# BMS-986143

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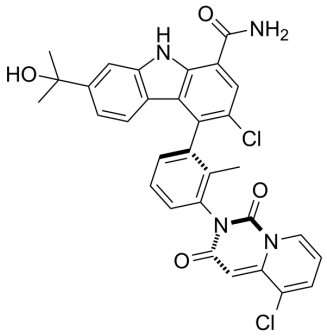
| **Cat. No.:** | HY-145373 |
| **CAS No.:** | 1643372-83-1 |
| **Molecular Formula:** | $C_{31}H_{24}Cl_2N_4O_4$ |
| **Molecular Weight:** | 587.45 |
| **Target:** | Btk |
| **Pathway:** | Protein Tyrosine Kinase/RTK |
| **Storage:** | Please store the product under the recommended conditions in the Certificate of Analysis. |



## BIOLOGICAL ACTIVITY

**Description**

BMS-986143 is an orally active, reversible BTK inhibitor with an $IC_{50}$ of 0.26 nM. BMS-986143 also inhibits TEC, BLK, BMX, TXK FGR, YES1, ITK with $IC_{50}$s of 3 nM, 5 nM, 7 nM, 10 nM, 15 nM,19 nM, 21 nM, respectively. BMS-986143 can be used for the research of autoimmune diseases[1].

**In Vitro**

BMS-986143 inhibits BTK with $IC_{50}$s of 6.9±3.4 and 25±19 nM in Ramos cellular assay and the human whole blood assay, respectively[1].

BMS-986143 provides potent inhibition of end points derived from IgG-containing immune complex low affinity activating Fc γ receptor signaling in peripheral blood mononuclear cells (PBMC) ($IC_{50}$=2 nM)[1].

BMS-986143 inhibits the expression of CD63 on the surface of basophils in human whole blood, driven by FcεRI signaling ($IC_{50}$ of 54 nM)[1].

BMS-986143 inhibits calcium flux in Ramos B Cells, proliferation of human peripheral B Cells, CD86 surface expression in peripheral B Cells, and TNFα from human PBMC Cells with $IC_{50}$s of 7±3, 1±0.4, 1±0.5, and 2 nM, respectively[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**In Vivo**

BMS-986143 demonstrates desirable efficacy in mouse models of collagen-induced arthritis (CIA) and anticollagen antibody-induced arthritis (CAIA)[1].

BMS-986143 exhibits high oral bioavailability (mouse 100%, dog 82%) and moderate $C_{max}$ (mouse 4.3, dog 1.2 μM) following oral administration (mouse 6, dog 2 mg/kg)[1].

BMS-986143 exhibits long elimination half-lives (mouse 3.6, dog 7.9 h) due to moderate plasma clearance (8.6, 4.4 mL/min/kg respectively) combined with low volumes of distribution (1.8, 2.6 L/kg respectively) following intravenous administration (mouse 3.0, dog 1.0 mg/kg)[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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| Animal Model: | DBA/1 male mice (8-10wk of age) bearing CIA model[1] |
| Dosage: | 15 and 45 mg/kg |
| Administration: | Oral gavage; BID |
| Result: | 15 and 45 mg/kg provided dose-dependent inhibition of observed clinical disease progression (63% and 80%, respectively), representing 17 and 19 h coverage of the mouse whole blood $IC_{50}$ (130 nM). |

## REFERENCES

[1]. Anurag S Srivastava, et al. Driving Potency with Rotationally Stable Atropisomers: Discovery of Pyridopyrimidinedione-Carbazole Inhibitors of BTK. ACS Med Chem Lett. 2020 Sep 16;11(11):2195-2203.



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