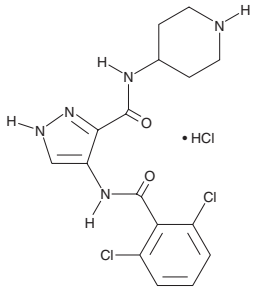
PRODUCT INFORMATION

AT7519 (hydrochloride)

Item No. 16231

CAS Registry No.:	902135-91-5
Formal Name:	4-[(2,6-dichlorobenzoyl)amino]-N-4-piperidinyl-1H-pyrazole-3-carboxamide, monohydrochloride
MF:	$C_{16}H_{17}Cl_2N_5O_2 \bullet HCl$
FW:	418.7
Purity:	≥98%
UV/Vis.:	λ_{max}: 268 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

AT7519 (hydrochloride) is supplied as a crystalline solid. A stock solution may be made by dissolving the AT7519 (hydrochloride) in the solvent of choice. AT7519 (hydrochloride) is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide, which should be purged with an inert gas. The solubility of AT7519 (hydrochloride) in these solvents is approximately 5, 25, and 20 mg/ml, respectively.

Further dilutions of the stock solution into aqueous buffers or isotonic saline should be made prior to performing biological experiments. Ensure that the residual amount of organic solvent is insignificant, since organic solvents may have physiological effects at low concentrations. Organic solvent-free aqueous solutions of AT7519 (hydrochloride) can be prepared by directly dissolving the crystalline solid in aqueous buffers. The solubility of AT7519 (hydrochloride) in PBS, pH 7.2, is approximately 0.5 mg/ml. We do not recommend storing the aqueous solution for more than one day.

Description

AT7519 is an ATP-competitive inhibitor of cyclin-dependent kinases (Cdks) with IC_{50} values of 210, 47, 100, 13, 170, and <10 nM for Cdk1, 2, 4, 5, 6, and 9, respectively.[1] It is less potent against Cdk3 and Cdk7 and inactive against non-Cdk kinases save for GSK3β (IC_{50} = 89 nM).[1] AT7519 demonstrates antiproliferative activity against a wide variety of human tumor cell lines (IC_{50}s = 40-940 nM *in vitro*), inhibiting cell cycle progression and inducing apoptosis, and prevents tumor growth in human tumor xenograft models.[1,2] AT7519 induces activation of GSK3β by down-regulating GSK3β phosphorylation, which contributes to AT7519-induced apoptosis.[2]

References

1. Squires, M.S., Feltell, R.E., Wallis, N.G., *et al.* Biological characterization of AT7519, a small-molecule inhibitor of cyclin-dependent kinases, in human tumor cell lines. *Mol. Cancer Ther.* **8(2)**, 324-332 (2009).
2. Santo, L., Vallet, S., Hideshima, T., *et al.* AT7519, a novel small molecule multi-cyclin-dependent kinase inhibitor, induces apoptosis in multiple myeloma *via* GSK-3β activation and RNA polymerase II inhibition. *Oncogene* **29(16)**, 2325-2336 (2010).

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