MNK1/2-IN-7

Cat. No.: HY-163479

CAS No.: 2548283-27-6

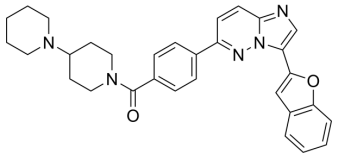
Molecular Formula: $C_{31}H_{31}N_5O_2$

Molecular Weight: 505.61

Target: Eukaryotic Initiation Factor (eIF); MNK

Pathway: Cell Cycle/DNA Damage; MAPK/ERK Pathway

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



BIOLOGICAL ACTIVITY

Description

MNK1/2-IN-7 (compound 20j) is an orally available inhibitor of MNK1/2 with anticancer activity and hERG safety. MNK1/2-IN-7 also inhibits the phosphorylation of eIF4E, inhibiting the MNK/eIF4E signaling pathway and cancer cell proliferation. MNK1/2-IN-7 is synergistic with Ibrutinib (HY-109970).[15][1].

IC_{50} & Target

MNK1	MNK2
4.4 nM (IC_{50}, [1])	0.4 nM (IC_{50}, [1])

In Vitro

MNK1/2-IN-7 (1.25-5 μM; 24 h) inhibits the phosphorylation of eIF4E in Hela cells (IC_{50}=90.5 nM) and downregulates the phosphorylation of eIF4E and 4E-BP1 in A549 cells [1].

MNK1 /2-IN-7 shows stability in liver microparticles of humans, dogs, and rats, with $T_{1/2}$ being 62.6 min, >120 min, and 64.6 min respectively[1].br /

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

Western Blot Analysis[1]

Cell Line:	A549 cell line
Concentration:	1.25 μM, 2.5 μM, 5 μM
Incubation Time:	24 h
Result:	Downregulated the phosphorylation of eIF4E and 4E-BP1.

In Vivo

MNK1/2-IN-7 (5 mg/kg; po; single dose) exhibits acceptable exposure and bioavailability in rats and is orally effective [1].

MNK1/2-IN-7 (10 mg/kg; po; 17 d) effectively caused tumor regression in a DOHH2 xenograft mouse model without affecting mouse body weight. MNK1/2-IN-7 also has a synergistic effect with Ibrutinib (HY-109970)[1].

Pharmacokinetic Analysis in SD Rats[1]

Route	Dose (mg/kg)	$T_{1/2}$ (h)	T_{max} (h)	C_{max} (μg/mL)	AUC_{0-t} (h·μg/mL)	$AUC_{0-\infty}$ (h·μg/mL)	Cl (mL/h/kg)	F (%)
i.v.	1	13.8	0.083	1.3	10.0	14.4	70.2	/

p.o.	5	>24	6	1.5	23.3	NA	/	46.86

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Animal Model:	GCB-DLBCL DOHH2 xenograft tumors model in mouse[1]
Dosage:	10 mg/kg
Administration:	po; once daily for 17 days; or combination of 3 mg/kg Ibrutinib
Result:	Resulted tumor regression Achieved a greater TGI value of 54% for combination group at the end of treatment compared to the value for a single administration or ibrutinib administration.

REFERENCES

[1]. Yuan X, et al. Development of an Imidazopyridazine-Based MNK1/2 Inhibitor for the Treatment of Lymphoma[J]. Journal of Medicinal Chemistry, 2024.

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