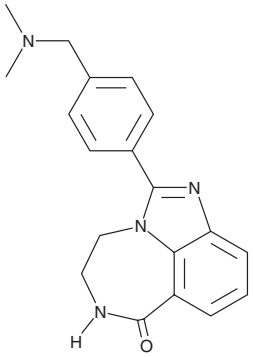
PRODUCT INFORMATION

AG-14361

Item No. 24677



CAS Registry No.:	328543-09-5
Formal Name:	2-[4-[(dimethylamino)methyl]phenyl]-5,6-dihydro-imidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
MF:	$C_{19}H_{20}N_4O$
FW:	320.4
Purity:	≥98%
UV/Vis.:	λ_{max}: 210, 240, 312 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

AG-14361 is supplied as a crystalline solid. A stock solution may be made by dissolving the AG-14361 in the solvent of choice. AG-14361 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide, which should be purged with an inert gas. The solubility of AG-14361 in these solvents is approximately 2, 20, and 10 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 AG-14361 can be prepared by directly dissolving the crystalline solid in aqueous buffers. The solubility of AG-14361 in PBS, pH 7.2, is approximately 0.2 mg/ml. We do not recommend storing the aqueous solution for more than one day.

Description

AG-14361 is an inhibitor of poly(ADP-ribose) polymerase 1 (PARP1; K_i = 6.3 nM for the human enzyme).[1] It inhibits PARP1 activity in permeabilized and intact SW620 cells (IC_{50}s = 29 and 14 nM, respectively).[2] AG-14361 (0.4 µM) potentiates the growth inhibitory effects of temozolomide (Item No. 14163) in HCT116, A2480, and CP70 cells and of the topoisomerase I inhibitor topotecan (Item No. 14129) by greater than three-fold in $PARP1^{+/+}$ primary embryonic fibroblasts.[3,4] It slows the rejoining of camptothecin-induced DNA strand breaks.[4] AG-14361 also inhibits cell growth in a PARP1-independent manner with GI_{50} values of 66 and 65 µM, respectively, in cell lines derived from $PARP1^{+/+}$ and $PARP1^{-/-}$ mice.[2] AG-14361 (15 mg/kg), in combination with temozolomide, leads to tumor regression in an SW620 mouse xenograft model.

References

1. Skalitzky, D.J., Marakovits, J.T., Maegley, K.A., *et al. J. Med. Chem.* **46(2)**, 210-213 (2003).
2. Calabrese, C.R., Almassy, R., Barton, S., *et al. J. Natl. Cancer Inst.* **96(1)**, 56-67 (2004).
3. Curtin, N.J., Wang, L.Z., Yiakouvaki, A., *et al. Clin. Cancer Res.* **10(3)**, 881-889 (2004).
4. Smith, L.M., Willmore, E., Austin, C.A., *et al. Clin. Cancer Res.* **11(23)**, 8449-8457 (2005).

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