AKN-028

Cat. No.: HY-118304

CAS No.: 1175017-90-9

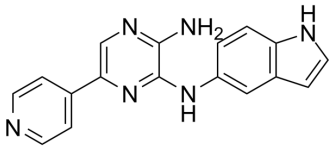
Molecular Formula: $C_{17}H_{14}N_6$

Molecular Weight: 302.33

Target: FLT3; Apoptosis; Caspase

Pathway: Protein Tyrosine Kinase/RTK; Apoptosis

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (413.46 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	3.3076 mL	16.5382 mL	33.0764 mL
	5 mM	0.6615 mL	3.3076 mL	6.6153 mL
	10 mM	0.3308 mL	1.6538 mL	3.3076 mL

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

BIOLOGICAL ACTIVITY

Description

AKN-028, a novel tyrosine kinase (TK) inhibitor, is a potent, orally active FMS-like receptor tyrosine kinase 3 (FLT3) inhibitor with an IC_{50} value of 6 nM. AKN-028 inhibits FLT3 autophosphorylation. AKN-028 induces dose-dependent cytotoxic response (mean IC_{50}=1 μM). AKN-028 induces apoptosisby activation of caspase 3. AKN-028 can be used in research of acute myeloid leukemia (AML)[1].

IC_{50} & Target

IC50: 6 nM (FLT3), 140 nM (CLK1), 220 nM (RPS6KA), 520 nM (VEGFR2), and 120 nM (FGFR2)[1]

In Vitro

AKN-028 (0.1 nM-100 μM; 15 h; mouse embryonal fibroblasts and human acute megakaryoblastic leukemia M07 cells) inhibits FLT3 and KIT autophosphorylation in a dose-dependent manner[1].

AKN-028 (10 μM; 72 h; tumor cell lines) is cytotoxic to AML cell lines and induces apoptosis in the AML cell line MV4-11[1].

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

Western Blot Analysis[1]

Cell Line:	Mouse embryonal fibroblasts either overexpressing FLT-wt, FLT3-TKD or FLT3-ITD and human acute megakaryoblastic leukemia M07 cells overexpressing KIT

Concentration:	0.1 nM-100 μM
Incubation Time:	15 hours
Result:	Inhibited FLT3 and KIT autophosphorylation.

Cell Cytotoxicity Assay[1]

Cell Line:	Tumor cell lines
Concentration:	10 μM
Incubation Time:	72 hours
Result:	Had cytotoxic activity was highest in MV4-11 and MOLM-13 (IC_{50}<50 nM), followed by the three other AML cell lines (IC_{50}=0.5-6 μM).

In Vivo

AKN-028 (15 mg/kg; i.h.; twice daily, for 6 days; male C57 black mice with MV4-11 xenografts) inhibits growth of primary AML and MV4-11 cells in mice[1].

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

Animal Model:	Male C57 black mice with MV4-11 xenografts[1]
Dosage:	15 mg/kg
Administration:	Subcutaneous injection; twice daily, for 6 days
Result:	Inhibited tumor growth and did not affect body weight.

REFERENCES

[1]. A Eriksson, et al. The Novel Tyrosine Kinase Inhibitor AKN-028 Has Significant Antileukemic Activity in Cell Lines and Primary Cultures of Acute Myeloid Leukemia. Blood Cancer J. 2012 Aug 3;2(8):e81.

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