BMS-986202

Cat. No.: HY-131968

CAS No.: 1771691-34-9

Molecular Formula: $C_{22}H_{18}D_3FN_6O_3$

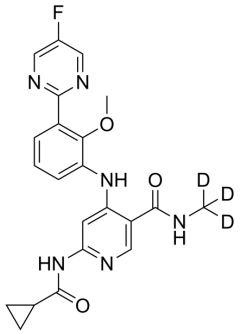
Molecular Weight: 439.46

Target: JAK; Cytochrome P450

Pathway: Epigenetics; JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Stem Cell/Wnt; Metabolic Enzyme/Protease

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (568.88 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2755 mL	11.3776 mL	22.7552 mL
5 mM	0.4551 mL	2.2755 mL	4.5510 mL
10 mM	0.2276 mL	1.1378 mL	2.2755 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 (4.73 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.73 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BMS-986202 is a potent, selective and orally active Tyk2 inhibitor that binds to Tyk2 JH2 with an IC_{50} value of 0.19 nM and a K_i of 0.02 nM. BMS-986202 is remarkably selective over other kinases including Jak family members. BMS-986202 is also a weak inhibitor of CYP2C19 with an IC_{50} value of 14 μM. BMS-986202 can be used for IL-23-driven acanthosis, anti-CD40-induced colitis, and spontaneous lupus research. BMS-986202 is a de novo deuterium[1].

IC_{50} & Target

Tyk2 JH2	Tyk2 JH2	CYP2C19
0.19 nM (IC_{50})	0.02 nM (Ki)	14 μM (IC_{50})

In Vitro

Stable heavy isotopes of hydrogen, carbon, and other elements have been incorporated into drug molecules, largely as

tracers for quantitation during the drug development process. Deuteration has gained attention because of its potential to affect the pharmacokinetic and metabolic profiles of drugs[1].
Potential advantages of deuterated compounds:
(1) Extend the half-life in vivo. Deuterated compounds may be able to prolong the pharmacokinetic characteristics of the compound, that is, prolong the half-life in vivo. This can improve compound safety, efficacy and tolerability, and increase ease of administration.
(2) Improve oral bioavailability. Deuterated compounds may reduce the degree of unwanted metabolism (first-pass metabolism) in the gut wall and liver, allowing a greater proportion of the unmetabolized drug to reach its target site of action. High bioavailability determines its activity at low doses and better tolerance.
(3) Improve metabolic characteristics. Deuterated compounds may reduce the formation of toxic or reactive metabolites and improve drug metabolism.
(4) Improve drug safety. Deuterated compounds may reduce or eliminate adverse side effects of pharmaceutical compounds and are safe.
(5) Preserve the therapeutic properties. Deuterated compounds are expected to retain similar biochemical potency and selectivity to hydrogen analogs in previous studies.
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

BMS-986202 (Compound 7; 3-30 mg/kg; p.o.; daily; for 9 days) treatment inhibits IL-23-driven acanthosis in mice[1].
BMS-986202 (Compound 7; 0.4-10 mg/kg; p.o.) treatment inhibits IL-12/IL-18-induced IFNγ production in mice. BMS-986202 dose-dependently inhibits IFNγ production by 46% and 80% at doses of 2 mg/kg and 10 mg/kg, respectively[1].
BMS-986202 (Compound 7; 7-10 mg/kg; p.o.) is stable in liver microsomes, with half lives of greater than 120 min in mouse, rat, monkey, and humans and 89 min in dog. The serum protein binding for BMS-986202 in these species ranges from 89.3% to 96.0%, leaving a good range of free fraction of drug available. BMS-986202 shows the oral bioavailability up to 62-100%[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	C57BL/6 female mice (9-11 weeks) injected with IL-23[1]
Dosage:	3 mg/kg, 10 mg/kg, and 30 mg/kg
Administration:	Oral administration; daily; for 9 days
Result:	Inhibited ear swelling in a dose-responsive manner in IL-23-induced acanthosis in mice.

REFERENCES

[1]. Chunjian Liu, et al. Discovery of BMS-986202: A Clinical Tyk2 Inhibitor that Binds to Tyk2 JH2. J Med Chem. 2021 Jan 14;64(1):677-694.

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