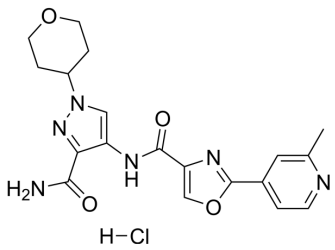
AS2444697

Cat. No.:	HY-18992
CAS No.:	1287665-60-4
Molecular Formula:	$C_{19}H_{21}ClN_6O_4$
Molecular Weight:	432.86
Target:	IRAK
Pathway:	Immunology/Inflammation
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 12.5 mg/mL (28.88 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	2.3102 mL	11.5511 mL	23.1022 mL
5 mM	0.4620 mL	2.3102 mL	4.6204 mL
10 mM	0.2310 mL	1.1551 mL	2.3102 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 1.67 mg/mL (3.86 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.67 mg/mL (3.86 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AS2444697 is an orally active IRAK-4 inhibitor with an IC_{50} of 21 nM[1]. AS2444697 potently inhibits human and rat IRAK-4 activity. AS2444697 exhibits renoprotective effects through anti-inflammatory action[2].

IC_{50} & Target

IRAK4
21 nM (IC_{50})

In Vivo

AS2444697 is efficacious in the rat adjuvant-induced arthritis (ED_{50} 2.7 mg/kg, BID, PO) and the rat collagen-induced arthritis (ED_{50} 1.6 mg/kg, BID, PO) disease models. Good bioavailability was seen in rat (F% 50) and dog (F% 78) pharmacokinetic studies[1].

AS2444697 (0.3-3 mg/kg) significantly increases the plasma levels of IL-1β, IL-6, TNF-α, MCP-1, and aminotransferases (ALT

and AST) in LPS/GalN-treated mice. Single administration of AS2444697 (0.3-3 mg/kg) dose-dependently decreases plasma levels of these all parameters, and these effects were significant at doses of 1 mg/kg or higher[2].
After oral administration of AS2444697 (3 mg/kg) to 5/6 Nx rats, plasma, and tissue (liver and kidney) concentrations of the unchanged drug peaked at 1 h and then gradually decreased, with a terminal half-life of 2.7-2.9 h[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male 6-week-old Wistar rats and Balb/c mice[2]
Dosage:	0.3-3 mg/kg
Administration:	Single administration; orally
Result:	The plasma levels of IL-1β, IL-6, TNF-α, MCP-1, and aminotransferases (ALT and AST) were significantly increased.

REFERENCES

[1]. JohnHynesJr, et al. Chapter Nine - Advances in the Discovery of Small-Molecule IRAK4 Inhibitors. Annu Rep Med Chem. 2014 (49):117-133.

[2]. Mitsuhiro Kondo, et al. Renoprotective effects of novel interleukin-1 receptor-associated kinase 4 inhibitor AS2444697 through anti-inflammatory action in 5/6 nephrectomized rats. Naunyn Schmiedebergs Arch Pharmacol. 2014 Oct;387(10):909-19.

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