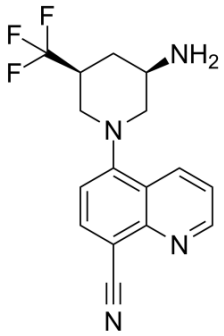
Enpatoran

Cat. No.:	HY-134581
CAS No.:	2101938-42-3
Molecular Formula:	$C_{16}H_{15}F_3N_4$
Molecular Weight:	320.31
Target:	Toll-like Receptor (TLR)
Pathway:	Immunology/Inflammation
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Enpatoran (M5049) is an orally active and dual TLR7/8 inhibitor with IC_{50}s of 11.1 nM and 24.1 nM in HEK293 cells, respectively. Enpatoran can block both innate and adaptive autoimmunity. Enpatoran is inactive against TLR3, TLR4 and TLR9. Enpatoran (M5049) can block molecule synthetic ligands and natural endogenous RNA ligands. Enpatoran (M5049) inhibits cytokine release, causing great potency in pharmacokinetic/pharmacodynamic properties[1].

IC_{50} & Target

TLR7 11.1 nM (IC_{50}, in HEK293 cells)	TLR8 24.1 nM (IC_{50}, in HEK293 cells)	TLR7 68.3 nM (IC_{50}, in peripheral blood mononuclear cells (PBMCs))	TLR8 620 nM (IC_{50}, in peripheral blood mononuclear cells (PBMCs))
TLR7 2.2 nM (IC_{50}, in whole blood (WB) cells)	TLR8 120 nM (IC_{50}, in whole blood (WB) cells)		

In Vitro

Enpatoran (0.01 nM-10 μM) inhibits production of IL-6 stimulated by all the ligands (miR-122, Let7c RNA, Alu RNA, and R848) with IC_{50} values ranging from 35 to 45 nM[1].

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

In Vivo

Pre-treatment with Enpatoran (M5049; oral gavage; 1 mg/kg) before R848 (intraperitoneal injection of 25 μg) dose-dependently inhibits the production of IL-6 and IFN-α in mice[1].

Enpatoran (M5049) exhibits high oral bioavailability (mouse 100%, rat 87%, dog 84%) following oral administration (mouse, rat and dog 1.0 mg/kg)[1].

Enpatoran exhibits moderate half-lives (mouse 1.4, rat 5.0 and dog 13 h) due to high plasma clearance (1.4, 1.2 and 0.59 L/h/kg, respectively) combined with large volumes of distribution (2.7, 8.7 and 5.7 L/kg, respectively) following intravenous administration (mouse, rat and dog 1.0 mg/kg)[1].

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

Animal Model:	Female C57BL/6 mice[1]
Dosage:	0.1 mg/kg and 1 mg/kg
Administration:	Oral gavage; administered 1 hour prior to R848 challenge

Result:	The TLR7/8 agonist R848 stimulated both IFN-α and IL-6 production in mice. Enpatoran decreased IFN-α and IL-6 production stimulated by R848.

Animal Model:	Female CD1 mice, Female Wistar rats, Female beagle dogs[1]
Dosage:	1 mg/kg (Pharmacokinetic Analysis)
Administration:	Intravenous (i.v.) or oral gavage
Result:	$T_{1/2}$s of 1.4, 5.0 and 13 h for mice, rats and dogs, respectively.

REFERENCES

[1]. Jaromir Vlach, et al. Discovery of M5049: A Novel Selective TLR7/8 Inhibitor for Treatment of Autoimmunity. J Pharmacol Exp Ther. 2020 Dec 16;JPET-AR-2020-000275.

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