Proteins

USP25/28 inhibitor AZ1

Cat. No.: HY-117370 CAS No.: 2165322-94-9

Molecular Weight: 422.21

Molecular Formula:

Target: Deubiquitinase

Pathway: Cell Cycle/DNA Damage

Powder -20°C Storage: 3 years

 $C_{17}H_{16}BrF_4NO_2$

2 years

-80°C In solvent 6 months

> -20°C 1 month

Product Data Sheet

SOLVENT & SOLUBILITY

In Vitro

DMSO: $\geq 250 \text{ mg/mL} (592.12 \text{ mM})$

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Mass Concentration	1 mg	5 mg	10 mg
	1 mM	2.3685 mL	11.8424 mL	23.6849 mL
	5 mM	0.4737 mL	2.3685 mL	4.7370 mL
	10 mM	0.2368 mL	1.1842 mL	2.3685 mL

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

In Vivo

- 1. Add each solvent one by one: corn oil Solubility: 25 mg/mL (59.21 mM); Suspended solution; Need ultrasonic
- 2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 2.08 mg/mL (4.93 mM); Clear solution
- 3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: 2.08 mg/mL (4.93 mM); Suspended solution; Need ultrasonic
- 4. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.08 mg/mL (4.93 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

USP25/28 inhibitor AZ1 (AZ1) is an orally active, selective, noncompetitive, dual ubiquitin specific protease (USP) 25/28 inhibitor with IC $_{50}$ s of 0.7 μ M and 0.6 μ M, respectively. USP25/28 inhibitor AZ1 attenuates colitis and tumorigenesis in the $mice\ model^{[1][2]}$.

IC₅₀ & Target IC50: 0.7 μM (USP25) and 0.6 μM (USP28)^[1] In Vivo USP25/28 inhibitor AZ1 (AZ1; 40 mg/kg; gavage; daily; for 7 days) protects from dextran sulfate sodium (DSS)-induced weight loss and diarrhea and impaired colon shortening[1]. USP25/28 inhibitor AZ1 (20 mg/kg/day; gavage; 6 times a week in the 1, 3, 6 weeks) treatment significantly reduces tumor numbers in colons. Expression of Wnt-related genes and levels of pSTAT3 are decreased and levels of SOCS3 are increased in tumors. AZ1 gavage does not alleviate DSS-induced colitis in Usp25^{-/-} mice or the spontaneous colitis of Il10^{-/-} mice^[1]. USP25/28 inhibitor AZ1 (20 mg/kg/day; gavage; every 3 days from 13-20 weeks) significantly inhibits tumorigenesis in the colon and prolonged the survival of AOM/Vil-Cre;Trp53fl/fl (VP) mice. AZ1 treatment has minimal effect on tumorigenesis in the USP25-deficient background^[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only. 12-week old male Usp25^{+/+} and Usp25^{-/-} mice^[1] Animal Model: Dosage: 40 mg/kg Administration: Gavage; daily; for 7 days Result: Protected from dextran sulfate sodium (DSS)-induced weight loss and diarrhea and impaired colon shortening and potentiated the expression of proinflammatory cytokines

CUSTOMER VALIDATION

• Biochem Pharmacol. 2022 Nov 25;115355.

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REFERENCES

[1]. Wrigley JD, et al. Identification and Characterization of Dual Inhibitors of the USP25/28 Deubiquitinating EnzymeSubfamily. ACS Chem Biol. 2017 Dec 15;12(12):3113-3125.

[2]. Xiao-Meng Wang, et al. The deubiquitinase USP25 supports colonic inflammation and bacterial infection and promotes colorectal cancer. Nature Cancer volume 1, pages811–825(2020).

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

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and antibacterial peptides in colons of Usp25^{-/-} mice compared to control counterparts.

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