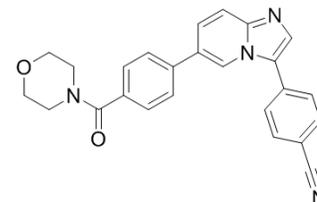


ETC-206

Cat. No.:	HY-112424		
CAS No.:	1464151-33-4		
Molecular Formula:	C ₂₅ H ₂₀ N ₄ O ₂		
Molecular Weight:	408.45		
Target:	MNK		
Pathway:	MAPK/ERK Pathway		
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 : ≥ 50 mg/mL (122.41 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration \ Mass	1 mg	5 mg	10 mg
	1 mM	2.4483 mL	12.2414 mL	24.4828 mL
5 mM	0.4897 mL	2.4483 mL	4.8966 mL	
10 mM	0.2448 mL	1.2241 mL	2.4483 mL	

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

In Vivo

- Add each solvent one by one: **10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline**
Solubility: ≥ 5 mg/mL (12.24 mM); Clear solution
- Add each solvent one by one: **10% DMSO >> 90% (20% SBE-β-CD in saline)**
Solubility: ≥ 5 mg/mL (12.24 mM); Clear solution
- Add each solvent one by one: **10% DMSO >> 90% corn oil**
Solubility: ≥ 5 mg/mL (12.24 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ETC-206 is a selective MNK1 and MNK2 inhibitor with IC₅₀s of 64 nM and 86 nM, respectively.

IC₅₀ & Target

MNK1 64 nM (IC ₅₀)	MNK2 86 nM (IC ₅₀)
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In Vitro	ETC-206 inhibits eIF4E phosphorylation in HeLa cell line with an IC ₅₀ of 321 nM. The anti-proliferative effects of ETC-206 are assessed in vitro, using CellTiter-Glo viability assay against 25 hematological cancer cell lines including the K562 cell line that overexpresses eIF4E (K562 o/e eIF4E). The IC ₅₀ s are 1.71 μM, 3.36 μM, 3.70 μM, 4.81 μM, 5.13 μM, 5.05 μM, 6.70 μM, 9.76 μM, and 48.8 μM for SU-DHL-6, GK-5, MC 116, P3HR-1, DOHH2, MPC-11, Ramos.2G6.4C10, AHH-1, and K562 o/e eIF4E cells, respectively ^[1] .
In Vivo	The antitumor effect of ETC-206 is then assessed in a K562 e/o eIF4E mouse xenograft model after oral administration at 25, 50, or 100 mg/kg alone or in combination with a 2.5 mg/kg fixed dose of Dasatinib throughout the study. Dasatinib at 2.5 mg/kg elicits a tumor growth inhibition (TGI) of 88% with one tumor-free animal. In contrast, ETC-206 alone only yields a maximum TGI of 23% at the highest administered dose of 100 mg/kg, which does not impede tumor growth, and is similar to the nontreated animals. ETC-206 with 2.5 mg/kg of Dasatinib not only increases tumor growth inhibition in a dose-dependent manner but, more importantly leads to 2, 5, and 8 out of 8 tumor-free animals at 25, 50, and 100 mg/kg, respectively. The combination of ETC-206 and Dasatinib inhibits tumor growth at all tested doses, and no weight loss is recorded. Both the combination of ETC-206 and Dasatinib and, on the other hand, the dual MNK1/2 and BCR-ABL1 inhibitors prevent tumor growth in the same mouse xenograft model. ETC-206 has moderate terminal elimination half-life (t _{1/2} =1.7 h, and 1.77 h for mouse (1 mg/kg, i.v.), mouse (5 mg/kg, p.o.)) ^[1] .

PROTOCOL

Cell Assay ^[1]	The anti-proliferative effects of ETC-206 are assessed in vitro, using CellTiter-Glo viability assay against 25 hematological cancer cell lines including the K562 cell line that overexpresses eIF4E (K562 o/e eIF4E). The IC ₅₀ s are in general in the micromolar range ^[1] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration ^[1]	Mice ^[1] CD-1 female mice (6-8 weeks old) are weighed, and those selected for dosing are 24±2 g. Three mice are randomly grouped per time point. Mice are administered a single dose of 1 mg/kg of ETC-206 via tail vein injection or a single dose of 5 mg/kg of ETC-206 via oral gavage . The volume of injection for intravenous (i.v.) and oral (p.o.) administration is 4 mL/kg and 8 mL/kg, respectively ^[1] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Yang H, et al. Optimization of Selective Mitogen-Activated Protein Kinase Interacting Kinases 1 and 2 Inhibitors for the Treatment of Blast Crisis Leukemia. J Med Chem. 2018 May 24;61(10):4348-4369.

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

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