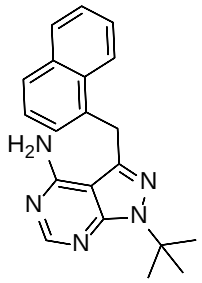
Product data sheet

MedKoo Cat#: 406395 Name: 1NM-PP1 CAS#: 221244-14-0 Chemical Formula: $C_{20}H_{21}N_5$ Exact Mass: 331.1797 Molecular Weight: 331.41	
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:
1NM-PP1 is a potent Mutant Kinases Inhibitor.

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	46.75	141.06
DMF	30.0	90.52
DMF:PBS (pH 7.2) (1:5)	0.15	0.45
Ethanol	2.0	6.03

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.02 mL	15.09 mL	30.17 mL
5 mM	0.60 mL	3.02 mL	6.03 mL
10 mM	0.30 mL	1.51 mL	3.02 mL
50 mM	0.06 mL	0.30 mL	0.60 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. Haan C, Rolvering C, Raulf F, Kapp M, Drückes P, Thoma G, Behrmann I, Zerwes HG. Jak1 has a dominant role over Jak3 in signal transduction through γc-containing cytokine receptors. Chem Biol. 2011 Mar 25;18(3):314-23. doi: 10.1016/j.chembiol.2011.01.012. PMID: 21439476.

In vivo study

1. Sugi T, Kato K, Kobayashi K, Kurokawa H, Takemae H, Gong H, Recuenco FC, Iwanaga T, Horimoto T, Akashi H. 1NM-PP1 treatment of mice infected with Toxoplasma gondii. J Vet Med Sci. 2011 Oct;73(10):1377-9. doi: 10.1292/jvms.11-0085. Epub 2011 Jun 16. PMID: 21685719.
2. Wang X, Ratnam J, Zou B, England PM, Basbaum AI. TrkB signaling is required for both the induction and maintenance of tissue and nerve injury-induced persistent pain. J Neurosci. 2009 Apr 29;29(17):5508-15. doi: 10.1523/JNEUROSCI.4288-08.2009. PMID: 19403818; PMCID: PMC2720992.

7. Bioactivity
Biological target: 1-NM-PP1 is a Src family kinases inhibitor with IC50s of 4.3 nM and 3.2 nM for v-Src-as1 and c-Fyn-as1, respectively.

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In vitro activity

Treatment of cells expressing Jak1WT/Jak3WT with IL-2 and 1NM-PP1, a prototype analog-sensitive kinase inhibitor, did not lead to reduced STAT5 phosphorylation indicating that the inhibitor did not affect Jak1WT or Jak3WT activity (left panel in Figure 3). Interestingly, treatment of cells expressing either AS-Jak1/Jak3WT or Jak1WT/AS-Jak3 with IL-2 and 1NM-PP1 led to a hyperphosphorylation of the respective analog sensitive Jak (lanes 3 and 6 in Figure 3). In addition, the trans-phosphorylation of Jak3 by AS-Jak1 and of Jak1 by AS-Jak3 was reduced by 1NM-PP1. Importantly, STAT5 phosphorylation was effectively inhibited by 1NM-PP1 in cells expressing AS-Jak1/Jak3WT but not in cells expressing Jak1WT/AS-Jak3 (lanes 3 and 6 in Figure 3) again indicating that specific inhibition of Jak3 kinase activity does not result in efficient abrogation of signal transduction initiated by the IL-2 receptor.

Reference: Chem Biol. 2011 Mar 25;18(3):314-23.
https://www.sciencedirect.com/science/article/pii/S1074552111000408?via%3Dihub

In vivo activity

The contribution of the receptor tyrosine kinase, type 2 (TrkB) to the generation and maintenance of injury-induced persistent pain was evaluated. Wild-type mice and transgenic (TrkB(F616A)) mice that express mutant but fully functional TrkB receptors were studied. By injecting a small molecule derivative of the protein kinase inhibitor protein phosphatase 1 (1NM-PP1), it is possible to produce highly selective inhibition of TrkB autophosphorylation in adult mice, without interfering with the activity of other protein kinases. Oral administration of 1NM-PP1, at doses that blocked phosphorylation of TrkB in the spinal cord, had no effect in behavioral tests of acute heat, mechanical, or chemical pain sensitivity. However, the same pretreatment with 1NM-PP1 prevented the development of tissue- or nerve injury-induced heat and mechanical hypersensitivity. Established hypersensitivity was transiently reversed by intraperitoneal injection of 1NM-PP1. Although interfering with TrkB signaling altered neither acute capsaicin nor formalin-induced pain behavior, the prolonged mechanical hypersensitivity produced by these chemical injuries was prevented by 1NM-PP1 inhibition of TrkB signaling. These results suggest that TrkB signaling is not only an important contributor to the induction of heat and mechanical hypersensitivity produced by tissue or nerve injury but also to the persistence of the pain.

Reference: J Neurosci. 2009 Apr 29;29(17):5508-15. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2720992/