

BMS-066

Chemical Properties

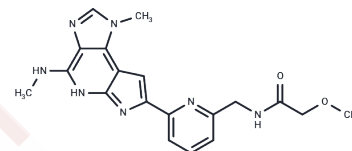
CAS No. : 914946-88-6

Formula: C₁₉H₂₁N₇O₂

Molecular Weight: 379.42

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Actual storage temperature shall be subject to the COA.



Biological Description

Description	BMS-066 is an IKK β /Tyk2 pseudokinase inhibitor with IC ₅₀ s of 9 nM and 72 nM, respectively.
Targets(IC ₅₀)	I κ B/IKK,JAK,Tyrosine Kinases
In vitro	BMS-066 demonstrates significant inhibition of IKK β -catalyzed phosphorylation in vitro, with a potent IC ₅₀ of 9 nM, exhibiting over 500-fold selectivity towards IKK β compared to IKK α . In assays with six kinases that were more than 75% inhibited at 10 μ M, BMS-066 displayed over 30-fold selectivity over the next most susceptible kinase (Brk), indicating its specificity. Additionally, BMS-066 showed IC ₅₀ values of 72 and 1020 nM in Tyk2 pseudokinase domain probe displacement and IL-23-stimulated reporter assays respectively. A broader selectivity assessment against 155 kinases at 10 μ M revealed that only six were inhibited more than 75%, confirming BMS-066's greater than 400-fold selectivity for IKK β over 95% of the kinases tested. BMS-066 also effectively inhibits LPS-stimulated cytokine production in human peripheral blood mononuclear cells (PBMCs) at both protein and mRNA levels, with similar IC ₅₀ values around 200 nM, and it inhibits IKK β -mediated phosphorylation of I κ B α in LPS-stimulated cells with a comparable efficacy.
In vivo	Clear reduction of inflammation is also evident in the low dose of BMS-066 (5 mg/kg) and the bone resorption seems to be more focal and less severe compared with the control. The joints from animals receiving 10 mg/kg BMS-066 are normal or show minimal changes in both inflammation and bone resorption. Bone density measurements also show a clear dose-dependent benefit of treatment with BMS-066. Microcomputed tomography of the hind limbs also show that BMS-066 provides a dose-dependent protection against the pitting, loss of bone mass, woven porous bone, and fusion of the small bones evident in the rats. Serum drug level measurements in satellite animals on the first day of dosing show that a single dose provides coverage for approximately 3 h (6 h daily with twice daily dosing) of the mouse whole-blood IC ₅₀ value against LPS-induced TNF- α . It is also showed that IKK β inhibitors suppress TNF- α and IL-1 β production within these tissues in experimental arthritis model[1].

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.6356 mL	13.178 mL	26.356 mL
5 mM	0.5271 mL	2.6356 mL	5.2712 mL
10 mM	0.2636 mL	1.3178 mL	2.6356 mL
50 mM	0.0527 mL	0.2636 mL	0.5271 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Gillooly KM, et al. Periodic, partial inhibition of IkappaB Kinase beta-mediated signaling yields therapeutic benefit in preclinical models of rheumatoid arthritis. *J Pharmacol Exp Ther.* 2009 Nov;331(2):349-60.

Tokarski JS, et al. Tyrosine Kinase 2-mediated Signal Transduction in T Lymphocytes Is Blocked by Pharmacological Stabilization of Its Pseudokinase Domain. *J Biol Chem.* 2015 Apr 24;290(17):11061-74.

Inhibitor · Natural Compounds · Compound Libraries · Recombinant Proteins

This product is for Research Use Only · Not for Human or Veterinary or Therapeutic Use

Tel:781-999-4286 E_mail:info@targetmol.com Address:34 Washington Street,Wellesley Hills,MA 02481