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Produktinformation

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- Diagnostik & molekulare Diagnostik
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Lieferung & Zahlungsart

siehe unsere Liefer- und Versandbedingungen

Zuschläge

- Mindermengenzuschlag
- Trockeneiszuschlag
- Gefahrgutzuschlag
- Expressversand

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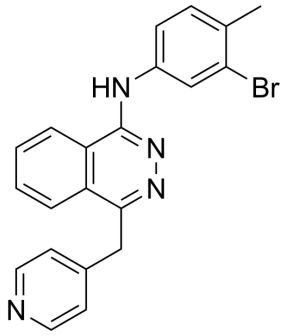
NVP-ACC789

Cat. No.:	HY-19624
CAS No.:	300842-64-2
Molecular Formula:	$C_{21}H_{17}BrN_4$
Molecular Weight:	405.29
Target:	VEGFR; PDGFR
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (61.68 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4674 mL	12.3368 mL	24.6737 mL
	5 mM	0.4935 mL	2.4674 mL	4.9347 mL
	10 mM	0.2467 mL	1.2337 mL	2.4674 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.17 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.17 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

NVP-ACC789 is an inhibitor of human VEGFR-1, VEGFR-2 (mouse VEGFR-2), VEGFR-3 and PDGFR-β with IC_{50}s of 0.38, 0.02 (0.23), 0.18, 1.4 μM, respectively.

IC_{50} & Target

VEGFR-2 0.02 μM (IC_{50})	VEGFR-1 0.38 μM (IC_{50})	mVEGFR-2 0.23 μM (IC_{50})	VEGFR-3 0.18 μM (IC_{50})
PDGFR-β 1.4 μM (IC_{50})			

In Vitro

The enzymatic kinase assays demonstrate that NVP-ACC789 is an inhibitor of human VEGFR-1, VEGFR-2 (mouse VEGFR-2),

	VEGFR-3 and PDGFR-β with IC_{50}s of 0.38, 0.02 (0.23), 0.18, 1.4 μM, respectively. In VEGF-treated cultures, addition of the VEGFR-2 inhibitor NVP-ACC789 reduces BME cell number to baseline levels from 1 μM. Likewise, bFGF-induced BME cell proliferation is reduced markedly by NVP-ACC789 from 1 to 10 μM, without however reaching basal levels. NVP-ACC789 is found to be a potent inhibitor of VEGF-induced HUVE cell proliferation with an IC_{50} of 1.6 nM. NVP-ACC789 also completely inhibits VEGF-induced BME and BAE cell invasion and VEGF-C-induced BAE cell invasion. The inhibition is dose-dependent in both cell types with a maximal effect from 1 μM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	NVP-ACC789 which is given in daily oral doses for 6 days blocks VEGF-induced angiogenesis in a dose-dependent manner. NVP-ACC789 also inhibits the response to bFGF to some extent, but the dose-response curve is not linear for NVP-ACC789[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Human VEGFR-2-transfected CHO cells are seeded into 6-well plates and grown to about 80% confluency. NVP-ACC789 is added in serial dilutions and the cells incubated for 2 h at 37°C in medium without fetal calf serum (FCS). VEGF (20 ng/mL) is then added. After a 5-min incubation at 37°C, the cells are washed twice with ice-cold phosphate-buffered saline and lysed. Nuclei are removed by centrifugation for 10 min at 4°C. Protein concentrations of the lysates are determined[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	HUVE cell proliferation is determined. Cells are seeded into 1.5% gelatin-coated 96-well plates (5×10^3 cells per well) and incubated in endothelial cell growth medium containing 5% fetal calf serum (FCS) for 24 h. The medium is replaced with essential basic medium (1.5% FCS), and the cells are incubated for another 24 h. Essential basic medium is then replaced with fresh medium containing either 50 ng/mL VEGF or 0.5 ng/mL bFGF. NVP-ACC789 is added just before addition of growth factors. The cells are incubated for a further 24 h before adding the BrdU labeling solution. Twenty four hours later, the labeling solution is removed, the cells are fixed, and the incorporated BrdU is visualized with a peroxidase-labeled anti-BrdU antibody and TMB substrate[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Porous Teflon chambers (volume, 0.5 mL) filled with 0.8% w/v agar-containing heparin (20 U/mL) with or without VEGF (2 μg/mL) or bFGF (0.3 μg/mL) are implanted subcutaneously on the dorsal flank of female mice. The mice are treated with NVP-ACC789 (p.o. once daily) or vehicle (5% dimethyl sulfoxide, 1% Tween 80 in water) starting 1 day before implantation of the chamber and continuing for 5 days thereafter. At the end of the treatment period, the mice are killed, and the chambers are removed. The vascularized tissue growing around the chamber is removed carefully and weighed, and the blood content is assessed by measuring hemoglobin levels. The percentage inhibition of the angiogenic response (increase in tissue weight or total blood) is calculated. EC_{50} values are estimated from the dose response curves (% inhibition versus dose). Each experiment is performed with six animals per dose group and each dose is tested in at least two independent experiments[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Tille JC, et al. Vascular endothelial growth factor (VEGF) receptor-2 antagonists inhibit VEGF- and basicfibroblast growth factor-induced angiogenesis in vivo and in vitro. J Pharmacol Exp Ther. 2001 Dec;299(3):1073-85.

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