LeuRS-IN-1 hydrochloride

Cat. No.: HY-139987A

CAS No.: 1364683-67-9

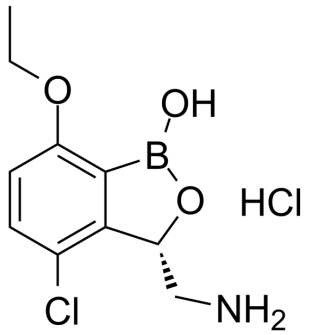
Molecular Formula: $C_{10}H_{14}BCl_2NO_3$

Molecular Weight: 277.94

Target: Bacterial

Pathway: Anti-infection

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

LeuRS-IN-1 hydrochloride is a potent, orally active M. tuberculosis leucyl-tRNA synthetase (M.tb LeuRS) inhibitor. LeuRS-IN-1 hydrochloride has IC_{50} and Kd values of 0.06 μM, 0.075 μM for M.tb LeuRS, respectively[1]. LeuRS-IN-1 hydrochloride inhibits human cytoplasmic LeuRS (IC_{50}=38.8 μM), and HepG2 protein synthesis (EC_{50}=19.6 μM)[2].

IC_{50} & Target

M.tb LeuRS	M.tb LeuRS	human cytoplasmic LeuRS	HepG2 protein synthesis
0.06 μM (IC_{50})	0.075 μM (Kd)	38.8 μM (IC_{50})	19.6 μM (EC50)

In Vitro

LeuRS-IN-1 (compound 13) hydrochloride has a MIC value of 0.02 μg/mL for M.tb H37Rv bacteria[1].

LeuRS-IN-1 (compound 3a) (48 h) hydrochloride induces HepG2 cell toxicity with an EC_{50} value of 65.8 μM[2].

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

In Vivo

LeuRS-IN-1 (100 mg/kg; orally daily for 14 days) hydrochloride reduces lung CFU value in acute tuberculosis (TB) mice[1].

LeuRS-IN-1 (33 mg/kg; orally 5 days a week for 4 weeks) hydrochloride reduces lung and spleen CFU values in chronic TB mice[1].

Murine pharmacokinetic parameters[1]:

Administration	Dose (mg/kg)	C_{max} (μg/ml) at 5 min	CL (ml/h/kg)	V_{ss} (ml/kg)	MRT (h)	$AUC_{0-\infty}$ (h · μg/ml)	α (h) (
i.v.	30	13.6	582	3,142	5.4	51.6	0.

Administration	Dose (mg/kg)	C_{max} (μg/ml)	T_{max} (h)	AUC_{0-24} (h · μg/ml)	Terminal $t_{1/2}$ (h)	Bioavail (%) (h ·
p.o.	30	6.4	0.25	47.5	3.1	9.

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

Animal Model:	Murine GKO (C57BL/6-Ifngtm1ts) model of acute TB[1]

Dosage:	100 mg/kg
Administration:	Orally daily for 14 days after 10 days of infection (start) with M. tuberculosis Erdman.
Result:	Reduced lung CFU value in mice.

Animal Model:	Murine BALB/c model of chronic TB infection[1]
Dosage:	33 mg/kg
Administration:	Orally 5 days a week for 4 weeks after infection with M. tuberculosis Erdman with a low-dose aerosol 21 days prior (start).
Result:	Reduced lung and spleen CFU values in mice.

REFERENCES

[1]. Palencia A, et al. Discovery of Novel Oral Protein Synthesis Inhibitors of Mycobacterium tuberculosis That Target Leucyl-tRNA Synthetase. Antimicrob Agents Chemother. 2016;60(10):6271-6280. Published 2016 Sep 23.

[2]. Li X, et al. Discovery of a Potent and Specific M. tuberculosis Leucyl-tRNA Synthetase Inhibitor: (S)-3-(Aminomethyl)-4-chloro-7-(2-hydroxyethoxy)benzo[c][1,2]oxaborol-1(3H)-ol (GSK656). J Med Chem. 2017 Oct 12;60(19):8011-8026.

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