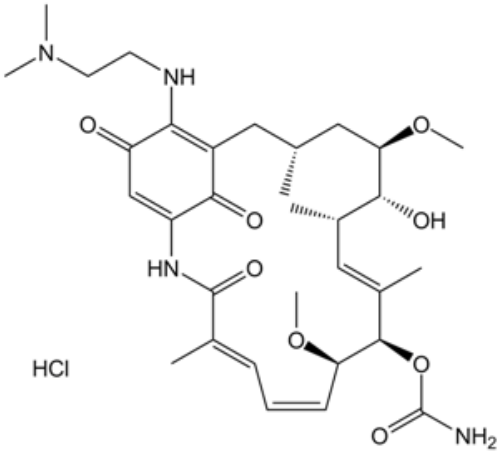
Product Data Sheet

Product Name: 17-DMAG (Alvespimycin) HCl
Cat. No.: GC13044

Chemical Properties

Cas. No.	467214-21-7		
Chemical Name	[(3R,5S,6R,7S,8E,10S,11S,12Z,14E)-21-[2-(dimethylamino)ethylamino]-6-hydroxy-5,11-dimethoxy-3,7,9,15-tetramethyl-16,20,22-trioxo-17-azabicyclo[16.3.1]docosa-1(21),8,12,14,18-pentaen-10-yl] carbamate;hydrochloride		
SMILES	CC1CC(C(C(C=C(C(C(C=CC=C(C(=O)NC2=CC(=O)C(=C(C1)C2=O)NCCN(C)C)C)OC)OC(=O)N)C)C)O)OC.Cl		
Formula	$C_{32}H_{48}N_4O_8$.HCl	M.Wt	653.21
Solubility	≥ 26.2mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Kinase experiment [1]:

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Preparation Method	Fluorescence polarization (FP)-based competition binding assay： This assay utilized a boron difluoride dipyrromethene (BODIPY) labeled geldanamycin analogue (BODIPY-AG) as a probe and measured fluorescence polarization upon binding of the probe to a protein. Native human Hsp90 protein (α+β isoforms) is isolated from HeLa cells. BODIPY-AG solution was freshly prepared in FP assay buffer (20mM HEPES-KOH, pH 7.3, 1.0mM EDTA, 100mM KCl, 5.0mM $MgCl_2$, 0.01% NP-40, 0.1mg/mL fresh bovine γ-globulin (BGG), 1.0mM fresh DTT, and protease inhibitor from stock solution in DMSO). Competition curves were obtained by mixing 10μL each of a solution containing BODIPY-AG and Hsp90, and a serial dilution of 17-DMAG (Alvespimycin) HCl freshly prepared in FP assay buffer from stock solution in DMSO. Final concentrations were 10nM BODIPY-AG, 40 or 60nM Hsp90, varying concentration of 17-DMAG (Alvespimycin) HCl (0.10nM~10μM), and ≤ 0.25% DMSO in a 384-well microplate. After 3-hr incubation at 30°C, fluorescence anisotropy (γEx=485nm, γEm=535nm) was measured on an EnVision 2100 multilabel plate reader. The IC_{50} value of 17-DMAG was obtained from the competition curves.
Reaction Conditions	0.1nM-10μM; 3h
Applications	The IC_{50} value of 17-DMAG (Alvespimycin) HCl for human Hsp90 is 62nM.

Cell experiment [2]:

Cell lines	CD19-selected B cells from CLL patients

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Preparation Method	A total of 1 × 10^6 CD19-selected B cells from CLL patients were incubated for 24 or 48h in 17-DMAG (Alvespimycin) HCl, or vehicle. Apoptosis was determined by staining with annexin V-fluorescein isothiocyanate and propidium iodide (PI). After exposure to drugs, cells were washed with phosphate-buffered saline and stained in 1 time binding buffer. Cell death was assessed by flow cytometry using a Beckman-Coulter model EPICS XL cytometer.
Reaction Conditions	50nM-500nM; 24 or 48h
Applications	17-DMAG (Alvespimycin) HCl treatment significantly and dose- and time-dependently induces cysteine aspartate-dependent apoptosis in chronic lymphocytes.

Animal experiment [2]:

Animal models	SCID mice engrafted with TCL1 leukemia cells
Preparation Method	SCID mice were housed in a clean environment and supplied with sterile food and water ad libitum. CD19-selected transformed B cells (1 × 10^6) from the spleen of a TCL1 transgenic mouse with active leukemia were engrafted by tail vein into an SCID mouse. Ten or 11 mice in each treatment group were treated with dimethyl sulfoxide (vehicle control) or 10mg/kg of 17-DMAG (Alvespimycin) HCl administered by intraperitoneal injection 5 times per week beginning 2 weeks after injection of leukemia cells. Blood was collected at various time points throughout treatment for RNA isolation and assessment of gene expression.
Dosage form	10mg/kg/day; 5 times per week for 16 days; i.p.
Applications	17-DMAG (Alvespimycin) HCl treatment significantly reduced the number of white blood cells in the blood of TCL1-SCID transplanted mouse models and prolonged their survival period.

Caution: Product has not been fully validated for medical applications. For research use only.
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References:
[1] Ge J, Normant E, Porter JR, et al. Design, synthesis, and biological evaluation of hydroquinone derivatives of 17-amino-17-demethoxygeldanamycin as potent, water-soluble inhibitors of Hsp90. *J Med Chem*. 2006;49(15):4606-4615.
[2] Hertlein E, Wagner AJ, Jones J, et al. 17-DMAG targets the nuclear factor-kappaB family of proteins to induce apoptosis in chronic lymphocytic leukemia: clinical implications of HSP90 inhibition. *Blood*. 2010;116(1):45-53.

Background

17-DMAG (Alvespimycin) HCl is an effective inhibitor of Hsp90, with an IC_{50} value of 62nM [1]. 17-DMAG (Alvespimycin) HCl binds to the ATP binding motif of Hsp90 and inhibits its protein folding protection activity, resulting in the misfolding and degradation of the target proteins of Hsp90 (such as EGFR, AKT, mutant p53 and IKK) [2]. 17-DMAG (Alvespimycin) HCl has anti-tumor effects and can be used in cancer research such as lung cancer, liver cancer, and colon cancer [3-4].

In vitro, 17-DMAG (Alvespimycin) HCl (50-500nM; 24 or 48h) treatment significantly and dose- and time-dependently led to depletion of the target protein IKK in chronic lymphocytic leukemia (CLL) cells and cysteine aspartate-dependent apoptosis, reducing the binding of NF-κB p50/p65 DNA and the transcription of NF-κB target genes [5]. 17-DMAG (Alvespimycin) HCl (0-1000nM; 24h) treatment inhibits the proliferation of osteosarcoma cells in a dose-dependent manner and inhibits the activation of MET protein and the cell cycle progression [6].

In vivo, 17-DMAG (Alvespimycin) HCl (10mg/kg/day; 5 times per week for 16 days; i.p.) treatment significantly reduces the number of white blood cells in the blood of TCL1-SCID transgenic mouse models and prolongs survival [5]. The treatment with 17-DMAG (Alvespimycin) HCl (5mg/kg/day; 3 times per week; i.p.) reduced the incidence and severity of abdominal aortic aneurysms induced by ANG II in mice, weakened the remodeling of the aortic wall, the inflammatory response and the formation of new blood vessels, and decreased the expression of MMP-2 and MMP-9, the level of MDA and the secretion of MCP-1 [7].

References:

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[1] Ge J, Normant E, Porter JR, et al. Design, synthesis, and biological evaluation of hydroquinone derivatives of 17-amino-17-demethoxygeldanamycin as potent, water-soluble inhibitors of Hsp90. *J Med Chem*. 2006;49(15):4606-4615.
[2] Sun X, Bristol JA, Iwahori S, Hagemeier SR, Meng Q, Barlow EA, Fingeroth JD, Tarakanova VL, Kalejta RF, Kenney SC. Hsp90 inhibitor 17-DMAG decreases expression of conserved herpesvirus protein kinases and reduces virus production in Epstein-Barr virus-infected cells. J Virol. 2013 Sep;87(18):10126-38.
[3] Chang Y J, Huang C Y, Hung C S, et al. Glucose-regulated protein 78 mediates the therapeutic efficacy of 17-DMAG in colon cancer cells[J]. Tumor Biology, 2015, 36(6): 4367-4376.
[4] Mellatyar H, Talaei S, Pilehvar-Soltanahmadi Y, et al. Targeted cancer therapy through 17-DMAG as an Hsp90 inhibitor: Overview and current state of the art[J]. Biomedicine & Pharmacotherapy, 2018, 102: 608-617.
[5] Hertlein E, Wagner AJ, Jones J, et al. 17-DMAG targets the nuclear factor-kappaB family of proteins to induce apoptosis in chronic lymphocytic leukemia: clinical implications of HSP90 inhibition. *Blood*. 2010;116(1):45-53.
[6] Kawano M, Tanaka K, Itonaga I, Iwasaki T, Kubota Y, Tsumura H. The anti-oncogenic effect of 17-DMAG via the inactivation of HSP90 and MET pathway in osteosarcoma cells. Oncol Res. 2023 Jul 21;31(5):631-643.
[7] Qi J, Yang P, Yi B, et al. Heat shock protein 90 inhibition by 17-DMAG attenuates abdominal aortic aneurysm formation in mice[J]. American Journal of Physiology-Heart and Circulatory Physiology, 2015, 308(8): H841-H852.

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