# LeuRS-IN-1

**Cat. No.:** HY-139987

**CAS No.:** 1364914-72-6

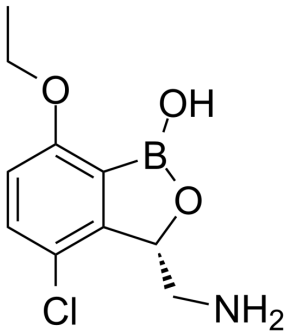
**Molecular Formula:** $C_{10}H_{13}BClNO_3$

**Molecular Weight:** 241.48

**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 is a potent, orally active M. tuberculosis leucyl-tRNA synthetase (M.tb LeuRS) inhibitor. LeuRS-IN-1 has $IC_{50}$ and Kd values of 0.06 μM, 0.075 μM for M.tb LeuRS, respectively[1]. LeuRS-IN-1 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) has a MIC value of 0.02 μg/mL for M.tb H37Rv bacteria[1].
LeuRS-IN-1 (compound 3a) (48 h) 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) reduces lung CFU value in acute tuberculosis (TB) mice[1].
LeuRS-IN-1 (33 mg/kg; orally 5 days a week for 4 weeks) 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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