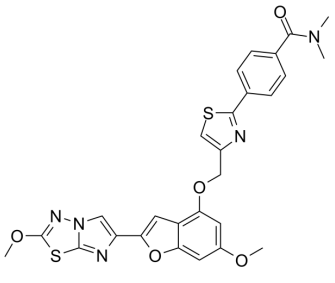
BMS-986141

Cat. No.:	HY-150790
CAS No.:	1478711-48-6
Molecular Formula:	$C_{27}H_{23}N_5O_5S_2$
Molecular Weight:	561.63
Target:	Protease Activated Receptor (PAR)
Pathway:	GPCR/G Protein
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	BMS-98614 is an orally active, selective thrombin receptor protease-activated receptor-4 (PAR-4) antagonist with an IC_{50} value of 0.4 nM. BMS-98614 has excellent antithrombotic effect[1][2].
IC_{50} & Target	PAR4 0.4 nM (IC_{50})
In Vitro	BMS-986141 (compound 49) (0-1 μM) inhibits platelet aggregation induced by PAR4 agonist peptide with an IC_{50} value of 2.2 nM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	BMS-986141 (compound 49) shows a slight but significant prolongation of KBT (kidney bleeding time) and demonstrates excellent anti-thrombotic efficacy at 0.5 mg/kg in cynomolgus monkey[1][2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Monkey arterial thrombosis (AT) and mesenteric bleeding time (MBT) models[2]
Dosage:	0.05, 0.1, 0.5 mg/kg
Administration:	p.o., 2 hours
Result:	Inhibited PAR4-AP-induced platelet aggregation in human and monkey blood with IC50 of 1.8 and 1.3 nM, respectively. Reduced the thrombus weight by 36%, 63% and 88% at concentrations of 0.05, 0.1 and 0.5 mg/kg, respectively in AT model. Increased MBT by 1.2 times.

Animal Model:	Rat, dog and monkey[1]
Dosage:	0.5, 1, 2 mpk
Administration:	i.v., 0.5 mpk, 10 min or p.o., 2 mpk for rat, 1 mpk for dog and monkey
Result:	The pharmacokinetic parameters of BMS-986141 (compound 49)

Parameters	rat	dog	monkey
$t_{1/2}$(h)	3.7 ± 0.4	13	75 ± 12
CL (mL/min/kg)	14.3 ± 0.4	8.5	12 ± 2
Vss(L/kg)	2.7 ± 0.3	2.7	14 ± 5
F (%)	31	25	36

REFERENCES

[1]. E Scott Priestley, et al. Discovery of Two Novel Antiplatelet Clinical Candidates (BMS-986120 and BMS-986141) That Antagonize Protease-Activated Receptor 4. J Med Chem. 2022 Jul 14;65(13):8843-8854.

[2]. P Wong, et al. Favorable therapeutic index of an orally-active small-molecule antagonist of the platelet protease-activated receptor-4, BMS-986141, compared with the P2Y12 antagonist ticagrelor in cynomolgus monkeys. European Heart Journal, Volume 41, Issue Supplement_2, November 2020.

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