PF-06446846 hydrochloride

Cat. No.: HY-120088A

CAS No.: 1632250-50-0

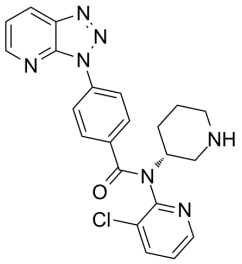
Molecular Formula: $C_{22}H_{21}Cl_2N_7O$

Molecular Weight: 470.35

Target: Ser/Thr Protease

Pathway: Metabolic Enzyme/Protease

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 2 years; -20°C, 1 year (sealed storage, away from moisture)



H−Cl

SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (531.52 mM; Need ultrasonic)
H_2O : 100 mg/mL (212.61 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1261 mL	10.6304 mL	21.2608 mL
5 mM	0.4252 mL	2.1261 mL	4.2522 mL
10 mM	0.2126 mL	1.0630 mL	2.1261 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 100 mg/mL (212.61 mM); Clear solution; Need ultrasonic and warming and heat to 60°C
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.42 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.42 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.42 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PF-06446846 hydrochloride is an orally active and highly selective inhibitor of translation of Proprotein convertase subtilisin/kexin type 9 (PCSK9). PF-06446846 hydrochloride inhibits PCSK9 by inducing the ribosome to stall around codon 34[1].

IC_{50} & Target

PCSK9[1]

In Vitro	PF-06446846 inhibits the secretion of PCSK9 by Huh7 cells with an IC_{50} of 0.3 μM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	PF-06446846 (oral gavage; 5-50 mg/kg/day for 14 days) lowers plasma PCSK9 in a dose-dependent manner and lowers total cholesterol levels[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male Sprague-Dawley (Crl:CD [SD] rats, 6-8 wk old at initiation of dosing)[1]
Dosage:	5, 15, and 50 mg/kg
Administration:	Oral gavage; daily for 14 days
Result:	Lowered plasma PCSK9 in a dose-dependent manner and lowered total cholesterol levels.

CUSTOMER VALIDATION

- Protein Cell. 2021 Apr;12(4):240-260.

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REFERENCES

[1]. Lintner NG, et al. Selective stalling of human translation through small-molecule engagement of the ribosome nascent chain. PLoS Biol. 2017 Mar 21;15(3):e2001882.

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