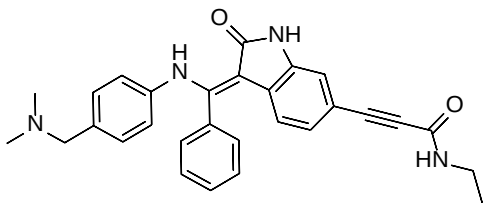
Product data sheet

MedKoo Cat#: 206543 Name: BI-847325 CAS#: 1207293-36-4 Chemical Formula: $C_{29}H_{28}N_4O_2$ Exact Mass: 464.2212 Molecular Weight: 464.57	
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:

BI-847325 is an orally available dual inhibitor of mitogen-activated protein kinase kinase (MEK) and Aurora kinases, with potential antineoplastic activity. Upon oral administration, MEK/Aurora kinase inhibitor BI 847325 selectively binds to and inhibits the activity of MEK, which both prevents the activation of MEK-dependent effector proteins and inhibits growth factor-mediated cell signaling. BI 847325 also binds to and inhibits the activity of the Aurora kinases A, B and C which may disrupt the assembly of the mitotic spindle apparatus, prevent chromosome segregation, and inhibit both cellular division and proliferation in Aurora kinase-overexpressing tumor cells.

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
DMF	16.0	34.44
DMF:PBS (pH 7.2) (1:6)	0.14	0.30
DMSO	13.56	29.19
Ethanol	0.65	1.40

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.15 mL	10.76 mL	21.53 mL
5 mM	0.43 mL	2.15 mL	4.31 mL
10 mM	0.22 mL	1.08 mL	2.15 mL
50 mM	0.04 mL	0.22 mL	0.43 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. Sini P, Gürtler U, Zahn SK, Baumann C, Rudolph D, Baumgartinger R, Strauss E, Haslinger C, Tontsch-Grunt U, Waizenegger IC, Solca F, Bader G, Zoephel A, Treu M, Reiser U, Garin-Chesa P, Boehmelt G, Kraut N, Quant J, Adolf GR. Pharmacological Profile of BI 847325, an Orally Bioavailable, ATP-Competitive Inhibitor of MEK and Aurora Kinases. Mol Cancer Ther. 2016 Oct;15(10):2388-2398. doi: 10.1158/1535-7163.MCT-16-0066. Epub 2016 Aug 5. PMID: 27496137.

In vivo study

1. Sini P, Gürtler U, Zahn SK, Baumann C, Rudolph D, Baumgartinger R, Strauss E, Haslinger C, Tontsch-Grunt U, Waizenegger IC, Solca F, Bader G, Zoephel A, Treu M, Reiser U, Garin-Chesa P, Boehmelt G, Kraut N, Quant J, Adolf GR. Pharmacological Profile of BI 847325, an Orally Bioavailable, ATP-Competitive Inhibitor of MEK and Aurora Kinases. Mol Cancer Ther. 2016 Oct;15(10):2388-2398. doi: 10.1158/1535-7163.MCT-16-0066. Epub 2016 Aug 5. PMID: 27496137.

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7. Bioactivity

Biological target:

BI-847325 is an ATP competitive dual inhibitor of MEK and aurora kinases (AK) with IC50 values of 4 and 15 nM for human MEK2 and AK-C, respectively.

In vitro activity

The effects of BI 847325 in a cellular environment were investigated in a BRAFV600E-mutant melanoma cell line (A375) and a KRASQ61K-mutant NSCLC cell line (Calu-6). Proliferation was inhibited in both cell lines with GI50 values of 7.5 and 60 nmol/L, respectively. Western blot analysis indicated that in A375 cells, BI 847325 potently reduced the concentration of phospho-ERK, an indicator of MAPK pathway activity (partial to complete inhibition at 10–30 nmol/L), whereas about 10-fold higher concentrations were required in Calu-6 cells (Fig. 2A).

Reference: Mol Cancer Ther. 2016 Oct;15(10):2388-2398. https://mct.aacrjournals.org/content/15/10/2388.long

In vivo activity

BI 847325 induced gradual regression of A375 tumors in a mouse xenograft model that was sustained for the entire 4-week treatment period (Fig. 5A). In the Calu-6 model, sustained tumor stasis was observed upon treatment with BI 847325. Treatment with BI 847325 resulted in a profound decrease of phospho-HH3–positive cells in both models, whereas reduction in phospho-ERK was observed only in BRAF-mutant A375 xenografts.

Reference: Mol Cancer Ther. 2016 Oct;15(10):2388-2398. https://mct.aacrjournals.org/content/15/10/2388.long

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.