Data Sheet (Cat.No.T5001)

TargetMol

Nintedanib esylate

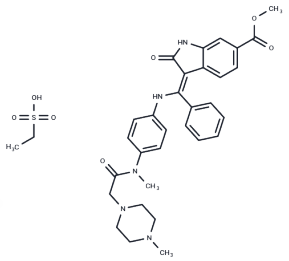
Chemical Properties

CAS No. : 656247-18-6

Formula: C31H33N5O4.C2H6O3S

Molecular Weight: 649.76

Storage: Keep away from direct sunlight,Keep away from moisture,Store at low temperature,Store under nitrogen
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	Nintedanib esylate (BIBF 1120 esylate) is a potent triple angiokinase inhibitor targeting VEGFR1/2/3, FGFR1/2/3, and PDGFRα/β.
Targets(IC50)	FGFR,PDGFR,VEGFR
In vitro	BIBF 1120 binds to the ATP-binding site in the cleft between the amino and carboxy terminal lobes of the kinase domain. BIBF 1120 inhibits proliferation of PDGF-BB stimulated BRPs with EC50 of 79 nM in cell assays. BIBF1120 (100 nM) blocks activation of MAPK after stimulation with 5% serum plus PDGF-BB. BIBF1120 prevents PDGF-BB stimulated proliferation with an EC50 of 69 nM in cultures of human vascular smooth muscle cells (HUASMC).
In vivo	BIBF1120, administered orally at doses ranging from 25-100 mg/kg daily, demonstrates high efficacy across various tumor models, including human tumor xenografts in nude mice and a syngeneic rat tumor model. Its effectiveness is confirmed through magnetic resonance imaging, which shows significant reductions in tumor perfusion, vessel density, and vessel integrity within 3 to 5 days, leading to substantial growth inhibition. Moreover, BIBF1120 is well-tolerated and exhibits promising results in in vivo tumor models, highlighting its potential as an effective oral therapeutic option.
Kinase Assay	Enzyme activity is assayed in the presence or absence of serial dilutions of BIBF1120 performed in 25% DMSO. Each microtiter plate contains internal controls such as blank, maximum reaction, and historical reference compound. All incubations are conducted at room temperature on a rotation shaker. 10 μL of each BIBF1120 dilution is added to 10 μL of diluted kinase (0.8 μg/mL VEGFR2, 10 mM Tris pH 7.5, 2 mM EDTA, and 2 mg/mL BSA) and preincubated for 1 hour. The reaction is started by addition of 30 μL of substrate mix containing 62.4 mM Tris pH 7.5, 2.7 mM DTT, 5.3 mM MnCl2, 13.3 mM Mg-acetate, 0.42 mM ATP, 0.83 mg/mL Poly-Glu-Tyr(4:1), and 1.7 μg/mL Poly-Glu-Tyr(4:1)-biotin and incubated for 1 hour. The reaction is stopped by addition of 50 μL of 250 mM EDTA, 20 mM HEPES, pH 7.4. 90 μL of the reaction mix is transferred to a streptavidin plate and incubated for 1-2 hours. After three washes with PBS the EU-labeled antibody, PY20 is added (recommended dilution 1:2000 of 0.5 mg/mL labeled antibody in DELFIA assay buffer). Excessive detection antibody is removed by three ishes of DELFIA washing

Kinase Assay	buffer. Then 10 minutes before measurement on the multilabel reader, each well is incubated with 100 μL of DELFIA enhancement solution.
Animal Research	Five-week-old to 6-wk-old athymic NMRI-nu/nu female mice (21-31 g) are used for the assay. After acclimatization, mice are inoculated with 1 to 5×106 (in 100 μL) FaDu, Caki-1, SKOV-3, H460, HT-29, or PAC-120 cells s.c. into the right flank of the animal. After acclimatization, F344 Fischer rats are injected with 5×106 (in 100 μL) GS-9L cells s.c. into the right flank of the animal. For pharmacokinetic analysis, blood is isolated at indicated time points from the retroorbital plexus of mice and plasma is analyzed using high performance liquid chromatography-mass spectrometry methodology.

Solubility Information

Solubility	DMSO: 101 mg/mL (155.44 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.539 mL	7.6951 mL	15.3903 mL
5 mM	0.3078 mL	1.539 mL	3.0781 mL
10 mM	0.1539 mL	0.7695 mL	1.539 mL
50 mM	0.0308 mL	0.1539 mL	0.3078 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

Roth GJ, et al. Design, synthesis, and evaluation of indolinones as triple angiokinase inhibitors and the discovery of a highly specific 6-methoxycarbonyl-substituted indolinone (BIBF 1120). J Med Chem, 2009, 52(14), 4466-4480.
Suzuki N, et al. Effect of a novel oral chemotherapeutic agent containing a combination of trifluridine, tipiracil and the novel triple angiokinase inhibitor nintedanib, on human colorectal cancer xenografts. Oncol Rep. 2016 Dec;36 (6):3123-3130.

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Tel:781-999-4286 E_mail:info@targetmol.com Address:34 Washington Street,Wellesley Hills,MA 02481