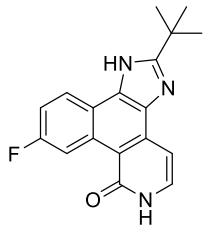
Product data sheet

MedKoo Cat#: 406781 Name: Pyridone 6 CAS#: 457081-03-7 Chemical Formula: $C_{18}H_{16}FN_3O$ Exact Mass: 309.1277 Molecular Weight: 309.34	
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:

Pyridone 6, also known CMP 6 or JAK Inhibitor I, is a pan-Janus-activated kinase inhibitor, Pyridone 6 interferes with JAK kinase activity by interacting within the ATP-binding cleft. It inhibits JAK1, 2, and 3 with IC50 values of 15, 1, and 5 nM, respectively. Pyridone 6 suppresses osteoclast formation and bone resorption through down-regulation of receptor activator of nuclear factor-kappaB (NF-kappaB) ligand (RANKL)-induced c-Fos and nuclear factor of activated T cells (NFAT) c1 expression. Pyridone 6 induces growth inhibition of multiple myeloma 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
DMSO	30.93	99.98
ethanol	15.47	50

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.23 mL	16.16 mL	32.33 mL
5 mM	0.65 mL	3.23 mL	6.47 mL
10 mM	0.32 mL	1.62 mL	3.23 mL
50 mM	0.06 mL	0.32 mL	0.65 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

Kwak HB, Kim HS, Lee MS, Kim KJ, Choi EY, Choi MK, Kim JJ, Cho HJ, Kim JW, Bae JM, Kim YK, Park BH, Ha H, Chun CH, Oh J. Pyridone 6, a pan-Janus-activated kinase inhibitor, suppresses osteoclast formation and bone resorption through down-regulation of receptor activator of nuclear factor-kappaB (NF-kappaB) ligand (RANKL)-induced c-Fos and nuclear factor of activated T cells (NFAT) c1 expression. Biol Pharm Bull. 2009 Jan;32(1):45-50. doi: 10.1248/bpb.32.45. PMID: 19122279.

In vivo study

Nakagawa R, Yoshida H, Asakawa M, Tamiya T, Inoue N, Morita R, Inoue H, Nakao A, Yoshimura A. Pyridone 6, a pan-JAK inhibitor, ameliorates allergic skin inflammation of NC/Nga mice via suppression of Th2 and enhancement of Th17. J Immunol. 2011 Nov 1;187(9):4611-20. doi: 10.4049/jimmunol.1100649. Epub 2011 Sep 28. PMID: 21957150.

7. Bioactivity

Biological target:

Pyridone 6 is a potent pan-JAK inhibitor; ATP-competitive inhibitor of JAK 1/2/3 and Tyk2

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In vitro activity

In this study, the effects of a pan-JAK inhibitor, pyridone 6, on osteoclast differentiation and bone-resorption in vitro and ex vivo were investigated. Pyridone 6 inhibited osteoclast differentiation in mouse bone marrow macrophage (BMM) cultures stimulated by the receptor activator of nuclear factor-kappaB (NF-kappaB) ligand (RANKL) and co-cultures of bone marrow cells and osteoblasts. Pyridone 6 suppressed the expression of c-Fos and nuclear factor of activated T cells (NFAT) c1 in BMMs. It also inhibited the bone resorptive activity of mature osteoclasts that was accompanied by disruption of actin rings. Pyridone 6 also suppressed I-kappaB degradation and extracellular signal-regulated kinase (ERK) in mature osteoclasts, suggesting that these are the key molecules that pyridone 6 targets in the inhibition of osteoclast function. These results demonstrate inhibition of JAK may be useful for the treatment of bone-resorptive diseases, such as osteoporosis.

Reference: Kwak HB, Kim HS, Lee MS, Kim KJ, Choi EY, Choi MK, Kim JJ, Cho HJ, Kim JW, Bae JM, Kim YK, Park BH, Ha H, Chun CH, Oh J. Pyridone 6, a pan-Janus-activated kinase inhibitor, suppresses osteoclast formation and bone resorption through down-regulation of receptor activator of nuclear factor-kappaB (NF-kappaB) ligand (RANKL)-induced c-Fos and nuclear factor of activated T cells (NFAT) c1 expression. Biol Pharm Bull. 2009 Jan;32(1):45-50. doi: 10.1248/bpb.32.45. PMID: 19122279.

In vivo activity

In the current study, pyridone 6 (P6), a pan-JAK inhibitor, delayed the onset and reduced the magnitude of skin disease in an AD-like skin-disease model of NC/Nga mice. P6 reduced IFN-γ and IL-13, whereas it enhanced IL-17 and IL-22 expression. In vitro, P6 also inhibited both Th1 and Th2 development, whereas it promoted Th17 differentiation from naive T cells when present within a certain range of concentrations. This was probably because P6 strongly inhibited STAT1, STAT5, and STAT6 phosphorylation, whereas STAT3 phosphorylation was less efficiently suppressed by P6 at the same concentration. Furthermore, IL-22 protects keratinocytes from apoptosis induced by IFN-γ, and administration of IL-17 and IL-22 partially ameliorated skin diseases in NC/Nga mice. These results suggested that the JAK inhibitor P6 is therapeutic for AD by modulating the balance of Th2 and Th17.

Reference: Nakagawa R, Yoshida H, Asakawa M, Tamiya T, Inoue N, Morita R, Inoue H, Nakao A, Yoshimura A. Pyridone 6, a pan-JAK inhibitor, ameliorates allergic skin inflammation of NC/Nga mice via suppression of Th2 and enhancement of Th17. J Immunol. 2011 Nov 1;187(9):4611-20. doi: 10.4049/jimmunol.1100649. Epub 2011 Sep 28. PMID: 21957150.