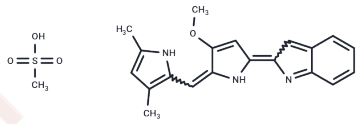
Data Sheet (Cat.No.T6275)

TargetMol

Obatoclax Mesylate

Chemical Properties



CAS No. : 803712-79-0

Formula: C20H19N3O·CH4O3S

Molecular Weight: 413.49

Appearance: no data available

Storage: keep away from direct sunlight
Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	Obatoclax Mesylate (GX15-070) is a Bcl-2 antagonist (Ki: 0.22 μM) and can induce apoptosis with up-regulation of Bim, induced cytochrome c release, and activation of caspase-3.
Targets(IC50)	Bcl-2 Family,Parasite,Autophagy
In vitro	Obatoclax (GX15-070) potently interfered with the direct interaction between MCL-1 and BAK in intact mitochondrial outer membrane and inhibited the association between MCL-1 and BAK in intact cells [1]. Obatoclax inhibited cell growth of HL-60, U937, OCI-AML3, and KG-1 cell lines. Obatoclax induced apoptosis in AML CD34+ progenitor cells with an average IC50 of 3.59 micromol/L although clonogenicity was inhibited at concentrations of 75 to 100 nmol/L [2]. Obatoclax reduced the viability of PANC-1 and BxPC-3 cell lines and synergistically enhanced TRAIL-mediated cytotoxicity [3].
In vivo	When formulated for i.v. administration, obatoclax (2 or 3.5 mg/kg) was found to have single-agent antitumor effects in several standard mouse tumor models. Antitumor activity without animal weight loss was observed in mice bearing solid tumors [1]. Thyroid cancer-carrying [Pten,Trp53]thyr?/? mice were treated with vehicle or Obatoclax for 6 days. Live thyrocytes in Obatoclax-treated mice exhibited a dramatic reduction in Lysotracker staining [4].
Cell Research	Cells were plated in logarithmic growth phase at 2,000-4,000 cells per well in 96-well clear bottom plates and cultured for 14 to 16 h before the start of drug treatment. Serial dilutions of obatoclax or companion drug were made in DMSO, diluted 1:50 in RPMI, and then added to tissue culture media at a final concentration of 0.2% DMSO. Cells were typically treated with a dose range of compound from 50 nM to 10 mM for 72 h. Cell viability was then determined using the ViaLight kit, according to the manufacturer's instructions. To obtain percentage viability, samples are expressed as a percentage of the signal obtained from DMSO-treated cells. Dose-response points were then plotted on a log scale, and IC50 values were determined using a best-fit sigmoidal dose-response curve with variable slope. The top of the curve was set to 100% [1].
Animal Research	Cells were transplanted s.c. into the flank of female BALB/c or CB17 SCID/SCID mice (6 to 8 weeks of age) as a suspension in PBS (1.0×10^6 cells/ml, 1.5×10^6 cells/ml, 2.0×10^6 cells/ml, or 5.0×10^6 cells/ml for SW480, C33A, PC3, and 4T1 cells respectively. After 7 (SW480), 14 (C33A), or 8 (PC3 and 4T1) days, treatment with drug was initiated, and body weight and tumor size were measured three times per week. The mean relative tumor size and volume (cohort of eight animals per treatment) were calculated as

follows: length (mm) ′ [width (mm)]2/2. Formulated obatoclax (tartrate salt) was administered intravenously (tail vein) once a day ′5 and cisplatin once every 3 days ′ 5 by the i.p. route. Obatoclax was formulated at the indicated concentration in 9.6% polyethylene glycol 300, 0.4% polysorbate 20, and 5% dextrose, except for the 4T1 tumor model where it was formulated at a concentration of 0.6 mg/ml in 9.48% polyethylene glycol, 0.38% polysorbate 20, 1.2 mg/ml mannitol, and 5% dextrose [1].

Solubility Information

Solubility	DMSO: 77 mg/mL (186.22 mM),Sonication is recommended. Ethanol: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.4184 mL	12.0922 mL	24.1844 mL
5 mM	0.4837 mL	2.4184 mL	4.8369 mL
10 mM	0.2418 mL	1.2092 mL	2.4184 mL
50 mM	0.0484 mL	0.2418 mL	0.4837 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Nguyen M, et al. Small molecule obatoclax (GX15-070) antagonizes MCL-1 and overcomes MCL-1-mediated resistance to apoptosis. Proc Natl Acad Sci U S A. 2007 Dec 4;104(49):19512-7. Epub 2007 Nov 26.
Konopleva M, et al. Mechanisms of Antileukemic Activity of the Novel Bcl-2 Homology Domain-3 Mimetic GX15-070 (Obatoclax). Cancer Res May 1, 2008 68; 3413
Huang S, et al. BH3 mimetic obatoclax enhances TRAIL-mediated apoptosis in human pancreatic cancer cells. Clin Cancer Res. 2009 Jan 1;15(1):150-9.
Champa D, et al. Obatoclax kills anaplastic thyroid cancer cells by inducing lysosome neutralization and necrosis. Oncotarget. 2016 Jun 7;7(23):34453-71.
Wei WJ, et al. Obatoclax and LY3009120 Efficiently Overcome RG7204 Resistance in Differentiated Thyroid Cancer. Theranostics. 2017 Feb 23;7(4):987-1001.

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