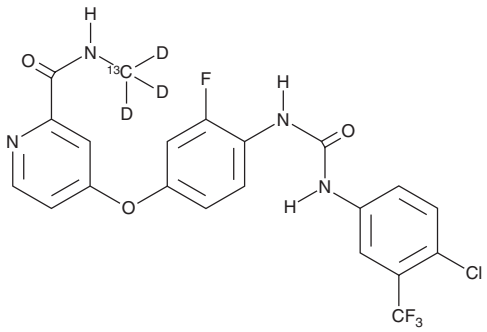
PRODUCT INFORMATION

Regorafenib-^{13}C-d$_3$

Item No. 25486

CAS Registry No.:	2126178-55-8
Formal Name:	4-[4-[[[[4-chloro-3-(trifluoromethyl) phenyl]amino]carbonyl]amino]-3-fluorophenoxy]-N-(methyl-^{13}C-d$_3$)-2-pyridinecarboxamide
MF:	$C_{20}[^{13}C]H_{12}D_3ClF_4N_4O_3$
FW:	486.8
Chemical Purity:	≥98% (Regorafenib)
Deuterium Incorporation:	≥99% deuterated forms (d_1-d_3); ≤1% d_0
Supplied as:	A solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

Regorafenib-^{13}C-d$_3$ is intended for use as an internal standard for the quantification of regorafenib (Item No. 18498) by GC- or LC-MS. The accuracy of the sample weight in this vial is between 5% over and 2% under the amount shown on the vial. If better precision is required, the deuterated standard should be quantitated against a more precisely weighed unlabeled standard by constructing a standard curve of peak intensity ratios (deuterated *versus* unlabeled).

Regorafenib-^{13}C-d$_3$ is supplied as a solid. A stock solution may be made by dissolving the regorafenib-^{13}C-d$_3$ in the solvent of choice. Regorafenib-^{13}C-d$_3$ is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of regorafenib-^{13}C-d$_3$ in ethanol is approximately 14 mg/ml and approximately 30 mg/ml in DMSO and DMF.

Description

Regorafenib is an orally bioavailable multi-kinase inhibitor with anticancer activity.[1] It inhibits RET, C-RAF, VEGFR2, c-Kit, VEGFR1, and PDGFRβ with IC_{50} values of 1.5, 2.5, 4.2, 7, 13, and 22 nM, respectively. Regorafenib also inhibits B-RAF, VEGFR3, FGFR, and Tie2 (IC_{50}s = 28, 46, 202, and 311 nM, respectively) as well as other kinases.[1-3] *In vivo*, regorafenib (10 mg/kg) reduces tumor size in the MDA-MB-231 breast and 786-O renal cancer mouse xenograft models.[1] It also reduces tumor microvessel area and inhibits tumor growth in a panel of mouse xenograft models. Formulations containing regorafenib have been used in the treatment of advanced gastrointestinal stromal tumors and metastatic colorectal cancer.

References

1. Wilhelm, S.M., Dumas, J., Adnane, L., *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* **129(1)**, 245-255 (2011).
2. Uitdehaag, J.C.M., de Roos, J.A.D.M., van Doornmalen, A.M., *et al.* Comparison of the cancer gene targeting and biochemical selectivities of all targeted kinase inhibitors approved for clinical use. *PLoS One* **9(3)**, 1-13 (2014).
3. Ravi, S. and Singal, A.K. Regorafenib: An evidence-based review of its potential in patients with advanced liver cancer. *Core Evid.* **9**, 81-87 (2014).

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