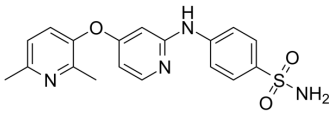
AZ12799734

Cat. No.:	HY-123900
CAS No.:	1117684-36-2
Molecular Formula:	$C_{18}H_{18}N_4O_3S$
Molecular Weight:	370.43
Target:	TGF-β Receptor
Pathway:	TGF-beta/Smad
Storage:	4°C, protect from light * In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (337.45 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6996 mL	13.4978 mL	26.9957 mL
	5 mM	0.5399 mL	2.6996 mL	5.3991 mL
	10 mM	0.2700 mL	1.3498 mL	2.6996 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

AZ12799734 is a selective, orally active TGFBR1 kinase inhibitor with an IC_{50} of 47 nM. AZ12799734 is also a pan BMP and TGF β inhibitor[1].

IC_{50} & Target

TGFBR1 47 nM (IC_{50})	ALK6 0.017 μM (Kd)	ALK5 0.74 μM (Kd)	ALK4 1 μM (Kd)
ACVR1 6.2 μM (Kd)	ALK1 7.1 μM (Kd)	BMPR1A 40 μM (Kd)	BMP

In Vitro

AZ12799734 inhibits ligand activated SMAD3/4 transcription[1].
AZ12799734 (10 nM; 24 h) inhibits phosphorylation of both SMAD1 and SMAD2[1].
AZ12799734 (500 nM; 36 h) inhibits TGFβ-induced migration in HaCaT epithelial cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	HaCaT cells and NIH3T3 cells

Concentration:	10 nM
Incubation Time:	10 days (HaCaT) or 24 h (NIH3T3)
Result:	Blocked TGFβ-mediated induction of SMAD2 phosphorylation. Inhibited phosphorylation of both SMAD1 and SMAD2.

Cell Migration Assay [1]

Cell Line:	HaCaT epithelial cells
Concentration:	500 nM
Incubation Time:	36 h
Result:	A dose-dependent decrease in TGFβ-induced migration was observed.

In Vivo

AZ12799734 (0-400 mg/kg/day; p.o.; 3-7 days) induces histopathologic heart valve lesions in rat[2].
AZ12799734 (50 mg/kg; p.o.; once) shows total and free pharmacokinetic (PK) levels in the nude mouse with time over in vitro IC_{50} of 0.01885 μM[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Ten-week-old female HsdHan:WIST rats[2]
Dosage:	200 and 400 mg/kg/day
Administration:	Oral, 3-7 days
Result:	Hemorrhage into the heart valves was evident at low magnification and the normal architecture of the leaflet was replaced by hemorrhage. Increased valvular interstitial cells in size and number and shows increased cytoplasm, an enlarged round to spindeloid nucleus, and frequently undergoing mitosis.

Animal Model:	Female BALB/c mice[1]
Dosage:	50 mg/kg
Administration:	Oral administration (Pharmacokinetic Analysis)
Result:	Showed total and free pharmacokinetic (PK) levels with time over in vitro IC_{50} of 0.01885 μM.

REFERENCES

[1]. Spender LC, et al. Preclinical Evaluation of AZ12601011 and AZ12799734, Inhibitors of Transforming Growth Factor β Superfamily Type 1 Receptors. Mol Pharmacol. 2019 Feb;95(2):222-234.

[2]. Anderton MJ, et al. Induction of heart valve lesions by small-molecule ALK5 inhibitors. Toxicol Pathol. 2011 Oct;39(6):916-24.

Caution: Product has not been fully validated for medical applications. For research use only.

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