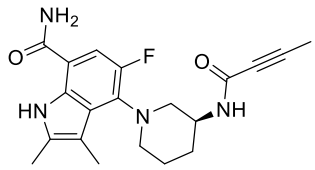
Product data sheet

MedKoo Cat#: 206954 Name: Branebrutinib CAS#: 1912445-55-6 Chemical Formula: $C_{20}H_{23}FN_4O_2$ Exact Mass: 370.1805 Molecular Weight: 370.4284	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

Branebrutinib, also known as BMS-986195, is a potent, covalent, irreversible inhibitor of Bruton's tyrosine kinase (BTK), a member of the Tec family of non-receptor tyrosine kinases essential in antigen-dependent B-cell signaling and function. BMS-986195 is more than 5000-fold selective for BTK over all kinases outside of the Tec family, and selectivity ranges from 9- to 1010-fold within the Tec family. BMS-986195 inactivated BTK in human whole blood with a rapid rate of inactivation (3.5×10-4 nM-1·min-1) and potently inhibited antigen-dependent interleukin-6 production, CD86 expression and proliferation in B cells (IC50 <1 nM) without effect on antigen-independent measures in the same cells.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	87.0	234.86
Ethanol	38.0	102.58

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.70 mL	13.50 mL	27.00 mL
5 mM	0.54 mL	1.70 mL	5.40 mL
10 mM	0.27 mL	1.35 mL	2.70 mL
50 mM	0.05 mL	0.27 mL	0.54 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Watterson SH, Liu Q, Beaudoin Bertrand M, Batt DG, Li L, Pattoli MA, Skala S, Cheng L, Obermeier MT, Moore R, Yang Z, Vickery R, Elzinga PA, Discenza L, D'Arienzo C, Gillooly KM, Taylor TL, Pulicicchio C, Zhang Y, Heimrich E, McIntyre KW, Ruan Q, Westhouse RA, Catlett IM, Zheng N, Chaudhry C, Dai J, Galella MA, Tebben AJ, Pokross M, Li J, Zhao R, Smith D, Rampulla R, Allentoff A, Wallace MA, Mathur A, Salter-Cid L, Macor JE, Carter PH, Fura A, Burke JR, Tino JA. Discovery of Branebrutinib (BMS-986195): A Strategy for Identifying a Highly Potent and Selective Covalent Inhibitor Providing Rapid in Vivo Inactivation of Bruton's Tyrosine Kinase (BTK). J Med Chem. 2019 Apr 11;62(7):3228-3250. doi: 10.1021/acs.jmedchem.9b00167. Epub 2019 Mar 29. PMID: 30893553.

In vivo study

1. Watterson SH, Liu Q, Beaudoin Bertrand M, Batt DG, Li L, Pattoli MA, Skala S, Cheng L, Obermeier MT, Moore R, Yang Z, Vickery R, Elzinga PA, Discenza L, D'Arienzo C, Gillooly KM, Taylor TL, Pulicicchio C, Zhang Y, Heimrich E, McIntyre KW, Ruan Q, Westhouse RA, Catlett IM, Zheng N, Chaudhry C, Dai J, Galella MA, Tebben AJ, Pokross M, Li J, Zhao R, Smith D, Rampulla R,

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Allentoff A, Wallace MA, Mathur A, Salter-Cid L, Macor JE, Carter PH, Fura A, Burke JR, Tino JA. Discovery of Branebrutinib (BMS-986195): A Strategy for Identifying a Highly Potent and Selective Covalent Inhibitor Providing Rapid in Vivo Inactivation of Bruton's Tyrosine Kinase (BTK). J Med Chem. 2019 Apr 11;62(7):3228-3250. doi: 10.1021/acs.jmedchem.9b00167. Epub 2019 Mar 29. PMID: 30893553.

7. Bioactivity

Biological target:

Branebrutinib (BMS-986195) is a covalent, irreversible inhibitor of Bruton's tyrosine kinase (BTK), with an IC50 of 0.1 nM.

In vitro activity

In B cells stimulated through the B cell receptor (BCR), 5a (Branebrutinib) potently inhibited signaling and functional end points, including calcium flux (IC50 = 7 nM), production of cytokines, proliferation, and surface expression of the costimulatory molecule CD86 (IC50 values of <1 nM). As expected, CD69 expression in peripheral B cells, when stimulated through CD40, was not impacted by 5a since this pathway is not dependent on the kinase activity of BTK to mediate downstream signaling, thus demonstrating the compound's functional selectivity. When evaluated against IgG-containing immune complex low affinity activating Fcγ (FcγRIIa and FcγRIII) receptor end points in peripheral blood mononuclear cells (PBMC), 5a was highly effective at inhibiting TNFα production with equivalent potency to those measured for the BCR-dependent end points in B cells. In human whole blood assays, 5a potently inhibited BCR-stimulated expression of CD69 on B cells with an IC50 of 11 nM.

Reference: J Med Chem. 2019 Apr 11;62(7):3228-3250. https://pubmed.ncbi.nlm.nih.gov/30893553/

In vivo activity

Microcomputed tomography of the hind limbs (Figure 14C) illustrated that 5a provided a dose-dependent protection against pitting, loss of bone mass, woven porous bone, and fusion of the small bones evident in the mice receiving only vehicle. The animals receiving 0.5 mg/kg showed essentially complete protection, as illustrated by the presence of a smooth bone surface and easily recognizable small individual bones of the foot and ankle. The compound was also effective at 0.5 mg/kg po, q.d. in blocking disease progression when dosed in a pseudoestablished dosing mode (data not shown).

Reference: J Med Chem. 2019 Apr 11;62(7):3228-3250. https://pubmed.ncbi.nlm.nih.gov/30893553/