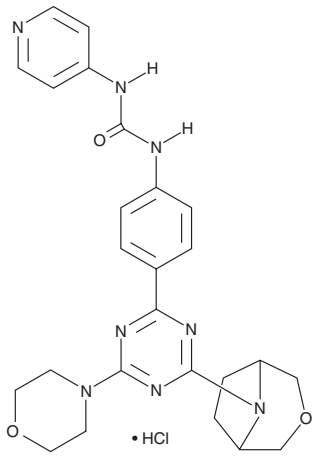
PRODUCT INFORMATION

PKI-179 (hydrochloride)

Item No. 21202



CAS Registry No.:	1463510-35-1
Formal Name:	N-[4-[4-(4-morpholinyl)-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl]-N'-4-pyridinyl-urea, monohydrochloride
MF:	$C_{25}H_{28}N_8O_3$ • HCl
FW:	525.0
Purity:	≥98%
UV/Vis.:	λ_{max}: 228, 297 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

PKI-179 (hydrochloride) is supplied as a crystalline solid. A stock solution may be made by dissolving the PKI-179 (hydrochloride) in the solvent of choice, which should be purged with an inert gas. PKI-179 (hydrochloride) is soluble in organic solvents such as DMSO and dimethyl formamide. The solubility of PKI-179 (hydrochloride) in these solvents is approximately 2.5 and 2 mg/ml, respectively. PKI-179 (hydrochloride) is also slightly soluble in ethanol.

PKI-179 (hydrochloride) is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, PKI-179 (hydrochloride) should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. PKI-179 (hydrochloride) has a solubility of approximately 0.25 mg/ml in a 1:3 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

PKI-179 is an orally bioavailable dual inhibitor of PI3K and mammalian target of rapamycin (mTOR).[1] In an *in vitro* enzymatic assay, it potently inhibits PI3K (IC_{50}s = 8, 24, 17, and 74 nM for isoforms α, β, δ, and γ, respectively), two common PI3Kα mutants, E545K and H1047R (IC_{50}s = 14 and 11 nM, respectively), and mTOR (IC_{50} = 0.42 nM). PKI-179 is selective for PI3K and mTOR over a panel of 361 other kinases at IC_{50} values up to 50 µM, hERG (IC_{50} > 30 µM), and cytochrome P450 (CYP) isoforms (IC_{50}s > 30 µM), but does have activity for CYP2C8 (IC_{50} = 3 µM). It inhibits proliferation through the Akt/mTOR signaling pathway in MDA-361 breast and PC3MM2 prostate cancer cell lines *in vitro* (IC_{50}s = 22 and 29 nM, respectively) and inhibits tumor growth in an MDA-361 mouse xenograft model when used at a dose of 50 mg/kg.

Reference

1. Venkatesan, A.M., Chen, Z., dos Santos, O., *et al.* PKI-179: An orally efficacious dual phosphatidylinositol-3-kinase (PI3K)/mammalian target of rapamycin (mTOR) inhibitor. *Bioorg. Med. Chem. Lett.* **20(19)**, 5869-5873 (2010).

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