IACS-010759 hydrochloride

Cat. No.: HY-112037A

CAS No.: 1807523-99-4

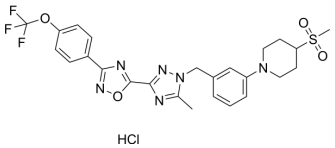
Molecular Formula: $C_{25}H_{26}ClF_3N_6O_4S$

Molecular Weight: 599.02

Target: Apoptosis; Mitochondrial Metabolism; Oxidative Phosphorylation

Pathway: Apoptosis; Metabolic Enzyme/Protease

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 60 mg/mL (100.16 mM; Need ultrasonic)
H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.6694 mL	8.3470 mL	16.6939 mL
5 mM	0.3339 mL	1.6694 mL	3.3388 mL
10 mM	0.1669 mL	0.8347 mL	1.6694 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.5 mg/mL (4.17 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

IACS-010759 hydrochlorideis an orally active, potent mitochondrial complex I of oxidative phosphorylation (OXPHOS) inhibitor. IACS-010759 hydrochlorideinhibits proliferation and induces apoptosis in models of brain cancer and acute myeloid leukemia (AML) reliant on OXPHOS. IACS-010759 hydrochloride has the potential for relapsed/refractory AML and solid tumors research[1][2].

IC_{50} & Target

OXPHOS[1]

In Vitro

IACS-010759 hydrochloride (10, 30, 100?nM; for 4 or 5 days) reduces viability and induces apoptosis in primary AML[1].
?IACS-010759 hydrochloride (0.001, 0.01, 0.1, 1, 10, 100, 1000 nM; 72 hurs) robustly inhibits both OCR and galactose-dependent H460 cell viability and has nearly identical IC50 values of 1.4?nM[1].
?IACS-010759 hydrochlorideis similarly active in mouse (average IC50?=?5.6?nM), rat (IC50?=?12.2?nM), and cynomolgus monkey (IC50?=?8.7?nM) cell lines[1].
?

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	IACS-010759 hydrochloride (5, 10, 25?mg/kg/day; oral; for 21 d) results in tumor regression with minimal body weight loss at the 5 or 10?mg/kg dose in mice bearing NB-1 (PGD-null) subcutaneous xenografts. IACS-010759 at the 25?mg/kg dose is not tolerated[1]. ?IACS-010759 HCl (10?mg/kg; orally; QD (daily) or QD×5 (5 d on/2 d off); for 35 d) increases median survival from 28 d to longer than 60 d, whereas less-frequent dosing schedules (Q2D or Q3D) enhances survival to a lesser extent[1]. ?IACS-010759 hydrochloride (0.3?mg/kg for iv; 1?mg/kg for oral) has low plasma clearance with a high volume of distribution, resulting in a prolonged terminal half-life (>24?h)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Discov. 2022 Oct 6;8(1):102.
- Nat Commun. 2023 Jul 14;14(1):4221.
- Cell Rep Med. 2022 Nov 3;100802.
- Biochem Biophys Res Commun. 2023 Jun 1.
- Biochem Biophys Res Commun. 2021 Mar 16;552:23-29.

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REFERENCES

[1]. Protopopova M. IACS-10759: A novel OXPHOS inhibitor which selectively kill tumors with metabolic vulnerabilities. [abstract]. In: Proceedings of the 106th Annual Meeting of the American Association for Cancer Research; 2015 Apr 18-22; Philadelphia, PA. Philadelphia (PA): AACR; Cancer Res 2015;75(15 Suppl):Abstract nr 4380. doi:10.1158/1538-7445.AM2015-4380

[2]. Jennifer R Molina, et al. An inhibitor of oxidative phosphorylation exploits cancer vulnerability. Nat Med. 2018 Jul;24(7):1036-1046.

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