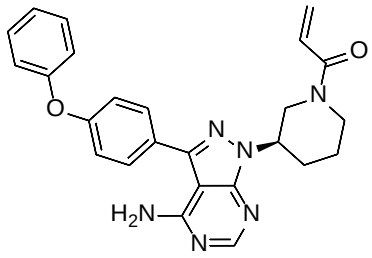
Product data sheet

MedKoo Cat#: 202171 Name: Ibrutinib CAS#: 936563-96-1 Chemical Formula: $C_{25}H_{24}N_6O_2$ Exact Mass: 440.1961 Molecular Weight: 440.50	
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:
Ibrutinib, also known as PCI-32765, is a potent and orally active BTK inhibitor. Ibrutinib binds to and inhibits BTK activity, preventing B-cell activation and B-cell-mediated signaling and inhibiting the growth of malignant B cells that overexpress BTK. Ibrutinib was approved by the US FDA on November 13, 2013 for the treatment of mantle cell lymphoma.

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	30.0	68.10
DMSO	48.01	108.99
DMSO:PBS (pH 7.2) (1:3)	0.25	0.57
Ethanol	0.25	0.57

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.27 mL	11.35 mL	22.70 mL
5 mM	0.45 mL	2.27 mL	4.54 mL
10 mM	0.23 mL	1.14 mL	2.27 mL
50 mM	0.05 mL	0.23 mL	0.45 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. Ninomoto J, Mokatrin A, Kinoshita T, Marimpietri C, Barrett TD, Chang BY, Sukbuntherng J, James DF, Crowther M. Effects of ibrutinib on in vitro platelet aggregation in blood samples from healthy donors and donors with platelet dysfunction. Hematology. 2020 Dec;25(1):112-117. doi: 10.1080/16078454.2020.1730080. PMID: 32131714.
2. Nam HY, Nam JH, Yoon G, Lee JY, Nam Y, Kang HJ, Cho HJ, Kim J, Hoe HS. Ibrutinib suppresses LPS-induced neuroinflammatory responses in BV2 microglial cells and wild-type mice. J Neuroinflammation. 2018 Sep 19;15(1):271. doi: 10.1186/s12974-018-1308-0. PMID: 30231870; PMCID: PMC6145206.

In vivo study

1. Chu Y, Lee S, Shah T, Yin C, Barth M, Miles RR, Ayello J, Morris E, Harrison L, Van de Ven C, Galardy P, Goldman SC, Lim MS, Hermiston M, McAllister-Lucas LM, Giulino-Roth L, Perkins SL, Cairo MS. Ibrutinib significantly inhibited Bruton's tyrosine kinase (BTK) phosphorylation,in-vitro proliferation and enhanced overall survival in a preclinical Burkitt lymphoma (BL) model. Oncoimmunology. 2018 Oct 11;8(1):e1512455. doi: 10.1080/2162402X.2018.1512455. PMID: 30546948; PMCID: PMC6287791.

Product data sheet

2. Nam HY, Nam JH, Yoon G, Lee JY, Nam Y, Kang HJ, Cho HJ, Kim J, Hoe HS. Ibrutinib suppresses LPS-induced neuroinflammatory responses in BV2 microglial cells and wild-type mice. J Neuroinflammation. 2018 Sep 19;15(1):271. doi: 10.1186/s12974-018-1308-0. PMID: 30231870; PMCID: PMC6145206.

7. Bioactivity

Biological target: Ibrutinib (PCI-32765) is a Btk inhibitor with an IC50 of 0.5 nM.

In vitro activity

To better understand the mechanism of ibrutinib in bleeding events, platelet-rich plasma was isolated from healthy donors (n = 8) and donors with conditions associated with impaired platelet function or with potentially increased bleeding risk (on hemodialysis, taking aspirin, or taking warfarin; n = 8 each cohort) and light transmission aggregometry was used to assess platelet aggregation in vitro after exposure to escalating concentrations of ibrutinib, spanning and exceeding the pharmacologic range of clinical exposure. Platelet aggregation was induced by agonists of 5 major platelet receptors: adenosine diphosphate (ADP), thrombin receptor-activating peptide 6 (TRAP6), ristocetin, collagen, or arachidonic acid (AA). Platelet aggregation induced by ADP, TRAP6, ristocetin, and AA was not meaningfully inhibited by the maximal concentrations of ibrutinib (10 μM). In contrast, collagen-induced platelet aggregation was dose-dependently inhibited by ibrutinib in all donor cohorts (maximum aggregation % with 10 μM ibrutinib, -64% to -83% of agonist activity compared to control agonist samples but without ibrutinib).

Reference: Hematology. 2020 Dec;25(1):112-117. https://www.tandfonline.com/doi/full/10.1080/16078454.2020.1730080

In vivo activity

The efficacy of ibrutinib in a dose dependent manner on tumor progression and survival was evaulated. Ibrutinib (12.5 mg/kg) treated mice had a significantly prolonged survival compared to phosphate-buffered saline (PBS) control mice ($p < 0.02$) with median survival of mice following ibrutinib treatment (32 days) compared to PBS control (24 days) (Figure 5A). The treatment experimental schema is shown in Figure 5B. Furthermore, a significant decrease of tumor progression was observed by measuring tumor luminescence signal intensity following ibrutinib treated Raji BL (Burkitt lymphoma) xenografted NSG mice at day 20 ($p < 0.001$) and at day 25 ($p < 0.05$) compared to control (Figure 5C and 5D).

Reference: Oncoimmunology. 2018 Oct 11;8(1):e1512455. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6287791/

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.