AMG PERK 44

Cat. No.: HY-12661A

CAS No.: 1883548-84-2

Molecular Formula: $C_{34}H_{29}ClN_4O_2$

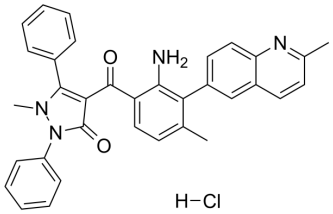
Molecular Weight: 561.07

Target: PERK; Autophagy

Pathway: Cell Cycle/DNA Damage; Autophagy

Storage: -20°C, sealed storage, away from moisture

* In solvent : -80°C, 1 years; -20°C, 6 months (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (44.56 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7823 mL	8.9115 mL	17.8231 mL
	5 mM	0.3565 mL	1.7823 mL	3.5646 mL
	10 mM	0.1782 mL	0.8912 mL	1.7823 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (3.71 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.71 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.71 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AMG PERK 44 is an orally active and highly selective PERK inhibitor with an IC_{50} of 6 nM. AMG PERK 44 has 1000-fold and 160-fold selectivity over GCN2 (IC_{50}=7300 nM) and B-Raf (IC_{50} >1000 nM), respectively. AMG PERK 44 induces autophagy[1][2].

IC_{50} & Target

IC50: 6 nM (PERK)[1]

In Vitro

AMG PERK 44 has an IC_{50} of 84 nM for cell pPERK[1].

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

In Vivo

AMG PERK 44 (orally; 3-100 mg/kg) robustly inhibits PERK autophosphorylation in this assay (ED_{50}=3 mg/kg; ED_{90}=60 mg/kg

at the 4 hours time point), and >50% target coverage is maintained for 24 h in a time course PD assay when dosed at 100 mg/kg po[1].

AMG PERK 44 (iv; 1 mg/kg) has a CL of 1.6 L/h•kg, a V_{ss} of 3.6 L/kg and MRT of 2.3 hours in Sprague-Dawley rats and male CD-1 mice[1].

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

Animal Model:	Four- to six-week old naive athymic nude mice[1]
Dosage:	3, 10, 30, 100 mg/kg
Administration:	Orally
Result:	Robustly inhibited PERK autophosphorylation in this assay (ED_{50}=3 mg/kg; ED_{90}=60 mg/kg at the 4 hours time point).

Animal Model:	Sprague-Dawley rats and male CD-1 mice[1]
Dosage:	1 mg/kg (Pharmacokinetic Analysis)
Administration:	Iv
Result:	Had a CL of 1.6 L/h•kg, a V_{ss} of 3.6 L/kg and a MRT of 2.3 hours.

CUSTOMER VALIDATION

- Cancer Res Commun. 2023 Nov 9.
- bioRxiv. 2023 Jul 27

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REFERENCES

[1]. Smith AL, et al. Discovery of 1H-pyrazol-3(2H)-ones as potent and selective inhibitors of protein kinase R-like endoplasmic reticulum kinase (PERK). J Med Chem. 2015 Feb 12;58(3):1426-41.

[2]. Roest G, et al. The ER Stress Inducer l-Azetidine-2-Carboxylic Acid Elevates the Levels of Phospho-eIF2α and of LC3-II in a Ca2+-Dependent Manner. Cells. 2018 Nov 30;7(12). pii: E239.

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

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