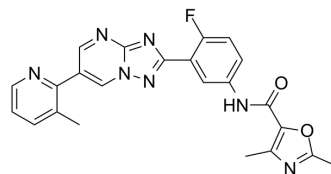


LXE408

Cat. No.:	HY-131350		
CAS No.:	1799330-15-6		
Molecular Formula:	C ₂₃ H ₁₈ FN ₇ O ₂		
Molecular Weight:	443.43		
Target:	Proteasome; Parasite		
Pathway:	Metabolic Enzyme/Protease; Anti-infection		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 16.67 mg/mL (37.59 mM); ultrasonic and warming and heat to 60°C)

Concentration	Solvent	Mass	1 mg			5 mg			10 mg		
			Concentration			Concentration			Concentration		
1 mM			2.2551 mL			11.2757 mL			22.5515 mL		
5 mM			0.4510 mL			2.2551 mL			4.5103 mL		
10 mM			0.2255 mL			1.1276 mL			2.2551 mL		

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

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 0.62 mg/mL (1.40 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 0.62 mg/mL (1.40 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 0.62 mg/mL (1.40 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

LXE408 is an orally active, non-competitive and kinetoplastid-selective proteasome inhibitor. LXE408 has an IC₅₀ of 0.04 μM for *L. donovani* proteasome and an EC₅₀ of 0.04 μM for *L. donovani*. LXE408 has a low propensity to cross the blood brain barrier. LXE408 has the potential for visceral leishmaniasis (VL) research^[1].

In Vitro

LXE408 (compound 1) can occupy the pocket as a ternary complex with the proteasome. LXE408 shows no inhibition of the hERG channel (IC₅₀>30 μM) in a manual patch clamp assay. LXE408 has a low propensity to cross the blood brain barrier (brain/plasma AUC ratio=0.03 in mice)^[1].

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

In Vivo

LXE408 (compound 1; 0.3-10 mg/kg; PO; twice daily for 8 days) potentially reduces the parasite burden in the liver in a dose-dependent manner^[1].

LXE408 (1, 3, 10, 20 mg/kg; p.o.; b.i.d.; for 10 days) effects robust healing of parasite-induced skin lesions at the base of the tail in BALB/c mice infected with *L. major*^[1].

LXE408 (5 mg/kg IV and 20 mg/kg PO) has a $T_{1/2}$ of 3.3 hours for mouse. LXE408 (3 mg/kg IV and 10 mg/kg PO) has a $T_{1/2}$ of 3.8 hours, a CL of 2.1 mL/min•kg, and a V_{SS} of 0.53 L/kg for male Sprague-Dawley rat^[1].

LXE408 (0.3 mg/kg IV and 1.0 mg/kg PO) has a $T_{1/2}$ of 3.8 hours for male beagle dog. LXE408 (0.3 mg/kg IV and 10 mg/kg PO) has a $T_{1/2}$ of 9.7 hours for male cynomolgus monkey^[1].

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

Animal Model:	Female BALB/c mice (6-8 weeks old) infected with <i>L. donovani</i> ^[1]
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Dosage:	0.3, 1, 3, 10 mg/kg
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Administration:	PO; twice daily for 8 days
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Result:	Led to a 95% and >99.84% reduction of parasite burden in the liver at 1 mg/kg and 10 mg/kg.
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Animal Model:	Balb/C mice ^[1]
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Dosage:	5 mg/kg IV and 20 mg/kg PO (Pharmacokinetic Analysis)
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Administration:	IV or PO
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Result:	Had a $T_{1/2}$ of 3.3 hours, a CL of 2.3 mL/min•kg, and a V_{SS} of 0.63 L/kg for mouse.
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REFERENCES

[1]. Advait Nagle, et al. Discovery and Characterization of Clinical Candidate LXE408 as a Kinetoplastid-Selective Proteasome Inhibitor for the Treatment of Leishmaniasis. *J Med Chem.* 2020 Jul 15.

Caution: Product has not been fully validated for medical applications. For research use only.

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