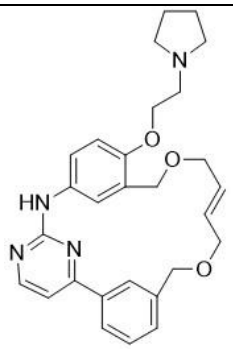
Product data sheet

MedKoo Cat#: 202571 Name: Pacritinib (SB1518) CAS#: 937272-79-2 Chemical Formula: $C_{28}H_{32}N_4O_3$ Exact Mass: 472.24744 Molecular Weight: 472.58	
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:

Pacritinib, also known as SB1518, is an orally bioavailable inhibitor of Janus kinase 2 (JAK2) and the JAK2 mutant JAK2V617F with potential antineoplastic activity. Pacritinib competes with JAK2 for ATP binding, which may result in inhibition of JAK2 activation, inhibition of the JAK-STAT signaling pathway, and so caspase-dependent apoptosis. JAK2 is the most common mutated gene in bcr-abl-negative myeloproliferative disorders; the JAK2V617F gain-of-function mutation involves a valine-to-phenylalanine modification at position 617. The JAK-STAT signaling pathway is a major mediator of cytokine activity.

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	5.0	10.6

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.12 mL	10.58 mL	21.16 mL
5 mM	0.42 mL	2.12 mL	4.23 mL
10 mM	0.21 mL	1.06 mL	2.12 mL
50 mM	0.04 mL	0.21 mL	0.42 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. Hosseini MM, Kurtz SE, Abdelhamed S, Mahmood S, Davare MA, Kaempf A, Elferich J, McDermott JE, Liu T, Payne SH, Shinde U, Rodland KD, Mori M, Druker BJ, Singer JW, Agarwal A. Inhibition of interleukin-1 receptor-associated kinase-1 is a therapeutic strategy for acute myeloid leukemia subtypes. Leukemia. 2018 Nov;32(11):2374-2387. doi: 10.1038/s41375-018-0112-2. Epub 2018 Mar 29. PMID: 29743719; PMCID: PMC6558520.

2. Jensen KV, Cseh O, Aman A, Weiss S, Luchman HA. The JAK2/STAT3 inhibitor pacritinib effectively inhibits patient-derived GBM brain tumor initiating cells in vitro and when used in combination with temozolomide increases survival in an orthotopic xenograft model. PLoS One. 2017 Dec 18;12(12):e0189670. doi: 10.1371/journal.pone.0189670. PMID: 29253028; PMCID: PMC5734728.

In vivo study

1. Jensen KV, Cseh O, Aman A, Weiss S, Luchman HA. The JAK2/STAT3 inhibitor pacritinib effectively inhibits patient-derived GBM brain tumor initiating cells in vitro and when used in combination with temozolomide increases survival in an orthotopic xenograft model. PLoS One. 2017 Dec 18;12(12):e0189670. doi: 10.1371/journal.pone.0189670. PMID: 29253028; PMCID: PMC5734728.

2. Hosseini MM, Kurtz SE, Abdelhamed S, Mahmood S, Davare MA, Kaempf A, Elferich J, McDermott JE, Liu T, Payne SH, Shinde U, Rodland KD, Mori M, Druker BJ, Singer JW, Agarwal A. Inhibition of interleukin-1 receptor-associated kinase-1 is a therapeutic strategy for acute myeloid leukemia subtypes. Leukemia. 2018 Nov;32(11):2374-2387. doi: 10.1038/s41375-018-0112-2. Epub 2018 Mar 29. PMID: 29743719; PMCID: PMC6558520.

7. Bioactivity

Biological target:

Pacritinib (SB1518) is a potent inhibitor of JAK2 (IC50=23 nM), JAK2V617F (IC50=19 nM), FLT3 (IC50=22 nM), and FLT3D835Y (IC50=6 nM).

In vitro activity

Pacritinib is in development as a treatment for myelofibrosis. In the previous kinome-wide screen, pacritinib was found to suppress phosphorylation of two other kinases of potential interest in myeloid diseases, specifically IRAK1 (IC50 = 13.6 nM) and CSF1R (IC50 = 46 nM). Pacritinib also inhibited the growth of FLT3-ITD–positive cells (MOLM-13, MOLM-14) at IC50 values of ~32 nM and 61 nM, respectively, and JAK3 mutation-positive cells (CMK) at an IC50 value of 262 nM. In addition, pacritinib inhibits FLT3 signaling in AML cell lines with the highest potency against cells harboring FLT3-ITD mutations. Pacritinib also inhibited growth of cell lines harboring various genetic mutations at IC50 values ranging from ~100 to ~500 nM for cell lines Kasumi-1, SKNO-1, OCI-AML5, GDM-1, THP1, and HL-60, and ranging from ~750 to ~1500 nM for cell lines. This showed that pacritinib has potent inhibitory effects on AML cell lines and primary AML samples harboring a wide variety of genetic mutations. Therefore, further clinical exploration of IRAK1 as a target for intervention with pacritinib and newer more specific agents is justified in AML and other neoplastic disorders associated with IRAK pathway activation

Leukemia. 2018 Nov; 32(11): 2374–2387.https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6558520/

In vivo activity

The efficacy of pacritinib, a JAK2 inhibitor currently in phase 3 trials was tested.The efficacy of pacritinib was tested in vivo in pharmacokinetic analyses, liver microsome analyses, and Kaplan-Meier survival studies. *In vivo*, systemic treatment with pacritinib demonstrated blood-brain barrier penetration and led to improved overall median survival in combination with TMZ, in mice orthotopically xenografted with an aggressive recurrent GBM BTIC culture. Thirty-two mice were xenografted with 5 x 10^4 BT147 cells each and randomized into treatment cohorts. Treatment began one week post cell implantation with mice randomized to vehicle (Ora-Plus), pacritinib (100mg/kg), TMZ (30mg/kg), or pacritinib (100 mg/kg) + TMZ (30 mg/kg) cohorts. Mice were treated for five weeks, three times per week for a total of 15 treatments. The combination of pacritinib and TMZ provided a significant improvement to overall median survival. *In vivo*, systemic treatment with pacritinib was tolerated and demonstrated favourable pharmacokinetic properties. While pacritinib was found to be unstable in mouse liver microsomes, the drug was stable in human liver microsomes. Despite the rapid metabolism of pacritinib, there was a significant increase in overall median survival in combination with TMZ in mice orthotopically xenografted with an aggressive recurrent GBM BTIC culture. These results suggest that benefits observed in our mouse model may hold further promise in humans, where the drug is not as rapidly metabolized and has promising safety profiles.

PLoS One. 2017; 12(12): e0189670. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5734728/

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.