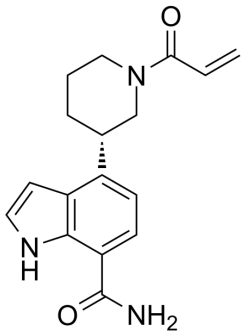
Elsubrutinib

Cat. No.:	HY-109143
CAS No.:	1643570-24-4
Molecular Formula:	$C_{17}H_{19}N_3O_2$
Molecular Weight:	297.35
Target:	Btk
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



BIOLOGICAL ACTIVITY

Description	Elsubrutinib (ABBV-105) is an orally active, potent, selective and irreversible Bruton's tyrosine kinase (BTK) inhibitor. The IC_{50} of Elsubrutinib for BTK catalytic domain is 0.18 μM. Elsubrutinib can be used for the research of inflammatory disease[1].
IC_{50} & Target	IC50: 0.18 μM (BTK)[1]
In Vitro	Elsubrutinib inhibits BTK (C481S) with an IC_{50} of 2.6 μM, indicating a significant loss in potency upon exchanging the targeted thiol nucleophile with an alcohol, suggesting Cys481 is important in the manner in which Elsubrutinib inhibits BTK. Elsubrutinib irreversibly inhibits BTK enzyme activity and blocks BTK-dependent cellular activation. Elsubrutinib inhibits histamine release from IgE-stimulated basophils and IL-6 release from IgG-stimulated monocytes, which utilize Fce and Fcc receptors respectively. Elsubrutinib inhibits IgM-mediated B cell proliferation, which is dependent on signaling through the BCR. Elsubrutinib also inhibits TNF-release from CpG-DNA stimulated PBMCs, which signals through TLR9, although it does not inhibit the function of TLRs that do not use ITAM motifs, namely, TNF release from PBMCs stimulated either through TLR4 (with LPS) or through TLR7/8 (with R848). Elsubrutinib has significant impacts on IgM-mediated B cell proliferation[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Elsubrutinib (10 mg/kg; p.o.) inhibits antibody responses to NP-Ficoll and NP-KLH, but not to NP-LPS or Prevnar-13[1]. Elsubrutinib (0.1~10 mg/kg; p.o.) results in dose-dependent inhibition of paw swelling throughout the course of disease and significantly prevents the onset of proteinuria and prolongs survival at the 10 mg/kg QD and BID doses, while lower doses does not significantly inhibit these endpoints[1]. Elsubrutinib demonstrates exposure-dependent inhibition of increases in paw volume. Elsubrutinib significantly inhibits bone volume loss in a dose dependent manner consistent with the observed anti-inflammatory effects[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female C57/BL6 mice[1]
Dosage:	10 mg/kg
Administration:	P.o.
Result:	Inhibited antibody responses to NP-Ficoll and NP-KLH, but not to NP-LPS or Prevnar-13.

Animal Model:	Lewis rats[1]
Dosage:	0.1~10 mg/kg
Administration:	P.o.
Result:	Resulted in dose-dependent inhibition of paw swelling throughout the course of disease.

Animal Model:	NZBWF1 mice[1]
Dosage:	0.1~10 mg/kg
Administration:	P.o.
Result:	Significantly prevented the onset of proteinuria and prolonged survival at the 10 mg/kg QD and BID doses, while lower doses did not significantly inhibit these endpoints.

REFERENCES

[1]. Goess C, et al. ABBV-105, a selective and irreversible inhibitor of Bruton's tyrosine kinase, is efficacious in multiple preclinical models of inflammation [published correction appears in Mod Rheumatol. 2019 May;29(3):v]. Mod Rheumatol. 2019;29(3):510-52

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