexual Maturation. Birth Defects Res B Dev Reprod Toxicol. 2015 Dec;104(6):244-52. doi: 10.1002/bdrb.21165. Epub 2015 Dec 1. PMID: 26626128.

Product data sheet

7. Bioactivity

Biological target:

Dabrafenib (GSK2118436, GSK2118436A) is a mutant BRAFV600 specific inhibitor with IC50 of 0.7 nM in cell-free assays, with 7- and 9-fold less potency against B-Raf(wt) and c-Raf, respectively.

In vitro activity

Vascular permeability was assessed to test the effects of dabrafenib on the PolyP-induced disruptions of the vascular barrier as the endothelial barrier integrity is cleaved by PolyP. Previous studies reported the PolyP parameters (50 μM and 4 h) that optimize the disruption of endothelial integrity. The cells were activated with PolyP (50 μM) for 4 h and then various concentrations of dabrafenib for 6 h. The results showed the inhibitory effects of dabrafenib on the PolyP-mediated hyperpermeability, with the optimal dose occurring at concentrations above 10 μM (Fig. 1A). Furthermore, dabrafenib alone (30 μM) did not alter the barrier integrity of the HUVECs (Fig. 1A).

Reference: Chem Biol Interact. 2016 Aug 25;256:266-73. https://linkinghub.elsevier.com/retrieve/pii/S0009-2797(16)30298-8

In vivo activity

Dabrafenib was intravenously injected into mice with PolyP-mediated hyperpermeability. The results showed that PolyP enhanced vascular permeability, and this was suppressed by dabrafenib (Fig. 1B). Because the average blood volume is 72 mL/kg and the average weight of the mice that were used in this study was 27 g, the amount of dabrafenib (5.2, 10.4, 20.8, or 31.1 μg/mouse) injected was equivalent to 5, 10, 20, or 30 μM in peripheral blood.

Reference: Chem Biol Interact. 2016 Aug 25;256:266-73. https://linkinghub.elsevier.com/retrieve/pii/S0009-2797(16)30298-8

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.