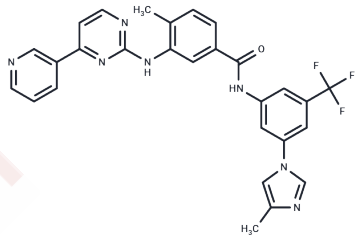
Data Sheet (Cat.No.T1524)

TargetMol

Nilotinib

Chemical Properties



CAS No. : 641571-10-0

Formula: C28H22F3N7O

Molecular Weight: 529.52

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	Nilotinib (AMN107) is a Bcr-Abl tyrosine kinase inhibitor with oral activity. Nilotinib has antitumor activity and may be used for the treatment of Imatinib-resistant chronic myelogenous leukemia (CML).
Targets(IC50)	Bcr-Abl,Autophagy
In vitro	**METHODS**: Ba/F3 cells expressing wild-type or mutant Bcr-Abl were treated with Nilotinib for 72 h, and cell viability was measured by methanethiosulfonate-based viability assay. **RESULTS**: Nilotinib inhibited the growth of cells expressing wild-type Bcr-Abl with 20-fold higher potency than imatinib (IC50:13 vs. 260 nmol/L). Similar improvements were maintained in all imatinib-resistant mutants tested except T315I. [1] **METHODS**: Melanoma cell line D04 was treated with Nilotinib (0.1-10 μM) for 3 h. Target protein expression levels were examined by Western Blot. **RESULTS**: Nilotinib stimulated robust MEK and ERK phosphorylation at concentrations as low as 100 nM. [2]
In vivo	**METHODS**: To test the antitumor activity in vivo, Nilotinib (25 mg/kg) and PD184352 (25 mg/kg) were administered by gavage to Balb/cJ mice bearing Ba/F3 allografts of BCR-ABL or BCR-ABLT315I once daily for twenty days. **RESULTS**: Nilotinib strongly inhibited the growth of BCR-ABL tumors, but not PD184352, nor did PD184352 enhance the growth inhibitory activity of Nilotinib. In contrast, BCR-ABLT315I tumors were insensitive to both Nilotinib and PD184352, but these drugs synergistically inhibited tumor growth. [2]
Kinase Assay	Kinase assays using wild-type and mutant glutathione S-transferase (GST)–Abl fusion proteins (c-Abl amino acids 220-498) were done as described, with minor alterations. GST-Abl fusion proteins were released from glutathione-Sepharose beads before use; the concentration of ATP was 5 μmol/L. Immediately before use in kinase autophosphorylation and in vitro peptide substrate phosphorylation assays, GST-Abl kinase domain fusion proteins were treated with LAR tyrosine phosphatase according to the manufacturer's instructions. After 1-hour incubation at 30°C, LAR phosphatase was inactivated by addition of sodium vanadate (1 mmol/L). Immunoblot analysis comparing untreated GST-Abl kinase to dephosphorylated GST-Abl kinase was routinely done using phosphotyrosine-specific antibody 4G10 to confirm complete (>95%) dephosphorylation of tyrosine residues and c-Abl antibody CST 2862 to confirm equal loading of GST-Abl kinase. The inhibitor concentration ranges for IC50 determinations

	were 0 to 5,000 nmol/L (imatinib and AMN107) or 0 to 32 nmol/L (BMS-354825). The BMS-354825 concentration range was extended to 1,000 nmol/L for mutant T315I. These same inhibitor concentrations were used for the in vitro peptide substrate phosphorylation assays. The three inhibitors were tested over these same concentration ranges against GST-Src kinase and GST-Lyn kinase [1].
Cell Research	Ba/F3 cell lines were plated in triplicate and incubated with escalating concentrations of imatinib, AMN107, or BMS-354825 for 72 hours. Proliferation was measured using a methanethiosulfonate-based viability assay. IC50 and IC90 values are reported as the mean of three independent experiments done in quadruplicate. The inhibitor concentration ranges for IC50 and IC90 determinations were 0 to 2,000 nmol/L (imatinib and AMN107) or 0 to 32 nmol/L (BMS-354825). The imatinib concentration range was extended to 6,400 nmol/L for mutants with IC50 >2,000 nmol/L. The BMS-354825 concentration range was extended to 200 nmol/L for mutant T315I [1].
Animal Research	The GIST xenograft lines GK1X, GK2X and GK3X in nude mice were established from GIST patients as described in our previous study [10]. These xenograft lines were maintained by continual passage in BALB/cSLc-nu/nu mice. Mice bearing GK1X, GK2X and GK3X tumors (6-8 mice per group) were treated daily with vehicle or 40 mg/kg imatinib or nilotinib for 4 weeks. Tumor volume (TV) was determined from caliper measurements of tumor length (L) and width (w) according to the formula LW2/2. TV was determined every two to three days and on the day of evaluation. Mice were sacrificed and the percentage of tumor growth inhibition (TGI) was calculated as follows: TGI (%) ?=? [1-(mean of treatment group tumor volume on evaluation day - mean of treatment group tumor volume on day 1)/(mean of control group tumor volume on evaluation day - mean of control group tumor volume on day 1)]×100 [2].

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), 10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2.6 mg/mL (4.91 mM),Suspension. Ethanol: < 1 mg/mL (insoluble or slightly soluble), DMSO: 13.75 mg/mL (25.97 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.8885 mL	9.4425 mL	18.885 mL
5 mM	0.3777 mL	1.8885 mL	3.777 mL
10 mM	0.1889 mL	0.9443 mL	1.8885 mL
50 mM	0.0378 mL	0.1889 mL	0.3777 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

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Kuang Y, Chai Y, Xu L, et al. Glabrone as a specific UGT1A9 probe substrate and its application in discovering the inhibitor glycycoumarin[J]. European Journal of Pharmaceutical Sciences. 2021: 105786.