Enpatoran hydrochloride

Cat. No.: HY-134581A

CAS No.: 2101945-93-9

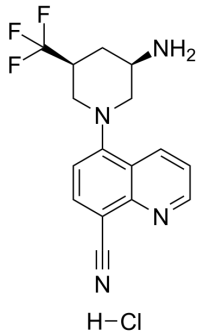
Molecular Formula: $C_{16}H_{16}ClF_3N_4$

Molecular Weight: 356.77

Target: Toll-like Receptor (TLR)

Pathway: Immunology/Inflammation

Storage: -20°C, sealed storage, away from moisture and light
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 16.67 mg/mL (46.72 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8029 mL	14.0146 mL	28.0293 mL
	5 mM	0.5606 mL	2.8029 mL	5.6059 mL
	10 mM	0.2803 mL	1.4015 mL	2.8029 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 mg/mL (5.61 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2 mg/mL (5.61 mM); Clear solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2 mg/mL (5.61 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Enpatoran (M5049) hydrochloride 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 hydrochloride is inactive against TLR3, TLR4 and TLR9. Enpatoran hydrochloride can block molecule synthetic ligands and natural endogenous RNA ligands. Enpatoran hydrochloride exhibits excellent pharmacokinetic properties in vivo. Enpatoran hydrochloride can be used for both innate and adaptive autoimmunity blocking research[1].

IC_{50} & Target	TLR7	TLR8
	11.1 nM (IC_{50})	24.1 nM (IC_{50})

In Vitro	Enpatoran hydrochloride (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 hydrochloride (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 hydrochloride exhibits high oral bioavailability (mouse 100%, rat 87%, dog 84%) following oral administration (mouse, rat and dog 1.0 mg/kg)[1]. Enpatoran hydrochloride 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 hydrochloride decreased IFN-α and IL-6 production stimulated by R848.

CUSTOMER VALIDATION

- 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.

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