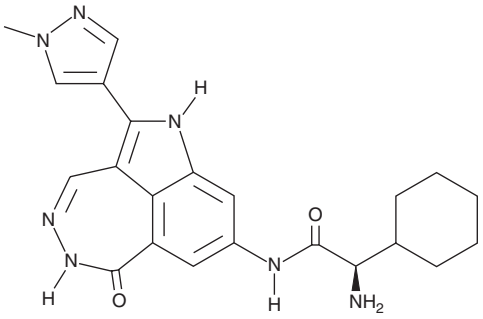
PRODUCT INFORMATION

PF-477736

Item No. 17859

CAS Registry No.:	952021-60-2
Formal Name:	(αR)-amino-N-[5,6-dihydro-2-(1-methyl-1H-pyrazol-4-yl)-6-oxo-1H-pyrrolo[4,3,2-ef][2,3]benzodiazepin-8-yl]-cyclohexaneacetamide
MF:	$C_{22}H_{25}N_7O_2$
FW:	419.5
Purity:	≥98%
UV/Vis.:	λ_{max}: 265, 330 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

PF-477736 is supplied as a crystalline solid. A stock solution may be made by dissolving the PF-477736 in the solvent of choice, which should be purged with an inert gas. PF-477736 is soluble in organic solvents such as DMSO and dimethyl formamide. The solubility of PF-477736 in these solvents is approximately 30 mg/ml.

PF-477736 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, PF-477736 should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. PF-477736 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.

Description

Checkpoint kinase 1 (Chk1) regulates S and G_2-M phase cell cycle checkpoints in response to DNA damage. PF-477736 is an ATP-competitive inhibitor of Chk1 with a K_i value of 0.49 nM that demonstrates 100-fold selectivity over Chk2.[1] When used in combination with various chemotherapeutics, PF-477736 abrogates DNA damage-induced cell cycle arrest, potentiating the antiproliferative effects of these compounds in tumor cell lines and xenografts.[1-3]

References

1. Blasina, A., Hallin, J., Chen, E., *et al.* Breaching the DNA damage checkpoint *via* PF-00477736, a novel small-molecule inhibitor of checkpoint kinase 1. *Mol. Cancer Ther.* **7(8)**, 2394-2404 (2008).
2. Zhang, C., Yan, Z., Painter, C.L., *et al.* PF-00477736 mediates checkpoint kinase 1 signaling pathway and potentiates docetaxel-induced efficacy in xenografts. *Clin. Cancer Res.* **15(14)**, 4630-4640 (2009).
3. Nguyen, T., Hawkins, E., Kolluri, A., *et al.* Synergism between bosutinib (SKI-606) and the Chk1 inhibitor (PF-00477736) in highly imatinib-resistant BCR-ABL$^+$ leukemia cells. *Leuk. Res.* **39**, 65-71 (2015).

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