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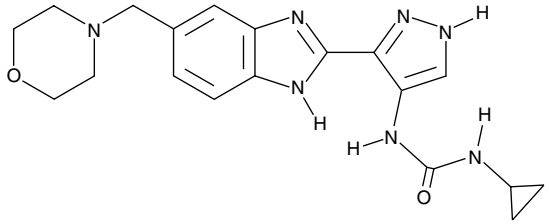
Product Information

AT-9283

Item No. 11496

CAS Registry No.: 896466-04-9
Formal Name: N-cyclopropyl-N'-[3-[6-(4-morpholinylmethyl)-1H-benzimidazol-2-yl]-1H-pyrazol-4-yl]-urea
MF: $C_{19}H_{23}N_7O_2$
FW: 381.4
Purity: ≥98%
Stability: ≥2 years at -20°C
Supplied as: A crystalline solid
UV/Vis.: λ_{max}: 214, 266, 306, 318 nm



Laboratory Procedures

For long term storage, we suggest that AT-9283 be stored as supplied at -20°C. It should be stable for at least two years.

AT-9283 is supplied as a crystalline solid. A stock solution may be made by dissolving the AT-9283 in the solvent of choice. AT-9283 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of AT-9283 in ethanol is approximately 10 mg/ml and approximately 30 mg/ml in DMSO and DMF.

AT-9283 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, AT-9283 should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. AT-9283 has a solubility of approximately 0.5 mg/ml in a 1:1 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

AT-9283 is a broad spectrum kinase inhibitor that potently inhibits Aurora A, Aurora B, JAK2, JAK3, and c-ABL (IC_{50}s = 3, 3, 1.2, 1.1, and 4 nM, respectively).[1] It also potently (IC_{50} = <1 µM) inhibits many other kinases, including serine/threonine kinases as well as receptor and non-receptor tyrosine kinases.[1] As Aurora kinases have roles in mitosis, inhibitors of these kinases, including AT-9283, have potential in cancer therapy.[2] Consistent with this, AT-9283 is effective in preventing proliferation of cancer cells both *in vitro* and *in vivo* and this effect may be enhanced by combination therapy with other chemotherapeutics.[3-4]

References

1. Howard, S., Berdini, V., Boulstridge, J.A., *et al.* Fragment-based discovery of the pyrazol-4-yl urea (AT9283), a multitargeted kinase inhibitor with potent aurora kinase activity. *J. Med. Chem.* **52(2)**, 379-388 (2009).
2. Curry, J., Angove, H., Fazal, L., *et al.* Aurora B kinase inhibition in mitosis: strategies for optimising the use of aurora kinase inhibitors such as AT9283. *Cell Cycle* **8(12)**, 1921-1929 (2009).
3. Qi, W., Liu, X., Cooke, L.S., *et al.* AT9283, a novel aurora kinase inhibitor, suppresses tumor growth in aggressive B-cell lymphomas. *Int. J. Cancer* **130(12)**, 2997-3005 (2012).
4. Santo, L., Hideshima, T., Cirstea, D., *et al.* Antimyeloma activity of a multitargeted kinase inhibitor, AT9283, *via* potent Aurora kinase and STAT3 inhibition either alone or in combination with lenalidomide. *Clin. Cancer Res.* **17(10)**, 3259-3271 (2011).

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