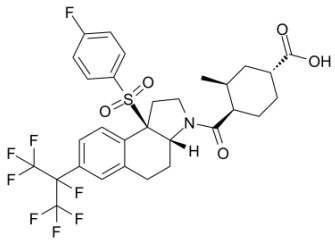
BMS-986251

Cat. No.:	HY-136527
CAS No.:	2460133-35-9
Molecular Formula:	$C_{30}H_{29}F_8NO_5S$
Molecular Weight:	667.61
Target:	ROR; Interleukin Related
Pathway:	Metabolic Enzyme/Protease; Immunology/Inflammation
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

BMS-986251 is an orally active and selective RORγt inverse agonist with an EC_{50} of 12 nM for RORγt GAL4. BMS-986251 inhibits IL-17 with an EC_{50} of 24 nM in human whole blood assay. BMS-986251 demonstrates robust efficacy in mouse acanthosis and Imiquimod-induced (HY-B0180) models (preclinical models of psoriasis)[1].

IC_{50} & Target

RORγt	IL-17	RORα	RORβ
12 nM (EC50)	24 nM (EC50)	>10 μM (EC50)	>10 μM (EC50)

In Vitro

BMS-986251 is against ROR family members (RORα GAL4: EC_{50}>10 μM; RORβ GAL4: EC_{50}>10 μM) and against other nuclear receptors (PXR: EC_{50}>5 μM; LXRα: EC_{50}>7.5 μM; LXRβ: EC_{50}>7.5 μM). BMS-986251 does not inhibit any of the CYP's[1].

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

In Vivo

BMS-986251 (5-45 mg/kg; orally; twice daily until day 9) results in reduced ear thickness[1].

BMS-986251 (0.13, 0.79, 4.76 mg/kg; orally; once a day) displays a dose-dependent reduction of the IL-17F produced in naïve C57BL/6 female mice (7-9 weeks)[1].

BMS-986251 (2 mg/kg of IV and 4 mg/kg of PO) has a $T_{1/2}$ of 7.7 hours, a CL of 2.7 mL/min•kg, and a V_{ss} of 1.9 L/kg for IV in mouse[1].

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

Animal Model:	C57BL/6 female mice with acanthosis[1]
Dosage:	5, 15, 45 mg/kg
Administration:	Orally; twice daily until day 9
Result:	Resulted in reduced ear thickness and significantly reduces imiquimod (IMQ)-induced skin thickening.

Animal Model:	Mouse or rat[1]
Dosage:	2 mg/kg of IV and 4 mg/kg of PO (Pharmacokinetic Analysis)
Administration:	IV or PO

Result:	Had a $T_{1/2}$ of 7.7 hours, a CL of 2.7 mL/min•kg, and a V_{ss} of 1.9 L/kg for IV in mouse. Had a C_{max} of 4.8 μM and an AUC of 37 μM•h for PO in mouse. Had a $T_{1/2}$ of 11 hours, a CL of 1.3 mL/min•kg, and a V_{ss} of 1.25 L/kg for IV in rat. Had a C_{max} of 4.7 μM and an AUC of 64 μM•h for PO in rat.

REFERENCES

[1]. Robert J. Cherney, et al. Discovery of BMS-986251: A Clinically Viable, Potent, and Selective RORγt Inverse Agonist. ACS Med. Chem. Lett. 2020, 11, 6, 1221–1227

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