H3B-6527

Cat. No.: HY-100491

CAS No.: 1702259-66-2

Molecular Formula: $C_{29}H_{34}Cl_2N_8O_4$

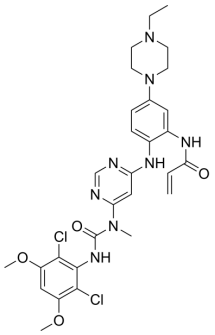
Molecular Weight: 629.54

Target: FGFR

Pathway: Protein Tyrosine Kinase/RTK

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 2.5 mg/mL (3.97 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.5885 mL	7.9423 mL	15.8846 mL
	5 mM	---	---	---
	10 mM	---	---	---

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

BIOLOGICAL ACTIVITY

Description

H3B-6527 is an orally active, highly selective and covalent FGFR4 inhibitor with an IC_{50} of <1.2 nM. H3B-6527 has at least 250-fold selectivity over FGFR1-3 with IC_{50}s of 320 nM, 1290 nM and 1060 nM respectively. H3B-6527 has potent anti-cancer activity[1].

IC_{50} & Target

FGFR4	FGFR1	FGFR2	FGFR3
<1.2 nM (IC_{50})	320 nM (IC_{50})	1290 nM (IC_{50})	1060 nM (IC_{50})

In Vitro

H3B-6527 inhibits TAOK2, JNK2, and CSF1R with IC_{50}s of 690 nM, >10000 nM, and >10000 nM, respectively[1].

H3B-6527 (10-10000 nM; 72 hours) results in a GI_{50} value of 25 nM[1].

H3B-6527 (10-10000 nM; 72 hours) leads cell death in HCC cell lines[1].

H3B-6527 (0.1-1000 nM; 1 hour) decreases the levels of pERK1/2 in a dose-dependent manner with maximal inhibition occurring at 100 nM[1].

H3B-6527 (1-1000 nM; 24 hours) causes a robust increase in CYP7A1 transcripts[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	Hepatocellular carcinoma (HCC) cell line Hep3B
Concentration:	10, 100, 1000, 10000 nM
Incubation Time:	72 hours
Result:	Resulted in a GI_{50} value of 25 nM.

Apoptosis Analysis[1]

Cell Line:	Hepatocellular carcinoma (HCC) cell line Hep3B
Concentration:	10, 100, 1000, 10000 nM
Incubation Time:	72 hours
Result:	Leaded cell death in HCC cell lines.

Western Blot Analysis[1]

Cell Line:	Hepatocellular carcinoma (HCC) cell line Hep3B
Concentration:	0.1, 0.3, 1, 3, 10, 100, 1000 nM
Incubation Time:	1 hour
Result:	Decreased the levels of pERK1/2 in a dose-dependent manner with maximal inhibition occurring at 100 nM.

RT-PCR[1]

Cell Line:	Hepatocellular carcinoma (HCC) cell line Hep3B
Concentration:	1, 10, 100, 1000 nM
Incubation Time:	24 hours
Result:	Caused a robust increase in CYP7A1 transcripts.

In Vivo

H3B-6527 (10-300 mg/kg; orally; twice-daily; for 15 days) significantly inhibits tumor growth at the 300 and 100 mg/kg and does not inhibit tumor growth at 30 and 10 mg/kg[1].

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Animal Model:	BALB/c nu/nu female mice approximately 8-week-old, weighing 18-20 g bearing Hep3B orthotopic xenografts in liver[1]
Dosage:	10, 30, 100, 300 mg/kg
Administration:	Orally; twice-daily; for 15 days
Result:	Inhibited tumor growth at the 300 and 100 mg/kg twice-daily dose.

REFERENCES

[1]. Joshi JJ, et al. H3B-6527 Is a Potent and Selective Inhibitor of FGFR4 in FGF19-Driven HepatocellularCarcinoma. Cancer Res. 2017 Dec 15;77(24):6999-7013.

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

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