Metallo-β-lactamase-IN-9

Cat. No.: HY-152105

CAS No.: 1802363-75-2

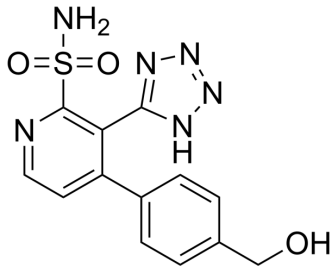
Molecular Formula: $C_{13}H_{12}N_6O_3S$

Molecular Weight: 332.34

Target: Bacterial; Beta-lactamase

Pathway: Anti-infection

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



BIOLOGICAL ACTIVITY

Description

Metallo-β-lactamase-IN-9 (Compound 23) is a pan metallo-beta-lactamase (MBL) inhibitor with IC_{50}s of 35, 269 and 369 nM against NDM-1, VIM-1 and IMP-1, respectively[1].

IC_{50} & Target

IC50: 35 nM (NDM-1), 269 nM (VIM-1), 369 nM (IMP-1)[1]

In Vivo

Metallo-β-lactamase-IN-9 (Compound 23) (10 and 50 mg/kg; s.c.; three times a day for 1 day) reduces bacterial burden in both the spleen and kidney in combination with Imipenem (HY-B1369A) in a Klebsiella pneumoniae MB9249 infection mice model[1].

Mouse Pharmacokinetic Properties of Metallo-β-lactamase-IN-9 (Compound 23)[d][1]

dose[a](iv, mpk)	AUC (μM·h)	MRT (h)	V_{dss} (L/kg)	Cl (mL/min/kg)
5[a]	27.08	5.2	2.97	9.33

dose (sc, mg/kg)	AUC (μM·h)	C_{max} (μM)	T_{max} (h)
10[b]	27.42	13.4	0.83
50[c]	111.28	69.1	0.5

[a]Formulation, 1.0 mg/mL 23 in 20% DMSO/60% PEG400/20% water (solution) with dose volume of 5 mL/kg.

[b]Formulation, 1.0 mg/mL of 23 in 30% captisol (solution) with dose volume 10 mL/kg.

[c]Formulation, 5.0 mg/mL of 23 in 30% captisol (solution) with dose volume of 10 mL/kg.

[d]AUC, area under the curve; Cl, clearance; iv, intravenous, MRT, mean residence time; V_{dss}, volume of distribution at steady state.

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

Animal Model:	Cytoxan-treated DBA-2 mice, Klebsiella pneumoniae MB9249 infection model[1]
Dosage:	10 and 50 mg/kg, in combination with 5mg/kg Imipenem (HY-B1369A)
Administration:	Subcutaneous injection, three times a day for 1 day
Result:	Demonstrated reduction of bacterial burden in both the spleen and kidney to a greater extent while combining with Imipenem (HY-B1369A) relative to Imipenem (HY-B1369A) alone.

Animal Model:	C57BL/6 mice[1]
Dosage:	Intravenous and subcutaneous injection
Administration:	5, 10 and 50 mg/kg (Pharmacokinetic Analysis)
Result:	Showed good pharmacokinetic properties.

REFERENCES

[1]. Mandal M, et al. Rapid Evolution of a Fragment-like Molecule to Pan-Metallo-Beta-Lactamase Inhibitors: Initial Leads toward Clinical Candidates. J Med Chem. 2022 Dec 22;65(24):16234-16251.

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