2,6-Dichloro-N-(2-(cyclopropanecarboxamido)pyridin-4-yl)benzamide

Cat. No.: HY-120469

CAS No.: 1258292-64-6

Molecular Formula: $C_{16}H_{13}Cl_2N_3O_2$

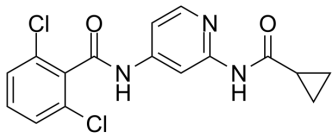
Molecular Weight: 350.2

Target: JAK

Pathway: Epigenetics; JAK/STAT Signaling; Stem Cell/Wnt

Storage: 4°C, protect from light

* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 62.5 mg/mL (178.47 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8555 mL	14.2776 mL	28.5551 mL
	5 mM	0.5711 mL	2.8555 mL	5.7110 mL
	10 mM	0.2856 mL	1.4278 mL	2.8555 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 (5.94 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.94 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GDC-046 is a potent, selective, and orally bioavailable TYK2 inhibitor with K_is of 4.8, 0.7, 0.7, and 0.4 nM for TYK2, JAK1, JAK2, and JAK3, respectively[1].

IC_{50} & Target

Tyk2	JAK1	JAK2	JAK3
4.8 nM (Ki)	0.7 nM (Ki)	0.7 nM (Ki)	0.4 nM (Ki)

In Vitro

In cell-based assays, GDC-046 demonstrates reasonable potency in blocking the IL-12 pathway (IL-12 pSTAT4 EC_{50}=380 nM) while displaying less activity in the EPO (JAK2) pathway (EPO pSTAT5 EC_{50}=1700 nM) and IL-6 (JAK1) pathway (IL-6 pSTAT3 EC_{50}=2000 nM)[1].

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

In Vivo	In mice, GDC-046 exhibits relatively high clearance (65 mL/min/kg) when dosed intravenously (i.v. 1 mg/kg) and exhibits modest oral exposure (AUC=2.6 μM·h at p.o. 5 mg/kg)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Jun Liang, et al. Lead Optimization of a 4-aminopyridine Benzamide Scaffold to Identify Potent, Selective, and Orally Bioavailable TYK2 Inhibitors. J Med Chem. 2013 Jun 13;56(11):4521-36.

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