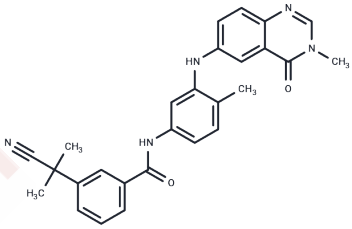
Data Sheet (Cat.No.T6318)

TargetMol

AZ 628

Chemical Properties



CAS No. : 878739-06-1

Formula: C27H25N5O2

Molecular Weight: 451.52

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	AZ628 is a new pan-Raf inhibitor for BRAF, BRAFV600E, and c-Raf-1 with IC50 of 105 nM, 34 nM and 29 nM, also inhibits VEGFR2, DDR2, Lyn, Flt1, FMS, etc.
Targets(IC50)	Apoptosis,Raf
In vitro	AZ628 prevents activation of number of tyrosine protein kinases including VEGFR2, DDR2, Lyn, Flt1, FMS and others. AZ628 suppresses anchorage-dependent and -independent growth, gives rise to cell cycle arrest, and induces apoptosis in colon and melanoma cell lines harboring B-RafV600E mutation. The profile of AZ628 cross-reactivity suggests that similar to sorafenib, AZ628 may be antiangiogenic based on prevention of VEGFR2. [1] AZ628-resistant clones are approximately 100-fold more resistant to AZ628 than the parental cell line, exhibiting IC50 of approximately 10 μM, compared with 0.1 μM for the parental cell line. Effective suppression of p-ERK1/2 levels is observed in the M14 parental cell line following treatment with increasing concentrations of AZ628. AZ628-resistant clones express elevated CRAF. Elevated CRAF expression is a potential mechanism of acquired resistance to continuous AZ628 exposure, resulting in sustained activation of ERK1/2. p-ERK1/2 activity is not significantly inhibited by exposure to AZ628 in one of these three AZ628-insensitive cell lines (Wm1552C). Unlike in the AZ628-resistant M14 cells in which AZ628 fails to suppress the activation of ERK, AZ628 treatment efficiently attenuates ERK activation in the NRAS mutant melanoma cells.[2]
Cell Research	Approximately 0.5-2.5 × 105 M14 cells are seeded in 12 or 24 - well plates, respectively, in medium supplemented with 5% FBS. After overnight incubation, the cells are treated with various concentrations of AZ628. Fresh medium and drug is replaced every 2 days until the untreated control wells reached confluence. At this time-point, the media is removed and the cells are fixed in 4% formaldehyde in PBS for 20 minutes at room temperature. Cells are then washed twice with PBS and stained with a 1:5000 solution of the fluorescent nucleic acid stain Syto60. Quantitation of fluorescent signal intensity is carried out at 700 nm, using an Odyssey Infrared Imager. Each experiment is performed in quadruplicate and the results shown represent the average of the four values compared to untreated wells. Error bars represent standard deviation of the 4 values from the mean. High-throughput cell growth/viability assays are performed.(Only for Reference)

Solubility Information

Solubility	DMSO: 250 mg/mL (553.69 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (4.43 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.2147 mL	11.0737 mL	22.1474 mL
5 mM	0.4429 mL	2.2147 mL	4.4295 mL
10 mM	0.2215 mL	1.1074 mL	2.2147 mL
50 mM	0.0443 mL	0.2215 mL	0.4429 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.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Khazak V, et al. Expert Opin Ther Targets. 2007, 11(12), 1587-1609.
Montagut C, et al. Cancer Res. 2008, 68(12), 4853-4861.