LY 3000328

Cat. No.: HY-15533

CAS No.: 1373215-15-6

Molecular Formula: $C_{25}H_{29}FN_4O_5$

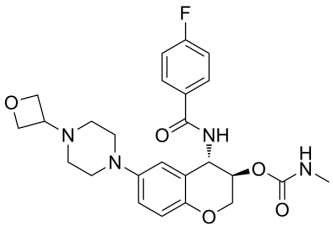
Molecular Weight: 484.52

Target: Cathepsin

Pathway: Metabolic Enzyme/Protease

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (103.19 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0639 mL	10.3195 mL	20.6390 mL
5 mM	0.4128 mL	2.0639 mL	4.1278 mL
10 mM	0.2064 mL	1.0319 mL	2.0639 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: ≥ 2.5 mg/mL (5.16 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.16 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.16 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

LY 3000328 (Z-FL-COCHO) is a potent and selective Cathepsin S (Cat S) inhibitor with IC_{50}s of 7.7 and 1.67 nM for hCat S and mCat S, respectively.

IC_{50} & Target

cathepsin S

In Vitro

LY 3000328 maintains excellent in vitro potency and selectivity. LY 3000328 shows low in vitro CYP450 inhibition (<15% at 10

	μM for CYP3A4, CYP2D6, and CYP2C9); low in vitro metabolism in mouse, rat, dog, and human liver microsomes (<20% after 30 min incubation at 4 μM); and good permeability (MDCK A-B>4%). At a 100 μM concentration of LY 3000328 there is only 6% displacement of [^{3}H]-astemizole in an assay with HEK293 membrane preparation, indicating low potential of hERG blockade[1]. LY 3000328 is a potent and specific inhibitor of cathepsin S (CatS). Inhibition of CatS activity in plasma would be 50% of maximal when LY 3000328 plasma concentration is approximately 60 ng/mL[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	The efficacies of LY 3000328 is studied in a mouse model of abdominal aortic aneurysm (AAA). In this model, inflammation is induced using $CaCl_2$ applied to the ablumenal surface. It is shown that features of the disease state in this model resemble those of human AAA. LY 3000328 exhibits a dose-responsive aortic diameter reduction at 1, 3, 10, and 30 mg/kg. At the lowest dose of 1 mg/kg of LY 3000328, the aortic diameter is reduced by 58%, then 83% at 3 mg/kg, and 87% at 10 mg/kg. The exposure (AUC) for both compounds increased in a dose-dependent manner, suggesting that the drug disposition properties of LY 3000328 are favorable[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cancer Cell. 2020 May 11;37(5):674-689.e12.
- Cell Chem Biol. 2021 Apr 27;S2451-9456(21)00213-0.
- J Virol. 2023 Sep 7;e0060123.
- Sci Rep. 2022 Jul 16;12(1):12197.
- Research Square Preprint. 2021 Dec.

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REFERENCES

[1]. Jadhav PK, et al. Discovery of Cathepsin S Inhibitor LY3000328 for the Treatment of Abdominal Aortic Aneurysm. ACS Med Chem Lett. 2014 Aug 27;5(10):1138-42.

[2]. Payne CD, et al. Pharmacokinetics and pharmacodynamics of the cathepsin S inhibitor, LY3000328, in healthy subjects. Br J Clin Pharmacol. 2014 Dec;78(6):1334-42.

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