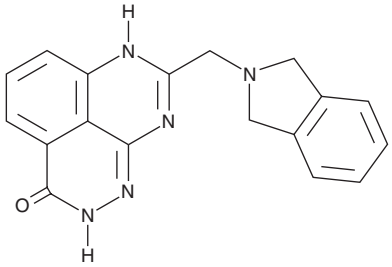
PRODUCT INFORMATION

E7449

Item No. 21658

CAS Registry No.:	1140964-99-3
Formal Name:	8-[(1,3-dihydro-2H-isoindol-2-yl)methyl]-1,2-dihydro-3H-pyridazino[3,4,5-de]quinazolin-3-one
MF:	$C_{18}H_{15}N_5O$
FW:	317.3
Purity:	≥98%
UV/Vis.:	λ_{max}: 207, 310 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

E7449 is supplied as a crystalline solid. A stock solution may be made by dissolving the E7449 in the solvent of choice. E7449 is soluble in organic solvents such as DMSO and dimethyl formamide, which should be purged with an inert gas. The solubility of E7449 in these solvents is approximately 0.2 mg/ml.

E7449 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, E7449 should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. E7449 has a solubility of approximately 0.2 mg/ml in a 1:2 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

E7449 is an inhibitor of poly(ADP-ribose) polymerase 1 (PARP1) and PARP2 (IC_{50}s = 1 and 1.2 nM, respectively) as well as tankyrase (TNKS) 1/2 (IC_{50}s = 50-100 nM).[1] It is selective for PARP1, PARP2, and TNKS1/2 over PARP3 and PARP6-15 (IC_{50}s = >3 µM). E7449 binds to chromatin in a concentration-dependent manner and inhibits growth of DT40 cells in a PARP-dependent manner (IC_{50}s = 3.2 and >15 µM for wild-type and $PARP^{-/-}$ cells, respectively). It also decreases expression of the Wnt/β-catenin signaling pathway proteins axin2, total and active β-catenin, and cyclin D1 in SW480 cells. *In vivo*, E7449 enhances tumor growth inhibition induced by temozolomide (TMZ; Item No. 14163) in a B16/F10 isograft model as well as antitumor activity of the DNA-crosslinking agent carboplatin (Item No. 13112) in an MX-1 mouse xenograft model. E7449 (30 and 100 mg/kg per day) inhibits tumor growth in a *BRCA1* mutant MDA-MB-436 breast cancer mouse xenograft model and induces complete inhibition of tumor cell PARP activity in an NCI-H460 lung cancer mouse xenograft model when administered at a dose of 100 mg/kg. It also delays hair regrowth, a TNKS-dependent process, in mice following hair removal.

Reference

1. McGonigle, S., Chen, Z., Wu, J., *et al.* E7449: A dual inhibitor of PARP1/2 and tankyrase1/2 inhibits growth of DNA repair deficient tumors and antagonizes Wnt signaling. *Oncotarget* **6(38)**, 41307-41323 (2015).

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