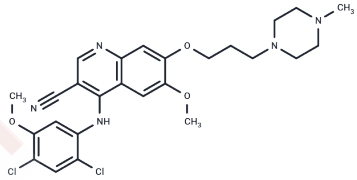
Data Sheet (Cat.No.T0152)

TargetMol

Bosutinib

Chemical Properties



CAS No. : 380843-75-4

Formula: C26H29Cl2N5O3

Molecular Weight: 530.45

Storage: Store at low temperature
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	Bosutinib (SKI-606) is a synthetic quinolone derivative and dual kinase inhibitor that targets both Abl (IC50: 1 nM) and Src (IC50: 1.2 nM) kinases.
Targets(IC50)	Bcr-Abl,Autophagy,Src
In vitro	Bosutinib has the antiproliferative activity against three different Bcr-Abl-positive leukemia cell lines (KU812, K562, and MEG-01). Bosutinib inhibited the proliferation of all three cell lines, with IC50s ranging from 5 nM in the KU812 line to 20 nM for the K562 and MEG-01 cell lines. Inhibition of proliferation by Bosutinib is associated with cell cycle arrest and cell death. Treatment with Bosutinib at 100 nM for 24 h (KU812) or 48 h (K562) resulted in a reduction of S and G2-M phase cells and an increase of cells with a DNA content of less than 2N. Treatment with Bosutinib at 100 nm also led to PARP degradation after 48 h. The potent antiproliferative activity of Bosutinib against CML lines was not a general property for leukemia cell lines. Molt-4, HL-60, Ramos, and other leukemia cell lines were unaffected by Bosutinib at concentrations less than 1 μM [2].
In vivo	Bosutinib (30/25 mg/kg, b.i.d) reduces tumor growth in unstaged and staged Src-transformed fibroblast mouse xenograft models. Bosutinib (100 mg/kg) also induces complete tumor regression in a K562 mouse xenograft model when administered once per day for five days [2].
Kinase Assay	The Src kinase activity is measured in an ELISA format. Src (3 units/reaction), reaction buffer (50 mM Tris-HCl pH 7.5, 10 mM MgCl2, 0.1 mM EGTA, 0.5 mM Na3VO4) and cdc2 substrate peptide are added to various concentration of Bosutinib and incubated at 30 °C for 10 minutes. The reaction is started by the addition of ATP to a final concentration of 100 μM, incubated at 30 °C for 1 hour and stopped by addition of EDTA. Instructions from the manufacturer are followed for subsequent steps. The Abl kinase assay is performed in a DELFIA solid phase europium-based detection assay format. Biotinylated peptide (2 μM) is bound to streptavidin-coated microtitration plates for 1.5 hours in 1 mg/mL ovalbumin in PBS. The plates are washed for 1 hour with PBS/0.1% Tween 80, followed by a PBS wash. The kinase reaction is incubated for 1 hour at 30°C. Abl kinase (10 units) is mixed with 50 mM Tris-HCl (pH 7.5), 10 mM MgCl2, 80 μM EGTA, 100 μM ATP, 0.5 mM Na3VO4, 1% DMSO, 1 mM HEPES (pH 7.0), 200 μg/mL ovalbumin and various concentration of Bosutinib. The reaction is stopped with EDTA at a final concentration of 50 mM. The reaction is monitored with Eu-labeled phosphotyrosine antibody and DELFIA

Kinase Assay	enhancement solution [2].
Cell Research	Cells are exposed to various concentrations of Bosutinib for 72 hours. Anchorage-independent proliferation of Abl-MLV-transformed fibroblasts is measured in 96-well ultra-low binding plates treated with Sigmacote to block residual cell attachment. Cell proliferation is measured with MTS or Cell-Glo. For the determination of cell cycle or cell death, cells are prepared for FACS analysis in the CycleTest Plus DNA reagent kit and analyzed on a fluorescence-activated cell sorter flow cytometer [2].
Animal Research	K562 cells were suspended to 50 million cells/ml in Matrigel (1 volume of cells with 1 volume of cold Matrigel). Nude female mice 6-7 weeks of age were given injections of 0.2 ml of this suspension. Tumors were staged for 10 days, at which time they entered the growth phase. At this time, the compound was administered by oral gavage in a 0.2-ml suspension with 0.5% methocel/0.4% Tween 80 [2].

Solubility Information

Solubility	DMSO: 65 mg/mL (122.54 mM),Sonication is recommended. Ethanol: 13.3 mg/mL (25.07 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 (3.77 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	1.8852 mL	9.426 mL	18.8519 mL
5 mM	0.377 mL	1.8852 mL	3.7704 mL
10 mM	0.1885 mL	0.9426 mL	1.8852 mL
50 mM	0.0377 mL	0.1885 mL	0.377 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

Boschelli DH, et al. Optimization of 4-phenylamino-3-quinolinecarbonitriles as potent inhibitors of Src kinase activity. J Med Chem. 2001 Nov 8;44(23):3965-77.
Cheng S, Jin P, Li H, et al. Evaluation of CML TKI Induced Cardiovascular Toxicity and Development of Potential Rescue Strategies in a Zebrafish Model. Frontiers in Pharmacology. 2021: 2866.
Golas JM, et al. SKI-606, a 4-anilino-3-quinolinecarbonitrile dual inhibitor of Src and Abl kinases, is a potent antiproliferative agent against chronic myelogenous leukemia cells in culture and causes regression of K562 xenografts in nude mice. Cancer Res. 2003 Jan 15;63(2):375-81.
Yan H, Wu W, Hu Y, et al.Regorafenib inhibits EphA2 phosphorylation and leads to liver damage via the ERK/MDM2/p53 axis.Nature Communications.2023, 14(1): 2756.
Golas JM, et al. SKI-606, a Src/Abl inhibitor with in vivo activity in colon tumor xenograft models. Cancer Res. 2005 Jun 15;65(12):5358-64.