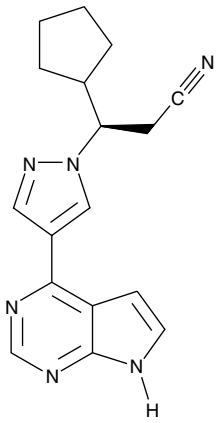
Product Information

Ruxolitinib

Item No. 11609



CAS Registry No.:	941678-49-5
Formal Name:	βR-cyclopentyl-4-(7H-pyrrolo[2,3-d] pyrimidin-4-yl)-1H-pyrazole-1-propanenitrile
Synonym:	INCB 018424
MF:	$C_{17}H_{18}N_6$
FW:	306.4
Purity:	≥98%
Stability:	≥2 years at -20°C
Supplied as:	A crystalline solid
UV/Vis.:	λ_{max}: 216, 224, 253, 309 nm

Laboratory Procedures

For long term storage, we suggest that ruxolitinib be stored as supplied at -20°C. It should be stable for at least two years.

Ruxolitinib is supplied as a crystalline solid. A stock solution may be made by dissolving the ruxolitinib in the solvent of choice. Ruxolitinib is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of ruxolitinib in ethanol is approximately 13 mg/ml and approximately 5 mg/ml in DMSO and DMF.

Ruxolitinib is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, ruxolitinib should first be dissolved in ethanol and then diluted with the aqueous buffer of choice. Ruxolitinib has a solubility of approximately 0.5 mg/ml in a 1:1 solution of ethanol:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Janus-associated kinases (JAKs) are cytoplasmic tyrosine kinases that are required for activating the signaling of certain cytokines and growth factor receptors.[1,2] A JAK2 gene fusion mutation, $JAK2^{V617F}$, that causes unchecked activation of various growth factors and cytokines, has been linked to myeloproliferative neoplasms (MPNs), including polycythemia vera, essential thrombocythemia, and primary myelofibrosis.[3] Ruxolitinib is a potent ATP mimetic that inhibits both JAK1 and JAK2 with IC_{50} values of 2.7 and 4.5 nM, respectively and is relatively less selective for JAK3 (IC_{50} = 322 nM).[3] It can block interleukin-6 (IL-6) signaling (IC_{50} = 281 nM) and proliferation of $JAK2^{V617F+}$ Ba/F3 cells (IC_{50} = 127 nM).[4] In primary cultures, ruxolitinib preferentially suppresses erythroid progenitor colony formation from $JAK2^{V617F+}$ polycythemia vera patients (IC_{50} = 67 nM) *versus* healthy donors (IC_{50} > 400 nM).[4] In a mouse model of $JAK2^{V617F+}$ MPN, 90 mg/kg ruxolitinib reduced splenomegaly, decreased circulating levels of IL-6 and TNF-α, eliminated neoplastic cells, and prolonged survival of the treated animals.[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. Verstovsek, S. Therapeutic potential of JAK2 inhibitors. *Hematology Am. Soc. Hematol. Educ. Program* **2009(1)**, 636-642 (2009).
4. Quintás-Cardama, A., Vaddi, K., Liu, P., *et al.* Preclinical characterization of the selective JAK1/2 inhibitor INCB018424: Therapeutic implications for the treatment of myeloproliferative neoplasms. *Blood* **115(15)**, 3109-3117 (2010).

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