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Lieferung & Zahlungsart

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Zuschläge

- Mindermengenzuschlag
- Trockeneiszuschlag
- Gefahrgutzuschlag
- Expressversand

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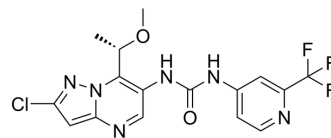
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MLT-943

Cat. No.:	HY-134820		
CAS No.:	1832576-04-1		
Molecular Formula:	C ₁₆ H ₁₄ ClF ₃ N ₆ O ₂		
Molecular Weight:	414.77		
Target:	MALT1		
Pathway:	Metabolic Enzyme/Protease; NF-κB		
Storage:	Powder	-20°C	3 years
	In solvent	-80°C	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro	DMSO : 250 mg/mL (602.74 mM; Need ultrasonic)				
		Solvent Concentration	Mass		
	Preparing Stock Solutions			1 mg	5 mg
		1 mM		2.4110 mL	12.0549 mL
		5 mM		0.4822 mL	2.4110 mL
	10 mM		0.2411 mL	1.2055 mL	
	Please refer to the solubility information to select the appropriate solvent.				
In Vivo	1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 2.08 mg/mL (5.01 mM); Clear solution				
	2. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.08 mg/mL (5.01 mM); Clear solution				

BIOLOGICAL ACTIVITY

Description	MLT-943 is a potent, selective and orally active MALT1 protease inhibitor. MLT-943 inhibits stimulated-IL-2 secretion in PBMC or in whole blood with a similar IC ₅₀ across species (0.07-0.09 μM in PBMC, 0.6-0.8 μM in whole blood). MLT-943 has anti-inflammatory activities and can be used for FcγR-mediated inflammation research ^[1] .
In Vitro	MLT-943 shows a high potency and selectivity in vitro. MLT-943 inhibits stimulated IL-2 secretion in PBMC or in whole blood with a similar IC ₅₀ across species (0.07-0.09 μM in PBMC, 0.6-0.8 μM in whole blood) ^[1] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	MLT-943 (oral gavage; 10 mg/kg; QD) prophylactic treatment in the rat collagen-induced arthritis model suppresses anti-collagen antibody production, fully prevents paw swelling, and normalizes joint histology scores in rat model ^[1] . MLT-943 (oral gavage; 5 mg/kg; QD; 10 consecutive days) effectively inhibits MALT1 protease activity and results in a

progressive reduction in the frequency of Foxp³⁺CD25⁺Treg cells in circulating CD4⁺T cells, which was maximal after 7 days of treatment. And Discontinuation of MLT-943 treatment after day 10 leads to Treg frequency progressively returning to their original values within 4 days. Suboptimal doses of MLT-943 (0.1 and 0.5 mg/kg QD; p.o.) does not impact the Treg frequency [1].

MLT-943 (oral gavage; 0, 5, 20 or 80 mg/kg/day; 4-13 weeks) causes a reduction in Treg and an increase in total T cell counts, in both 4- and 13-week rat toxicity studies at all dose levels. While a 4-Longer treatment induces severe immune-mediated pathology in multiple organs, with clinical onset starting around week 9 in rat^[1].

MLT-943 (p.o. administration; 3 mg/kg; single dose) exhibits a good PK parameters in vivo. The C_{max} values are 0.7 nM and 0.5 nM, respectively in rat and mice, respectively. And the F% are 86% and 50% in rat and mice, respective^[1].

For i.v. administration the compound is formed in NMP:PEG200 (30/70); For p.o. administration solution is formed in MC:Tween 80:Water (0.5:0.5:99) solution (Sourced from literature, for reference only)^[1].

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

Animal Model:	Naïve rats ^[1]
Dosage:	5 mg/kg
Administration:	Oral gavage; 5 mg/kg, 10 consecutive days or 0.1 mg/kg MLT-943
Result:	Induced a severe immune-mediated pathology after a prolonged treatment

REFERENCES

[1]. Kea Martin, et al. Pharmacological Inhibition of MALT1 Protease Leads to a Progressive IPEX-Like Pathology. Front Immunol

[2]. Jean Quancard, et al. Optimization of the In Vivo Potency of Pyrazolopyrimidine MALT1 Protease Inhibitors by Reducing Metabolism and Increasing Potency in Whole Blood. J Med Chem. 2020 Dec 10;63(23):14594-14608.

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

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