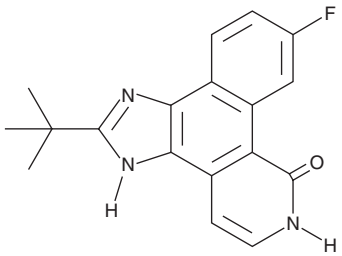
PRODUCT INFORMATION

JAK Inhibitor I

Item No. 15146

CAS Registry No.: 457081-03-7
Formal Name: 2-(1,1-dimethylethyl)-9-fluoro-1,6-dihydro-7H-benz[h]imidazo[4,5-f]isoquinolin-7-one
Synonyms: CMP 6, Janus-Associated Kinase Inhibitor I, Pyridone 6
MF: $C_{18}H_{16}FN_3O$
FW: 309.3
Purity: ≥98%
UV/Vis.: λ_{max}: 219, 260, 270, 328, 343, 359 nm
Supplied as: A crystalline solid
Storage: -20°C
Stability: ≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

JAK inhibitor I is supplied as a crystalline solid. A stock solution may be made by dissolving the JAK inhibitor I in the solvent of choice, which should be purged with an inert gas. JAK inhibitor I is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of JAK inhibitor I in ethanol is approximately 1 mg/ml and approximately 15 mg/ml in DMSO and DMF.

JAK inhibitor I is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, JAK inhibitor I should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. JAK inhibitor I has a solubility of approximately 0.3 mg/ml in a 1:2 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

Janus-associated kinases (JAKs) are cytoplasmic tyrosine kinases that are required for activating the signaling of certain cytokines and growth factor receptors.[1,2] JAK1 mostly activates IL-6, whereas JAK1 and JAK3 trigger IL-2 and IL-4 and JAK1 and JAK2 stimulates IFN-γ. JAK Inhibitor I is a pyridine-containing tetracycle that interferes with JAK kinase activity by interacting within the ATP-binding cleft. It inhibits JAK1, 2, and 3 with IC_{50} values of 15, 1, and 5 nM, respectively, while displaying significantly weaker affinities (IC_{50}s = 130 nM - >10 µM) for other protein tyrosine kinases.[3] It was shown to block IL-2 and IL-4-dependent proliferation of mouse T-cell lymphoma cells with IC_{50} values of 50-100 nM.[3] In a mouse model of atopic dermatitis, JAK Inhibitor I, supplied at 2 mg encapsulated in a PLGA nanoparticle, was shown to suppress IFN-γ/STAT1, IL-2/STAT5, and IL-4/STAT6 signaling pathways.[4]

References

1. Leonard, W.J. and O'Shea, J.J. JAKS and STATS: Biological implications. *Annu. Rev. Immunol.* **16**, 293-322 (1998).
2. Yamaoka, K., Saharinen, P., Pesu, M., *et al.* The janus kinases (Jaks). *Genome Biol.* **5(12)**, 1-6 (2004).
3. Thompson, J.E., Cubbon, R.M., Cummings, R.T., *et al.* Photochemical preparation of a pyridone containing tetracycle: A Jak protein kinase inhibitor. *Bioorg. Med. Chem. Lett.* **12(8)**, 1219-1223 (2002).
4. Nakagawa, R., Yoshida, H., Asakawa, M., *et al.* Pyridone 6, a pan-JAK inhibitor, ameliorates allergic skin inflammation of NC/Nga mice *via* suppression of Th2 and enhancement of Th17. *J. Immunol.* **187(9)**, 4611-4620 (2011).

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