Enpatoran

Cat. No.: HY-134581

CAS No.: 2101938-42-3

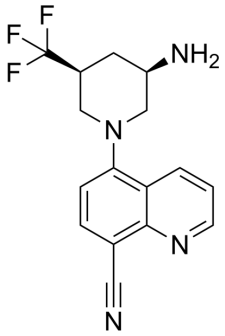
Molecular Formula: $C_{16}H_{15}F_3N_4$

Molecular Weight: 320.31

Target: Toll-like Receptor (TLR)

Pathway: Immunology/Inflammation

Storage: -20°C, sealed storage, away from moisture and light
* In solvent : -80°C, 2 years; -20°C, 1 year (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

Ethanol : 100 mg/mL (312.20 mM; Need ultrasonic)
DMSO : 24.44 mg/mL (76.30 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.1220 mL	15.6099 mL	31.2198 mL
5 mM	0.6244 mL	3.1220 mL	6.2440 mL
10 mM	0.3122 mL	1.5610 mL	3.1220 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.44 mg/mL (7.62 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.44 mg/mL (7.62 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Enpatoran (M5049) is a potent, orally active and dual TLR7/8 inhibitor with IC_{50}s of 11.1 nM and 24.1 nM in HEK293 cells, respectively. Enpatoran is inactive against TLR3, TLR4 and TLR9. Enpatoran can block molecule synthetic ligands and natural endogenous RNA ligands. Enpatoran exhibits excellent pharmacokinetic properties in vivo. Enpatoran can be used for both innate and adaptive autoimmunity blocking research [1].

IC_{50} & Target

TLR7	TLR8	TLR7	TLR8
11.1 nM (IC_{50}, in HEK293 cells)	24.1 nM (IC_{50}, in HEK293 cells)	68.3 nM (IC_{50}, in peripheral blood mononuclear cells (PBMCs))	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.

CUSTOMER VALIDATION

- Cell Commun Signal. 2023 Aug 18;21(1):215.
- J Innate Immun. 2023 Apr 11.

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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.

Caution: Product has not been fully validated for medical applications. For research use only.

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