Product Data Sheet

Product Name: AZD9496 maleate
Cat. No.: GC35450

Chemical Properties

Cas. No.	1639042-28-6		
SMILES	O=C(O)/C=C/C1=CC(F)=C([C@H]2N(CC(C)(F)C)[C@H](C)CC3=C2NC4=C3C=CC=C4)C(F)=C1.O=C(O)/C=C\C(O)=O		
Formula	$C_{29}H_{29}F_3N_2O_6$	M.Wt	558.55
Solubility	DMSO: ≥ 100 mg/mL (179.04 mM); Water: < 0.1 mg/mL (insoluble)	Storage	4°C, protect from light, stored under nitrogen
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	AZD9496 maleate		

Protocol

Cell experiment:

Effect of AZD9496, Fulvestrant, and Tamoxifen on ERα peptide turnover in MCF-7 cells. Cells are grown in steroid-free conditions in SILAC media containing 13C615N4 L-arginine to label ERα peptide as “heavy” (blue line) and then switched to grow in media containing unlabeled L-arginine to label newly synthesized protein as “normal” (red line) with 0.1% DMSO, 300 nM Tamoxife, 100 nM AZD9496, or 100 nM Fulvestrant for the time indicated. Data shown is representative of two independent experiments[1].

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Animal experiment:

Mice[1] In vivo efficacy of AZD9496 in MCF-7 xenograft model. MCF-7 xenografts, grown in male SCID mice, are dosed daily with either PEG/captisol (vehicle) or AZD9496 (0.02, 0.1, 0.5, 10, and 50 mg/kg, p.o., q.d.). Tumor growth is measured by caliper at regular intervals and mean tumor volumes plotted for each dosed group.

References:

[1]. Weir HM, et al. AZD9496: An Oral Estrogen Receptor Inhibitor That Blocks the Growth of ER-Positive and ESR1-Mutant Breast Tumors in Preclinical Models. Cancer Res. 2016 Jun 1;76(11):3307-18.
[2]. De Savi C, et al. Optimization of a Novel Binding Motif to (E)-3-(3,5-Difluoro-4-((1R,3R)-2-(2-fluoro-2-methylpropyl)-3-methyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)phenyl)acrylic Acid (AZD9496), a Potent and Orally Bioavailable Selective Estrogen Receptor Downregulator and Antagonist. J Med Chem. 2015 Oct 22;58(20):8128-40.

Background

AZD 9496 is a potent and selective estrogen receptor downregulator (SERD) with an IC_{50} value of 0.138 nM for estrogen receptor α (ERα) downregulation.[1] It is selective for

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ERα compared to other nuclear hormone receptors with IC_{50} values of 0.0008, 0.54, 9.2, and 30 μM for ERα, progesterone receptor (PR), glucocorticoid receptor (GR), and androgen receptor (AR), respectively. AZD 9496 decreases ERα activity (IC_{50} = 0.282 nM), measured *via* quantification of downstream PR activity, and reduces proliferation of MCF-7 breast cancer cells (IC_{50} = 0.0398 nM). It also inhibits MCF-7 xenograft growth in mice in a dose-dependent manner.

1.De Savi, C., Bradbury, R.H., Rabow, A.A., et al.Optimization of a novel binding motif to (E)-3-(3,5-difluoro-4-((1R,3R)-2-(2-fluoro-2-methylpropyl)-3-methyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)phenyl)acrylic acid (AZD9496), a potent and orally bioavailable selective estrogen receptor downregulator and antagonistJ. Med. Chem.58(20)8128-8140(2015)

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