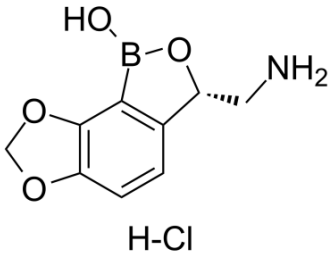
DS86760016

Cat. No.:	HY-124679
CAS No.:	1853176-89-2
Molecular Formula:	$C_9H_{11}BClNO_4$
Molecular Weight:	243.45
Target:	Bacterial
Pathway:	Anti-infection
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	DS86760016 is a potent leucyl-tRNA synthetase (LeuRS) inhibitor with activity against multidrug-resistant (MDR) Gram-negative bacteria, such as Escherichia coli, Klebsiella pneumoniae, and Pseudomonas aeruginosa. DS86760016 inhibits LeuRS enzymes from Escherichia coli, Pseudomonas aeruginosa, and Acinetobacter baumannii, with IC_{50}s of 0.38, 0.62, and 0.16 μM, respectively[1][2].
In Vitro	DS86760016 inhibits some Gram-negative bacteria with an MICs ranging from 0.25 to 2 μg/ml. The MIC of DS86760016 against Gram-positive bacteria is >32 μg/ml. DS86760016 is active against both susceptible and these MDR P. aeruginosa, E. coli, and K. pneumoniae strains, with an MIC_{90} of 2 μg/ml[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	DS86760016 (7.5-220 mg/kg; s.c.; q6h for 7 days) shows moderate spontaneous resistance (FSR)[1]. The pharmacokinetic (PK) parameters of DS86760016 in mouse, rat, monkey, and dog plasma by the intravenous (i.v.) route are test. DS86760016 shows lower intravenous plasma clearances (CL_p) of 11, 29, 5.6, and 4.5 ml/min/kg in mouse, rat, monkey, and dog plasma, respectively. The plasma half-lives ($t_{1/2}$) for DS86760016 are 1.9, 1.5, 8.6, and 8.3 h in mice, rats, monkeys, and dogs, respectively. The lower plasma clearance resulted in higher plasma exposures for DS86760016, with dose-normalized areas under the curve after i.v. administration ($DNAUC_{IV}$s) of 1.5, 0.6, 3.7, and 3.0 μg h kg/ml/mg in mice, rats, monkeys, and dogs, respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Immunocompetent female Swiss Webster mice (urinary tract infection, UTI model)[1]
Dosage:	7.5, 30, 220 mg/kg
Administration:	S.c.; q6h for 7 days
Result:	Bacteria resistant to DS86760016 were detected in a few animals after 1 day of treatment at doses of 7.5 and 30 mg/kg q6h; however, no resistant bacteria were detected at these doses after 7 days of treatment. No resistance was observed in any of the mice treated at a dose of 220 mg/kg q6h.

REFERENCES

[1]. Purnapatre KP, et al. In Vitro and In Vivo Activities of DS86760016, a Novel Leucyl-tRNA Synthetase Inhibitor for Gram-Negative Pathogens. Antimicrob Agents Chemother. 2018;62(4):e01987-17. Published 2018 Mar 27.

[2]. Kumar M, et al. DS86760016, a Leucyl-tRNA Synthetase Inhibitor with Activity against Pseudomonas aeruginosa. Antimicrob Agents Chemother. 2019;63(4):e02122-18. Published 2019 Mar 27.

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