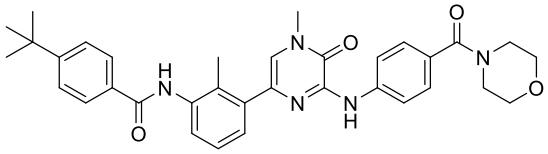
Product data sheet

MedKoo Cat#: 406102 Name: CGI1746 CAS#: 910232-84-7 Chemical Formula: $C_{34}H_{37}N_5O_4$ Exact Mass: 579.28455 Molecular Weight: 579.69	
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:

CGI1746 is a small-molecule Btk inhibitor chemotype with a new binding mode that stabilizes an inactive nonphosphorylated enzyme conformation. CGI1746 has exquisite selectivity for Btk and inhibits both auto- and transphosphorylation steps necessary for enzyme activation.

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	58.33	100.62
DMSO:PBS (pH 7.2) (1:3)	0.25	0.43
DMF	25.0	43.13
Ethanol	16.63	28.69

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.73 mL	8.63 mL	17.25 mL
5 mM	0.35 mL	1.73 mL	3.45 mL
10 mM	0.17 mL	0.86 mL	1.73 mL
50 mM	0.03 mL	0.17 mL	0.35 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. Yang Y, Shi J, Gu Z, Salama ME, Das S, Wendlandt E, Xu H, Huang J, Tao Y, Hao M, Franqui R, Levasseur D, Janz S, Tricot G, Zhan F. Bruton tyrosine kinase is a therapeutic target in stem-like cells from multiple myeloma. Cancer Res. 2015 Feb 1;75(3):594-604. doi: 10.1158/0008-5472.CAN-14-2362. Epub 2015 Jan 14. PMID: 25589346; PMCID: PMC4384656.

2. Di Paolo JA, Huang T, Balazs M, Barbosa J, Barck KH, Bravo BJ, Carano RA, Darrow J, Davies DR, DeForge LE, Diehl L, Ferrando R, Gallion SL, Giannetti AM, Gribling P, Hurez V, Hymowitz SG, Jones R, Kropf JE, Lee WP, Maciejewski PM, Mitchell SA, Rong H, Staker BL, Whitney JA, Yeh S, Young WB, Yu C, Zhang J, Reif K, Currie KS. Specific Btk inhibition suppresses B cell- and myeloid cell-mediated arthritis. Nat Chem Biol. 2011 Jan;7(1):41-50. doi: 10.1038/nchembio.481. Epub 2010 Nov 28. PMID: 21113169.

In vivo study

Product data sheet

1. Gu C, Peng H, Lu Y, Yang H, Tian Z, Yin G, Zhang W, Lu S, Zhang Y, Yang Y. BTK suppresses myeloma cellular senescence through activating AKT/P27/Rb signaling. Oncotarget. 2017 May 23;8(34):56858-56867. doi: 10.18632/oncotarget.18096. PMID: 28915637; PMCID: PMC5593608.
2. Yang Y, Shi J, Gu Z, Salama ME, Das S, Wendlandt E, Xu H, Huang J, Tao Y, Hao M, Franqui R, Levasseur D, Janz S, Tricot G, Zhan F. Bruton tyrosine kinase is a therapeutic target in stem-like cells from multiple myeloma. Cancer Res. 2015 Feb 1;75(3):594-604. doi: 10.1158/0008-5472.CAN-14-2362. Epub 2015 Jan 14. PMID: 25589346; PMCID: PMC4384656.

7. Bioactivity

Biological target:

CGI-1746 is an inhibitor of the Btk with IC50 of 1.9 nM.

In vitro activity

Next, this study asked whether CGI1746 inhibits HMCLs in vitro. Treatment of ARP1 and OPM2 cells with a dose range of drug (0.2 μM to 50 μM; 48 hrs) resulted in similar levels of cytotoxicity in both cell lines (IC50 ≅ 10 μM; Figure 1B).

Reference: Cancer Res. 2015 Feb 1; 75(3): 594–604. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4384656/

In vivo activity

To testify CGI-1746 in vivo, this study xenografted OCI-MY5 cells subcutaneously into NSG mice respectively (n = 5), CGI-1476 treatment was start 7 days after injection. Tumor diameter was measured twice per week to evaluate the tumor growth rate. After 30 days, the tumors from control group, PBS Treatment, were visibly smaller than their counterparts (Figure 6C). The average weight of control tumors and the ratio of tumor weight to body weight were higher than the treatment tumors (Figure 6D & 6E). Time course analysis of tumor growth demonstrated that CGI-1746 outstandingly lagged the MM tumor growth in vivo (Figure 6F).

Reference: Oncotarget. 2017 Aug 22; 8(34): 56858–56867. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5593608/

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.