Regorafenib monohydrate

Cat. No.: HY-10331A

CAS No.: 1019206-88-2

Molecular Formula: $C_{21}H_{17}ClF_4N_4O_4$

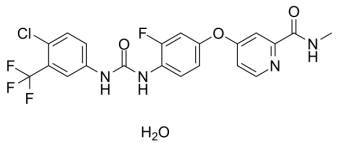
Molecular Weight: 500.83

Target: VEGFR; Autophagy; PDGFR; Raf; RET; FGFR; c-Kit; Tie

Pathway: Protein Tyrosine Kinase/RTK; Autophagy; MAPK/ERK Pathway

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 : 50 mg/mL (99.83 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9967 mL	9.9834 mL	19.9669 mL
	5 mM	0.3993 mL	1.9967 mL	3.9934 mL
	10 mM	0.1997 mL	0.9983 mL	1.9967 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 (4.99 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.99 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Regorafenib (BAY 73-4506) monohydrate is an orally active and potent multi-targeted receptor tyrosine kinase inhibitor, with IC_{50} values of 13/4.2/46, 22, 7, 1.5 and 2.5 nM for VEGFR1/2/3, PDGFRβ, Kit, RET and Raf-1, respectively. Regorafenib monohydrate shows very robust antitumor and antiangiogenic activity[1].

IC_{50} & Target

Raf-1 2.5 nM (IC_{50})	Tie2 311 ± 46 nM (IC_{50})	VEGFR2 4.2 nM (IC_{50})	VEGFR1 13 nM (IC_{50})
$BRaf^{V600E}$ 19 nM (IC_{50})	PDGFRβ 22 nM (IC_{50})	Braf 28 nM (IC_{50})	VEGFR3 46 nM (IC_{50})

In Vitro

Regorafenib monohydrate (0-10 μM, 96 h) shows anti-proliferation activity in GIST 882, Thyroid TT, MDA-MB-231, HepG2, A375 and SW620 cells[1].
Regorafenib monohydrate (0-3000 nM, 30 min) inhibits the autophosphorylation of VEGFR2, TIE2 and PDGFR-β, and inhibits FGFR and pERK1/2[1].
Regorafenib monohydrate causes a concentration-dependent decrease in Hep3B cell growth, with an IC_{50} of 5 μM.
Regorafenib subsequently increases the levels of phospho-c-Jun, a JNK target, but not total c-Jun in Hep3B cells[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	GIST 882, Thyroid TT, MDA-MB-231, HepG2, A375 and SW620 cells
Concentration:	10 μM and 5 nM
Incubation Time:	96 h
Result:	Showed anti-proliferation activity in GIST 882, Thyroid TT, MDA-MB-231, HepG2, A375 and SW620 cells, with IC_{50} values of 45 ± 20, 34 ± 8, 401 ± 88, 560 ± 200, 900, 967 ± 287 nM. respectively.

Western Blot Analysis[1]

Cell Line:	NIH-3T3/VEGFR2 cells, (CHO)-TIE2 cells, HAoSMCs cells, MCF-7 cells
Concentration:	0, 10, 30, 100, 300, 1000, 3000 nM
Incubation Time:	30 min
Result:	Inhibited the autophosphorylation of VEGFR2, TIE2 and PDGFR-β, with IC_{50} values of 3, 31, and 90 nM, respectively, inhibited FGFR signaling in MCF-7 breast cancer (BC) cells stimulated with FGF10, and showed inhibition of phosphorylated FGFR substrate 2 (pFRS2) and the downstream signaling kinase pERK1/2.

In Vivo

Regorafenib monohydrate (10 mg/kg, Orally, single dose or daily for 4 days) inhibits tumor vasculature and tumor growth in a rat GS9L glioblastoma model[1].
Regorafenib monohydrate (0-100 mg/kg, Orally, qd × 9) exhibits antitumorigenic and antiangiogenic effects in the Colo-205, MDA-MB-231 and 786-O model[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Rat GS9L glioblastoma xenograft[1]
Dosage:	10 mg/kg
Administration:	Orally, single dose or daily for 4 days
Result:	Inhibited tumor vasculature and tumor growth in a rat GS9L glioblastoma model.

Animal Model:	Female athymic NCr nu/nu mice, Multiple xenograft models, including models derived from CRC (Colo-205), BC (MDA-MB-231) and RCC (786-O) tumors[1]
Dosage:	0, 3, 10, 30, 100 mg/kg
Administration:	Orally, qd × 9
Result:	Effectively inhibited growth of the Colo-205, MDA-MB-231 and 786-O model. Significantly reduces tumor MVA, effectively inhibited the RAF/MEK/ERK signaling cascade, and

	drastically inhibited tumor cell proliferation.

CUSTOMER VALIDATION

- Cell Res. 2020 Sep;30(9):779-793.
- Cancer Discov. 2021 Jul;11(7):1716-1735.
- Cancer Discov. 2019 Dec;9(12):1686-1695.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Adv Sci (Weinh). 2023 Jun 17;e2206798.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Wilhelm SM, et al. Regorafenib (BAY 73-4506): a new oral multikinase inhibitor of angiogenic, stromal and oncogenic receptor tyrosine kinases with potent preclinical antitumor activity. Int J Cancer, 2011, 129(1), 245-255.

[2]. Heng DY, et al. Targeted therapy for metastatic renal cell carcinoma: current treatment and future directions. Ther Adv Med Oncol, 2010, 2(1), 39-49.

[3]. Carr BI, et al. Fluoro-Bay 43-9006 (Regorafenib) effects on hepatoma cells: growth inhibition, quiescence, and recovery. J Cell Physiol, 2013, 228(2), 292-297.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA