Nintedanib esylate

Cat. No.: HY-11106

CAS No.: 656247-18-6

Molecular Formula: $C_{33}H_{39}N_5O_7S$

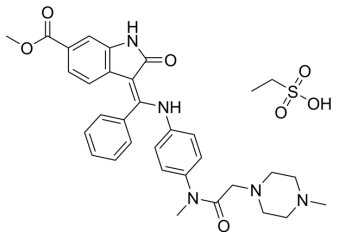
Molecular Weight: 649.76

Target: PDGFR; VEGFR; FGFR

Pathway: Protein Tyrosine Kinase/RTK

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 41.67 mg/mL (64.13 mM; ultrasonic and warming and heat to 60°C)

H_2O : 16.67 mg/mL (25.66 mM; Need ultrasonic)

Ethanol : 3.08 mg/mL (4.74 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.5390 mL	7.6951 mL	15.3903 mL
	5 mM	0.3078 mL	1.5390 mL	3.0781 mL
	10 mM	0.1539 mL	0.7695 mL	1.5390 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 20% HP-β-CD in saline
   Solubility: 20 mg/mL (30.78 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 50% PEG300 >> 50% saline
   Solubility: 10 mg/mL (15.39 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (3.85 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (3.85 mM); Clear solution
5. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (3.85 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Nintedanib esylate (BIBF 1120 esylate) is a potent triple angiokinase inhibitor for VEGFR1/2/3, FGFR1/2/3 and PDGFRα/β with IC_{50}s of 34 nM/13 nM/13 nM, 69 nM/37 nM/108 nM and 59 nM/65 nM, respectively.

IC_{50} & Target	VEGFR1 34 nM (IC_{50})	VEGFR2 13 nM (IC_{50})	VEGFR3 13 nM (IC_{50})	FGFR1 69 nM (IC_{50})
	FGFR2 37 nM (IC_{50})	FGFR3 108 nM (IC_{50})	PDGFRα 59 nM (IC_{50})	PDGFRβ 65 nM (IC_{50})

In Vitro

Nintedanib (BIBF 1120) binds to the ATP-binding site in the cleft between the amino and carboxy terminal lobes of the kinase domain. Nintedanib (BIBF 1120) inhibits proliferation of PDGF-BB stimulated BRPs with EC_{50} of 79 nM in cell assays. Nintedanib (BIBF 1120) (100 nM) blocks activation of MAPK after stimulation with 5% serum plus PDGF-BB. Nintedanib (BIBF 1120) prevents PDGF-BB stimulated proliferation with an EC_{50} of 69 nM in cultures of human vascular smooth muscle cells (HUASMC)[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Nintedanib (BIBF 1120) (25-100 mg/kg daily p.o.) is highly active in all tumor models, including human tumor xenografts growing in nude mice and a syngeneic rat tumor model. This is evident in the magnetic resonance imaging of tumor perfusion after 3 days, reducing vessel density and vessel integrity after 5 days, and profound growth inhibition[1]. Nintedanib (BIBF 1120) is orally available and displays encouraging efficacy in in vivo tumor models while being well tolerated[2].

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PROTOCOL

Animal Administration [1]

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 5×10^6 (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 5×10^6 (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[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nature Machine Intelligence. 2020 Jun.
- Sci Transl Med. 7 Jul 2022.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Sci Adv. 2022 Jun 17;8(24):eabn4564.
- Br J Cancer. 2020 Mar;122(7):986-994.

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REFERENCES

[1]. Hilberg F, et al. BIBF 1120: triple angiokinase inhibitor with sustained receptor blockade and good antitumor efficacy. Cancer Res, 2008, 68(12), 4774-4782.

[2]. 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.

[3]. 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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