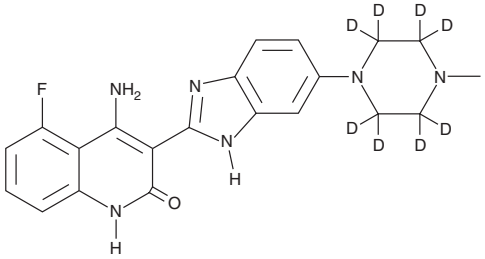
PRODUCT INFORMATION

Dovitinib-d_8

Item No. 28706

CAS Registry No.: 1246819-84-0
Formal Name: 4-amino-5-fluoro-3-(6-(4-methylpiperazin-1-yl-2,2,3,3,5,5,6,6-d_8)-1H-benzo[d]imidazol-2-yl)quinolin-2(1H)-one
MF: $C_{21}H_{13}D_8FN_6O$
FW: 400.5
Chemical Purity: ≥98% (Dovitinib)
Deuterium Incorporation: ≥99% deuterated forms (d_1-d_8); ≤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

Dovitinib-d_8 is intended for use as an internal standard for the quantification of dovitinib (Item No. 15220) 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).

Dovitinib-d_8 is supplied as a solid. A stock solution may be made by dissolving the dovitinib-d_8 in the solvent of choice, which should be purged with an inert gas. Dovitinib-d_8 is soluble in the organic solvent DMSO. Dovitinib-d_8 is also soluble in a 1:1 solution of acetonitrile:methanol.

Description

Dovitinib is a multi-kinase inhibitor.[1] It inhibits the receptor tyrosine kinases FLT3, CSF1R, and c-Kit (IC_{50}s = 1, 36, and 2 nM, respectively), as well as FGFR1, FGFR3, VEGFR1-3, PDFGRα, and PDGFRβ (IC_{50}s = 8, 9, 10, 13, 8, 27, and 210 nM, respectively). Dovitinib inhibits proliferation of human multiple myeloma cell lines expressing mutant, but not wild-type, FGFR3 (IC_{50}s = 90-550 and >2,500 nM, respectively). It decreases FGF-induced ERK1/2 phosphorylation and induces apoptosis in patient-derived multiple myeloma cells when used at a concentration of 500 nM. Dovitinib (3-300 mg/kg for eight days) inhibits bFGF-induced angiogenesis in a Matrigel™ plug assay in mice.[2] It reduces tumor growth in KM12L4A colon, DU145 prostate, and MV4-11 acute myelogenous leukemia mouse xenograft models with ED_{50} values of 17, 23, and 3 mg/kg per day, respectively.

References

1. Trudel, S., Li, Z.H., Wei, E., *et al.* CHIR-258, a novel, multitargeted tyrosine kinase inhibitor for the potential treatment of t(4;14) multiple myeloma. *Blood* **105(7)**, 2941-2948 (2005).
2. Renhowe, P.A., Pecchi, S., Shafer, C.M., *et al*. Design, structure-activity relationships and in vivo characterization of 4-amino-3-benzimidazol-2-ylhydroquinolin-2-ones: A novel class of receptor tyrosine kinase inhibitors. *J. Med. Chem.* **52(2)**, 278-292 (2009).

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