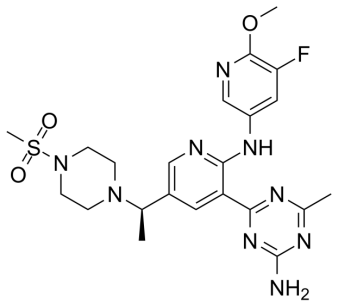
AMG 511

Cat. No.:	HY-13440
CAS No.:	1253573-53-3
Molecular Formula:	$C_{22}H_{28}FN_9O_3S$
Molecular Weight:	517.58
Target:	PI3K
Pathway:	PI3K/Akt/mTOR
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 : 33.33 mg/mL (64.40 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9321 mL	9.6603 mL	19.3207 mL
5 mM	0.3864 mL	1.9321 mL	3.8641 mL
10 mM	0.1932 mL	0.9660 mL	1.9321 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2 mg/mL (3.86 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

AMG 511 is a potent and orally available pan inhibitor of class I PI3Ks, with K_is of 4 nM, 6 nM, 2 nM and 1 nM for PI3Kα, β, δ and γ, respectively. AMG 511 significantly suppresses PI3K signaling that is indicated by p-Akt (Ser473) decrease. AMG 511 exhibits anti-tumor activity in mouse glioblastoma xenograft model[1].

IC_{50} & Target

PI3Kα	PI3Kβ	PI3Kδ	PI3Kγ
4 nM (Ki)	6 nM (Ki)	2 nM (Ki)	1 nM (Ki)

In Vitro

AMG 511 shows the inhibition of AKT (Ser473) phosphorylation in U87 malignant glioma (MG) cells with an IC_{50} of 4 nM[1].

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

In Vivo

AMG 511 potently blocks the targeted PI3K pathway in a mouse liver pharmacodynamic model (3-30 mg/kg; p.o.) and inhibits tumor growth in a U87 MG glioblastoma xenograft model (3-30 mg/kg; p.o.; daily; for 12 days)[1].

AMG 511 shows excellent in vivo efficacy and pharmacokinetic profile[1].

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

Animal Model:	Female CD1 NU/NU mice, with U87 MG glioblastoma xenograft model[1]
Dosage:	1 mg/kg, 3 mg/kg, 10 mg/kg
Administration:	Oral administration, daily, for 12 days
Result:	Inhibited tumor growth.

Animal Model:	Male Sprague-Dawley rats[1]
Dosage:	1 mg/kg
Administration:	Oral administration (Pharmacokinetic Analysis)
Result:	Had a superior pharmacokinetic profile with low clearance (0.4 L/h/kg, 12% of liver blood flow), good oral bioavailability (F = 60%), and a commensurate high oral exposure (AUC = 5.0 μM·h).

CUSTOMER VALIDATION

- Cancer Lett. 2022 Jun 28;536:215660.
- Exp Ther Med. 2021 Jun 8.

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REFERENCES

[1]. Mark H Norman, et al. Selective Class I Phosphoinositide 3-kinase Inhibitors: Optimization of a Series of Pyridyltriazines Leading to the Identification of a Clinical Candidate, AMG 511. J Med Chem. 2012 Sep 13;55(17):7796-816.

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