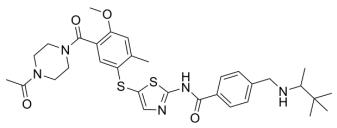
BMS-509744

Cat. No.:	HY-11092
CAS No.:	439575-02-7
Molecular Formula:	$C_{32}H_{41}N_5O_4S_2$
Molecular Weight:	624
Target:	Itk
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 1 year -20°C 6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 21.9 mg/mL (35.10 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6026 mL	8.0128 mL	16.0256 mL
	5 mM	0.3205 mL	1.6026 mL	3.2051 mL
	10 mM	0.1603 mL	0.8013 mL	1.6026 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: ≥ 2.5 mg/mL (4.01 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.01 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BMS-509744 is a potent, selective and ATP competitive Itk inhibitor with an IC_{50} of 19 nM.

IC_{50} & Target

IC50: 19 nM (Itk)[1]

In Vitro

BMS-509744 reduces T-cell receptor-induced functions including PLCγ1 tyrosine phosphorylation, calcium mobilization, IL-2 secretion, and T-cell proliferation in vitro in both human and mouse cells. BMS-488516 and BMS-509744 potently inhibit Itk in vitro with IC_{50} values of 96 and 19 nM, respectively. Both compounds exhibit competitive kinetics with respect to ATP, suggesting that they bind to the ATP binding site of the Itk kinase domain[1].

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

In Vivo	BMS-509744 and BMS-488516 suppress the production of IL-2 induced by anti-T-cell receptor antibody administered to mice. BMS-509744 exhibits a 50% inhibitory capacity when dosed at 50 mg/kg, irrespective of the amount of induction antibody. BMS-509744 also significantly diminishes lung inflammation in a mouse model of ovalbumin-induced allergy/asthma[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	BMS-509744 activity (IC_{50}) is determined by kinase assays. The kinase reactions are performed in the presence of 10 μM GST-SLP-76 and various concentrations of ATP for 10 min using 10 ng of enzyme. The concentrations of BMS-509744 MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: Balb/c mice are injected subcutaneously with the compounds (BMS-509744 and BMS-488516) or vehicle (H2O:ethanol:Tween 80) 90:5:5) 15 min before intravenous administration of anti-CD3 antibody. Serum is collected for the analysis of IL-2 and compound levels at 90 min after anti-CD3 antibody administration. IL-2 is measured by ELISA, and compound levels are measured by mass spectrometry[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Proc Natl Acad Sci U S A. 2022 Oct 25;119(43):e2207280119.
- Cancer Cell Int. 2019 Feb 14;19:32.
- Cancer Cell Int. 2019 Feb 14;19:32.
- Sci Rep. 2023 Sep 21;13(1):15678.
- Harvard Medical School LINCS LIBRARY

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REFERENCES

[1]. Lin TA, et al. Selective Itk inhibitors block T-cell activation and murine lung inflammation. Biochemistry.?2004 Aug 31;43(34):11056-62.

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