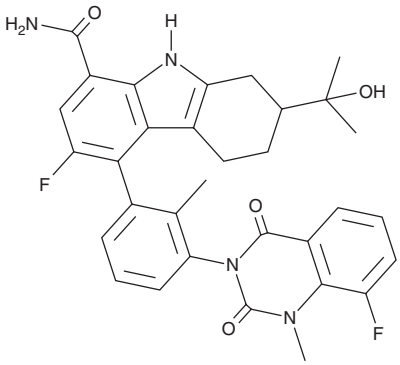
PRODUCT INFORMATION

BMS 986142

Item No. 30927

CAS Registry No.:	1643368-58-4
Formal Name:	(2S,5R)-6-fluoro-5-[(3S)-3-(8-fluoro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-2-methylphenyl]-2,3,4,9-tetrahydro-2-(1-hydroxy-1-methylethyl)-1H-carbazole-8-carboxamide
MF:	$C_{32}H_{30}F_2N_4O_4$
FW:	572.6
Purity:	≥98%
UV/Vis.:	λ_{max}: 222 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

BMS 986142 is supplied as a crystalline solid. A stock solution may be made by dissolving the BMS 986142 in the solvent of choice, which should be purged with an inert gas. BMS 986142 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of BMS 986142 in ethanol is approximately 15 mg/ml and approximately 30 mg/ml in DMSO and DMF.

BMS 986142 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, BMS 986142 should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. BMS 986142 has a solubility of approximately 0.25 mg/ml in a 1:3 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

BMS 986142 is a Bruton's tyrosine kinase (BTK) inhibitor (IC_{50} = 0.5 nM).[1] It is greater than 20-fold selective for BTK over a panel of 384 kinases. BMS 986142 inhibits calcium flux in Ramos B cells induced by B cell receptor (BCR) stimulation (IC_{50} = 9 nM), as well as BCR stimulation-induced proliferation of, and CD86 surface expression in, peripheral B cells (IC_{50}s = 3 and 4 nM, respectively). It inhibits TNF-α production in human peripheral blood mononuclear cells (PBMCs) induced by Fcγ receptor stimulation (IC_{50} = 3 nM). BMS 986142 (30 mg/kg per day) reduces the percentage of mice with severe proteinuria and increases survival in an NZB/W lupus-prone mouse model. It reduces hind paw tibiotarsal joint bone resorption and inflammation in a mouse model of collagen antibody-induced arthritis (CAIA) when administered at doses of 5 and 20 mg/kg.[2]

References

1. Watterson, S.H., De Lucca, G.V., Shi, Q., *et al.* Discovery of 6-Fluoro-5-(R)-(3-(S)-(8-fluoro-1-methyl-2,4-dioxo-1,2-dihydroquinazolin-3(4H)-yl)-2-methylphenyl)-2-(S)-(2-hydroxypropan-2-yl)-2,3,4,9-tetrahydo-1H-carbazole-8-carboxamide (BMS-986142): A reversible inhibitor of Bruton's tyrosine kinase (BTK) conformationally constrained by two locked atropisomers. *J. Med. Chem.* **59(19)**, 9173-9200 (2016).
2. Gillooly, K.M., Pulicicchio, C., Pattoli, M.A., *et al.* Bruton's tyrosine kinase inhibitor BMS-986142 in experimental models of rheumatoid arthritis enhances efficacy of agents representing clinical standard-of-care. *PLoS One* **12(7)**, e0181782 (2017).

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