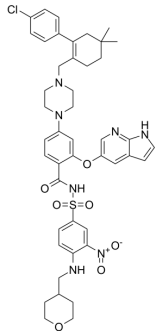
Venetoclax



Cat. No.: HY-15531

CAS No.: 1257044-40-8

Molecular Formula: $C_{45}H_{50}ClN_7O_7S$

Molecular Weight: 868.44

Target: Bcl-2 Family; Autophagy

Pathway: Apoptosis; Autophagy

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 : 77.5 mg/mL (89.24 mM; Need ultrasonic)

Ethanol : < 1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.1515 mL	5.7575 mL	11.5149 mL
5 mM	0.2303 mL	1.1515 mL	2.3030 mL
10 mM	0.1151 mL	0.5757 mL	1.1515 mL

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

In Vivo

1. Add each solvent one by one: 60% phosal 50 propylene glycol (PG), 30% polyethylene glycol 400 (PEG400), 10% ethanol
   Solubility: 20 mg/mL (23.03 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 15% Cremophor EL >> 85% Saline
   Solubility: 10 mg/mL (11.51 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 45% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: 10 mg/mL (11.51 mM); Suspended solution; Need ultrasonic
4. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: 5 mg/mL (5.76 mM); Suspended solution; Need ultrasonic and warming and heat to 49°C
5. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.5 mg/mL (2.88 mM); Suspended solution; Need ultrasonic
6. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (2.88 mM); Suspended solution; Need ultrasonic and warming

BIOLOGICAL ACTIVITY

Description	Venetoclax (ABT-199; GDC-0199) is a highly potent, selective and orally bioavailable Bcl-2 inhibitor with a K_i of less than 0.01 nM. Venetoclax induces autophagy[1][2][3].		
IC_{50} & Target	Bcl-2 0.01 nM (Ki)	Bcl-xL 48 nM (Ki)	Bcl-W 245 nM (Ki)
In Vitro	Venetoclax (ABT-199) potently kills FL5.12-BCL-2 cells (EC_{50}=4 nM), Venetoclax (ABT-199) shows much weaker activity against FL5.12-BCL-XL cells (EC_{50}=261 nM). ABT-199 also shows selectivity in cellular mammalian two-hybrid assays, where it disrupts BCL-2-BIM complexes (EC_{50}=3 nM) but is much less effective against BCL-XL-BCL-XS (EC_{50}=2.2 μM) or MCL-1-NOXA complexes[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.		
In Vivo	After a single oral dose of 12.5 mg per kg body weight in xenografts derived from RS4;11 cells (ALL), Venetoclax (ABT-199) causes a maximal tumor growth inhibition (TGI_{max}) of 47% (P<0.001) and tumor growth delay (TGD) of 26% (P<0.05)[1]. Treatment of established xenografted (a mouse xenograft model of the T-ALL cell line LOUCY) tumors with Venetoclax (ABT-199) 100 mg/kg for 4 days results in a significant reduction of leukemic burden[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.		

PROTOCOL

Cell Assay [1]	RS4;11 cells are seeded at 50,000 per well in 96-well plates and treated with compounds diluted in half-log steps starting at 1 μM and ending at 0.00005 μM. All other leukemia and lymphoma cell lines are seeded at 15,000-20,000 cells per well in the appropriate medium and incubated with Venetoclax or Navitoclax for 48 h. Effects on proliferation are determined using Cell TiterGlo reagent. EC_{50} values are determined by nonlinear regression analysis of the concentration-response data. Mouse FL5.12-BCL-2 and FL5.12-BCL-XL cells are propagated and assessed. $Bak^{-/-}$ $Bax^{-/-}$ double knockout mouse embryonic fibroblasts are seeded into 96-well microtiter plates at 5,000 cells per well in DMEM supplemented with 10% FBS. Venetoclax (ABT-199) in the same culture medium is added in half-log dilutions starting at 5 μM. The cells are then incubated at 37°C (5% CO_2) for 48 h, and the effects on proliferation are determined using Cell TiterGlo reagent[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice[2] Nonobese diabetic/severe combined immunodeficient γ (NSG) mice are injected at 6 weeks of age in the tail vein with 150 μL phosphate-buffered saline containing $5×10^6$ luciferase-labeled LOUCY cells. At regular time points, the bioluminescence is measured using the IVIS Lumina II imaging system. At 6 weeks, the cells are engrafted and the mice are randomly divided into 2 groups (with an equal number of males and females in both groups), and the treatment is started on day 0. Mice are treated with Venetoclax (ABT-199) 100 mg/kg body weight or with vehicle via oral gavage for 4 consecutive days. At days 0, 2, and 4 the bioluminescene is measured. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nature. 2023 Jan;613(7942):187-194.
- Nature. 2021 Mar;591(7850):477-481.
- Cell. 2022 Apr 28;185(9):1521-1538.e18.
- Cancer Cell. 2024 Apr 8;42(4):552-567.e6.
- Cancer Cell. 2020 Dec 14;38(6):872-890.e6.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Souers AJ, et al. ABT-199, a potent and selective BCL-2 inhibitor, achieves antitumor activity while sparing platelets. Nat Med. 2013 Feb;19(2):202-8.

[2]. Peirs S, et al. ABT-199 mediated inhibition of BCL-2 as a novel therapeutic strategy in T-cell acute lymphoblastic leukemia. Blood. 2014 Dec 11;124(25):3738-47.

[3]. Bi C, et al. Inhibition of 4EBP phosphorylation mediates the cytotoxic effect of mechanistic target of rapamycin kinase inhibitors in aggressive B-cell lymphomas. Haematologica. 2017 Apr;102(4):755-764.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA