Parsaclisib hydrochloride

Cat. No.: HY-109068A

CAS No.: 1995889-48-9

Molecular Formula: $C_{20}H_{23}Cl_2FN_6O_2$

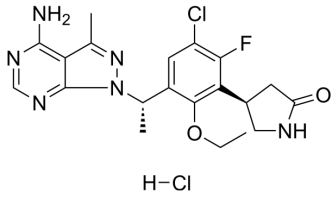
Molecular Weight: 469.34

Target: PI3K

Pathway: PI3K/Akt/mTOR

Storage: 4°C, stored under nitrogen

* In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 240 mg/mL (511.36 mM; Need ultrasonic)

H_2O : 100 mg/mL (213.07 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1307 mL	10.6533 mL	21.3065 mL
5 mM	0.4261 mL	2.1307 mL	4.2613 mL
10 mM	0.2131 mL	1.0653 mL	2.1307 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 50 mg/mL (106.53 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 6 mg/mL (12.78 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 6 mg/mL (12.78 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 6 mg/mL (12.78 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Parsaclisib hydrochloride (INCB050465 hydrochloride) is a potent, selective and orally active inhibitor of PI3Kδ, with an IC_{50} of 1 nM at 1 mM ATP. Parsaclisib hydrochloride shows approximately 20000-fold selectivity over other PI3K class I isoforms. Parsaclisib hydrochloride can be used for the research of relapsed or refractory B-cell malignancies[1][2][3].

IC_{50} & Target

PI3Kδ

1 nM (IC_{50})

In Vitro

Parsaclisib (0.1-3000 nM; 4 d) inhibits proliferation of MCL and DLBCL cell lines[2].

Parsaclisib (0.1-1000 nM; 2 h) inhibits anti-IgM-induced pAKT (Ser473) in the Ramos Burkitt's lymphoma cell line, with an IC_{50} of 1 nM[2].

Parsaclisib inhibits the proliferation of human, dog, rat, and mouse primary B cells after activation of these receptors, with IC_{50}s ranging from 0.2 to 1.7 nM[2].

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

Cell Proliferation Assay[2]

Cell Line:	Jeko-1, Mino, JVM2, Rec-1, Pfeiffer, SU-DHL-5, SU-DHL-6, WSU-NHL, SU-DHL-4, SU-DHL-8, and WILL-2 cells
Concentration:	0.1-3000 nM
Incubation Time:	4 days
Result:	Resulted in a maximal inhibition of 70-90%, with IC_{50}s of ≤10 nM in the four MCL cell lines. Pfeiffer, SU-DHL-5, SU-DHL-6, and WSU-NHL were highly sensitive, with IC_{50}s from 2 to 8 nM.

In Vivo

Parsaclisib (10 mg/kg; oral gavage twice daily for 7-19 days) inhibits tumor growth in the BALB/c mice bearing the A20 murine lymphoma cells[2].

Parsaclisib (0.1-10 mg/kg; p.o. twice daily) slows Pfeiffer xenograft tumor growth in a dose-dependent manner. And Parsaclisib was well tolerated[2].

Parsaclisib (0.5-1 mg/kg; a single p.o.) inhibits pAKT (Ser473) in Pfeiffer subcutaneous mouse xenograft models[2].

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

Animal Model:	Female BALB/c mice (5-9 weeks) were inoculated with A20 cells[2]
Dosage:	10 mg/kg
Administration:	Oral gavage twice daily for 7-19 days
Result:	Resulted in significant tumor growth inhibition (TGI). Reduced the percentage of Tregs ($CD4^+CD25^+FOXP3^+$) in tumors and spleens. Increased the ratio of $CD4^+$ and $CD8^+$ T cells to Tregs in spleens and tumors. Decreased the number of $CD4^+CD44^{high}$ and $CD8^+CD44^{high}$ T cells in both spleens and tumors.

REFERENCES

[1]. Shin N, et al. Abstract 2671: INCB050465, a novel PI3Kδ inhibitor, synergizes with PIM protein kinase inhibition to cause tumor regression in a model of DLBCL. Cancer Research. 2015, Aug. 75(15).

[2]. Shin N, et, al. Parsaclisib Is a Next-Generation Phosphoinositide 3-Kinase δ Inhibitor with Reduced Hepatotoxicity and Potent Antitumor and Immunomodulatory Activities in Models of B-Cell Malignancy. J Pharmacol Exp Ther. 2020 Jul;374(1):211-222.

[3]. Yue EW, et, al. INCB050465 (Parsaclisib), a Novel Next-Generation Inhibitor of Phosphoinositide 3-Kinase Delta (PI3Kδ). ACS Med Chem Lett. 2019 Oct 17;10(11):1554-1560.

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

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