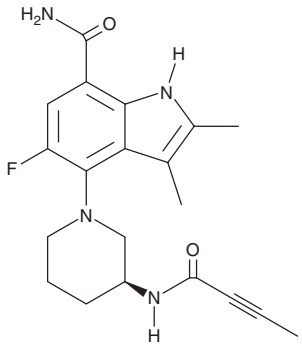
PRODUCT INFORMATION

Branebrutinib

Item No. 33462

CAS Registry No.:	1912445-55-6
Formal Name:	5-fluoro-2,3-dimethyl-4-[(3S)-3-[(1-oxo-2-butyn-1-yl)amino]-1-piperidinyl]-1H-indole-7-carboxamide
Synonym:	BMS-986195
MF:	$C_{20}H_{23}FN_4O_2$
FW:	370.4
Purity:	≥98%
UV/Vis.:	λ_{max}: 242, 329 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

Branebrutinib is supplied as a crystalline solid. A stock solution may be made by dissolving the branebrutinib in the solvent of choice, which should be purged with an inert gas. Branebrutinib is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of branebrutinib in ethanol is approximately 1 mg/ml and approximately 30 mg/ml in DMSO and DMF.

Branebrutinib is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, branebrutinib should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. Branebrutinib has a solubility of approximately 0.2 mg/ml in a 1:4 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

Branebrutinib is a covalent inhibitor of Bruton's tyrosine kinase (BTK; IC_{50} = 0.1 nM).[1] It is greater than 5,000-fold selective for BTK over a panel of 240 kinases but does inhibit the additional Tec family kinases Tec, BMX, and TMX (IC_{50}s = 0.9, 1.5, and 5 nM, respectively). Branebrutinib inhibits calcium flux in Ramos B cells induced by B cell receptor (BCR) stimulation (IC_{50} = 7.2 nM), as well as BCR stimulation-induced proliferation of, and CD86 surface expression in, peripheral B cells (IC_{50}s = 0.04 and 0.3 nM, respectively). It inhibits TNF-α production in human peripheral blood mononuclear cells (PMBCs) induced by Fcγ receptor stimulation (IC_{50} = 0.3 nM). Branebrutinib (0.5 mg/kg) is completely protective against bone destruction in a mouse model of collagen-induced arthritis. It also reduces proteinuria and glomerular IgG immune complex deposition and increases survival in an NZB/W lupus-prone mouse model.

Reference

1. Watterson, S.H., Liu, Q., Bertrand, M.B., *et al.* 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.* **62(7)**, 3228-3250 (2019).

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