Deucravacitinib

Cat. No.: HY-117287

CAS No.: 1609392-27-9

Molecular Formula: $C_{20}H_{19}D_3N_8O_3$

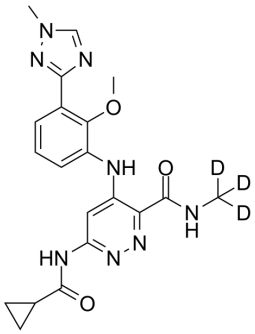
Molecular Weight: 425.46

Target: JAK; Interleukin Related; IFNAR

Pathway: Epigenetics; JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Stem Cell/Wnt; Immunology/Inflammation

Storage:

Powder	-20°C	3 years
In solvent	-80°C	1 year
	-20°C	6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 33.33 mg/mL (78.34 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3504 mL	11.7520 mL	23.5040 mL
	5 mM	0.4701 mL	2.3504 mL	4.7008 mL
	10 mM	0.2350 mL	1.1752 mL	2.3504 mL

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

In Vivo

1. Add each solvent one by one: 50% PEG300 >> 50% saline
   Solubility: 10 mg/mL (23.50 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: 3.83 mg/mL (9.00 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.88 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.88 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Deucravacitinib (BMS-986165) is a highly selective, orally bioavailable allosteric TYK2 inhibitor for the treatment of autoimmune diseases, which selectively binds to TYK2 pseudokinase (JH2) domain (IC_{50}=1.0 nM) and blocks receptor-mediated Tyk2 activation by stabilizing the regulatory JH2 domain. Deucravacitinib inhibits IL-12/23 and type I IFN pathways. Deucravacitinib, the FDA's world first de novo deuterium, is available for study in moderate to severe plaque psoriasis[1][2].

IC_{50} & Target	Tyk2 JH2 0.2 nM (IC_{50})	JAK1 JH2 1 nM (IC_{50})	IL-12	IL-23

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.

CUSTOMER VALIDATION

- Nat Chem Biol. 2022 Sep 12.
- Cell Death Differ. 2021 Feb;28(2):748-763.
- iScience. 2021, 102498.
- Int J Mol Sci. 2023 May 25, 24(11), 9243.
- Int J Mol Sci. 2022 May 1;23(9):5040.

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REFERENCES

[1]. Wrobleski ST, et al. Highly Selective Inhibition of Tyrosine Kinase 2 (TYK2) for the Treatment of Autoimmune Diseases: Discovery of the Allosteric Inhibitor BMS-986165. J Med Chem. 2019 Jul 18.

[2]. Catlett I, et al. SAT0226 A first-in-human, study of BMS-986165, a selective, potent, allosteric small molecule inhibitor of tyrosine kinase 2. Annals of the Rheumatic Diseases 2017;76:859.

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