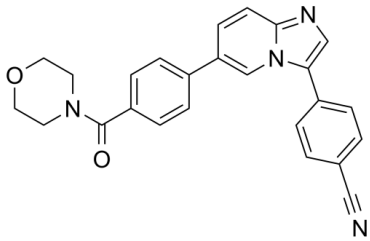
Data Sheet

Product Name:	ETC-206
Cat. No.:	CS-0046041
CAS No.:	1464151-33-4
Molecular Formula:	C25H20N4O2
Molecular Weight:	408.45
Target:	MNK
Pathway:	MAPK/ERK Pathway
Solubility:	DMSO : ≥ 50 mg/mL (122.41 mM)



BIOLOGICAL ACTIVITY:

ETC-206 is a selective **MNK1** and **MNK2** inhibitor with **IC_{50}**s of 64 nM and 86 nM, respectively. IC50 & Target: IC50: 64 nM (MNK1), 86 nM (MNK2)[1] **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 (Extracted from published papers and Only for reference)

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].

Animal Administration: ETC-206 is weighed and dissolved in 1/10 volumes of 100% DMA solution and 1/10 volumes of 100% CremophorEL (intravenous administration)[1].

ETC-206 is dissolved in a mixture of 0.5% methylcellulose and 0.1% Tween80 (oral administration)[1].[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].

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.

CAIndexNames:

Benzonitrile, 4-[6-[4-(4-morpholinylcarbonyl)phenyl]imidazo[1,2-a]pyridin-3-yl]-

SMILES:

N#CC1=CC=C(C2=CN=C3C=CC(C4=CC=C(C(N5CCOCC5)=O)C=C4)=CN32)C=C1

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