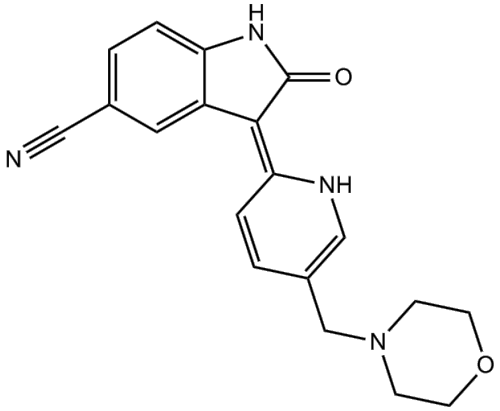
Product Data Sheet

Product Name: AZD1080
Cat. No.: GC16568

Chemical Properties

Cas. No.	612487-72-6		
Chemical Name	3-[5-(morpholin-4-ylmethyl)-1H-pyridin-2-ylidene]-2-oxo-1H-indole-5-carbonitrile		
SMILES	C1COCCN1CC2=CNC(=C3C4=C(C=CC(=C4)C#N)NC3=O)C=C2		
Formula	C19H18N4O2	M.Wt	334.37
Solubility	≥ 16.7mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C 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			

Protocol

Cell experiment [1]:

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Cell lines	3T3 fibroblasts engineered to stably express 4-repeat human tau
Preparation method	Limited solubility. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.
Reaction Conditions	37oC
Applications	AZD1080 inhibits phosphorylation of human tau protein in a concatenation-dependent manner (IC50 = 324 nM). The non-selective reference GSK3 inhibitor LiCl (IC50 = 1.5 mM) indicating that AZD1080 is several orders of magnitude more potent than LiCl.

Animal experiment [1]:

Animal models	11–12 days old male and female Sprague-Dawley rats
Dosage form	AZD1080 (3 or 10 lmol/kg); oral gavage (6 mL/kg).
Applications	6 h after administration of AZD1080, it inhibits the tau phosphorylation by maximal of 38±2% and 48±2% in hippocampus, indicating AZD1080 is effective at inhibiting tau phosphorylation at the P-Thr231 epitope, in a time- and dose-dependent manner in brain. In addition, AZD1080 reverses cognitive deficits in mice and rescues dysfunctional synapses.

Caution: Product has not been fully validated for medical applications. For research use only.
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Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

1. Georgievska B, Sandin J, Doherty J et al. AZD1080, a novel GSK3 inhibitor, rescues synaptic plasticity deficits in rodent brain and exhibits peripheral target engagement in humans. J Neurochem. 2013 May;125(3):446-56.

Background

AZD1080 is a novel, potent and selective inhibitor of Glycogen synthase kinase-3β (GSK3β) with the Ki values of 6.9 nM and 31 nM, respectively [1].

AZD1080 has been reported to inhibit GSK3β by binding within the ATP pocket by means of the high resolution X-ray crystal structure. In addition, AZD1080 has been noted to suppression recombinant human GSK3α and GSK3β with the Ki values of 6.9 nM and 31 nM, respectively. AZD1080 has also shown the selectivity against other kinases with the Ki values of 1150nM, 429nM,1980nM and >10μM for cdk2, cdk5, cdk2 and Erk2, respectively. Furthermore, AZD1080 has been revealed to concentration-dependently inhibit tau phosphorylation with the IC50 value of 324nM in 3T3 cell lines. Besides, AZD1080 has exhibited the good oral bioavailability the high blood – brain barrier permeability values of 8 ×10-3cm/min in rat [1].

References:
[1] Georgievska B1, Sandin J, Doherty J, Mörtberg A, Neelissen J, Andersson A, Gruber S, Nilsson Y, Schött P, Arvidsson PI, Hellberg S, Osswald G, Berg S, Fälting J, Bhat RV. AZD1080, a novel GSK3 inhibitor, rescues synaptic plasticity deficits in rodent brain and exhibits peripheral target engagement in humans. J Neurochem. 2013 May;125(3):446-56.

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