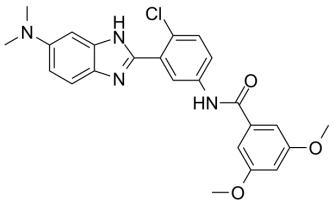
HhAntag

Cat. No.:	HY-15412
CAS No.:	496794-70-8
Molecular Formula:	$C_{24}H_{23}ClN_4O_3$
Molecular Weight:	450.92
Target:	Smo
Pathway:	Stem Cell/Wnt

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (221.77 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2177 mL	11.0884 mL	22.1769 mL
5 mM	0.4435 mL	2.2177 mL	4.4354 mL
10 mM	0.2218 mL	1.1088 mL	2.2177 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 3 mg/mL (6.65 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 3 mg/mL (6.65 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

HhAntag is a specific, potent and orally active small molecule SMO antagonist of the Hh pathway[1].

In Vitro

HhAntag (2-30 μM; 72 hours) demonstrates to be 10-times more potent than the natural product SMO antagonist, cyclopamine, at inhibiting Hh pathway activity and it inhibits Hh signalling pathway sensitivitive cells with IC_{50} values ranging from 2 μM to >30 μM[1].

HhAntag inhibits AsPC-1, BXPC-3, CFPAC, HPAC, HPAF-II, KP4, Panc 03.27, PA-TU-8902, PSN-1, SU.86.86 cells with IC_{50} values of 30 μM, 5.4 μM, 5.8 μM, 2.7 μM, 6.2 μM,10.3 μM, 2.5 μM, 2.9 μM, 5.8 μM and 2.7 μM, respectively[1].

HhAntag (100 nM) is needed to completely inhibit Hh signalling in a Hh-responsive human mesenchymal cell line (HEPM) expressing a GLI luciferase reporter construct (HEPM-rep), the IC_{50} of 5 nM 400-times lower than that required to inhibit cell

	growth by 50% in the most sensitive cancer cell line (1.9 μM)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	HhAntag (oral administraion; 75 mg/kg or 100 mg/kg; twice daily; 25 days) results in significant growth delay in HT55 and HT-29 colorectal cell line xenografts models, with average tumour growth inhibitions of 29% and 48%, respectively. Whereas HhAntag had no effect on the growth of DLD-1 xenografts[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Primary human xenografts in female CD1 nu/nu mice of 6–8 weeks (DLD-1, HT55 and HT-29 cells)[1]
Dosage:	75 mg/kg or 100 mg/kg
Administration:	Oral administraion; twice daily; 25 days
Result:	Resulted in growth delay of HT55 and HT-29 xenografts, but had no effects on DLD-1 xenografts.

REFERENCES

[1]. Neeraj Mahindroo, et al. Amide conjugates of ketoprofen and indole as inhibitors of Gli1-mediated transcription in the Hedgehog pathway. Bioorg Med Chem. 2010 Jul 1;18(13):4801-11.

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