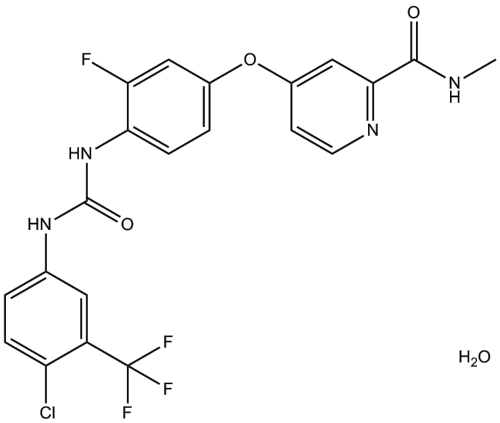
Product Data Sheet

Product Name: Regorafenib monohydrate
Cat. No.: GC14534

Chemical Properties

Cas. No.	1019206-88-2		
Chemical Name	4-[4-[[4-chloro-3-(trifluoromethyl)phenyl]carbamoylamino]-3-fluorophenoxy]-N-methylpyridine-2-carboxamide;hydrate		
SMILES	CNC(=O)C1=NC=CC(=C1)OC2=CC(=C(C=C2)NC(=O)NC3=CC(=C(C=C3)Cl)C(F)(F)F)F.O		
Formula	$C_{21}H_{17}ClF_4N_4O_4$	M.Wt	500.83
Solubility	100 mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment [1]:

Cell lines	Human umbilical vascular endothelial and human aortic smooth muscle cells

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Preparation method	The solubility of this compound in DMSO is >25.1mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37°C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.
Reacting condition	IC50: 2.6 and 146 nM
Applications	Regorafenib effectively inhibited proliferation of VEGF and FGF-2-stimulated human umbilical vascular endothelial and human aortic smooth muscle cells stimulated with the BB dimeric glycoprotein of PDGF with IC50 values of 2.6 and 146 nM, respectively.

Animal experiment [1]:

Animal models	CRC, breast cancer, and renal cell carcinoma mouse xenograft models
Dosage form	10 to 100 mg/kg
Application	In CRC, breast cancer, and renal cell carcinoma mouse xenograft models, Regorafenib monohydrate inhibited tumor growth in a dose-dependent way. Regorafenib also decreased pERK1/2, suggesting that the antiproliferative effects of Regorafenib were through RAF/MEK/ERK signaling cascade inhibition.
Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

Caution: Product has not been fully validated for medical applications. For research use only.
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References:

[1] Crona DJ, Keisler MD, Walko CM.Regorafenib: a novel multitargeted tyrosine kinase inhibitor for colorectal cancer and gastrointestinal stromal tumors.Ann Pharmacother. 2013 Dec;47(12):1685-96.

Background

Regorafenib monohydrate is a multitargetedinhibitor of tyrosine kinase with IC50 values of 13nM, 4.2nM, 46nM, 2.5nM, 28nM, 19nM, 202nM, 22nM, 7nM, 1.5nM and 311nM, respectively for VEGFR-1, mVEGFR-2, mVEGFR-3, Raf-1, BRAF WT, BRAFV600E, FGFR-1, PDGFR-β, c-KIT, RETand TIE2 [1].

Regorafenib is a multikinase inhibitor of both intracellular and membrane-bound RTKs. It shows potent inhibition of angiogenic and stromal RTKs like VEGF receptors-1-3, PDGFR-β and FGF receptor-1 with IC50 values ranging from4.2 to 311nM in biochemical assays. It also inhibits oncogenic RTKs, such as RET and c-KIT, with IC50 values ranging from 1.5 to 28nM in cellular assays [1].

Regorafenib is reported to have anti-tumor efficacy to various tumors including breast, pancreas, thyroid, melanoma, GIST, and CRC with a mean IC50 value less than 1μM. These inhibition effects of tumor growth are also found in mouse xenograft models after the treatment of regorafenib at dose ranging from 10 to 100 mg/kg [1].

References:
[1] Crona DJ, Keisler MD, Walko CM.Regorafenib: a novel multitargeted tyrosine kinase inhibitor for colorectal cancer and gastrointestinal stromal tumors.Ann Pharmacother. 2013 Dec;47(12):1685-96.

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