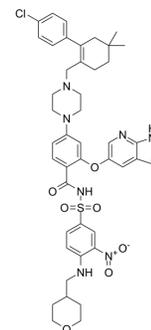


Venetoclax

Cat. No.:	HY-15531		
CAS No.:	1257044-40-8		
Molecular Formula:	C ₄₅ H ₅₀ ClN ₇ O ₇ S		
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	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 77.5 mg/mL (89.24 mM; Need ultrasonic)
Ethanol : < 1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent Concentration	Mass		
		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

- 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
- 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
- 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
- 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]}.

IC₅₀ & Target

Bcl-2	Bcl-xL	Bcl-W
-------	--------	-------

	0.01 nM (Ki)	48 nM (Ki)	245 nM (Ki)
In Vitro	<p>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].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>		
In Vivo	<p>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].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>		

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 μ M and ending at 0.00005 μ M. 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 μ M. The cells are then incubated at 37°C (5% CO₂) 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 μ L 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 bioluminescence 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. 2020 Dec 14;38(6):872-890.e6.
- Cancer Cell. 2018 Aug 13;34(2):271-285.e7.

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.
-

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

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