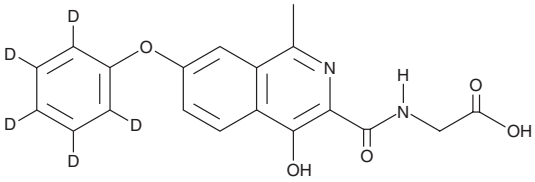
PRODUCT INFORMATION

Roxadustat-d_5

Item No. 34235

CAS Registry No.:	2043026-13-5
Formal Name:	N-[(4-hydroxy-1-methyl-7-phenoxy-d_5-3-isoquinolinyl)carbonyl]-glycine
MF:	$C_{19}H_{11}D_5N_2O_5$
FW:	357.4
Chemical Purity:	≥98% (Roxadustat)
Deuterium Incorporation:	≥99% deuterated forms (d_1-d_5); ≤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

Roxadustat-d_5 is intended for use as an internal standard for the quantification of roxadustat (Item No. 15294) 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).

Roxadustat-d_5 is supplied as a solid. A stock solution may be made by dissolving the roxadustat-d_5 in the solvent of choice, which should be purged with an inert gas. Roxadustat-d_5 is soluble in acetone and DMSO.

Description

Roxadustat is an inhibitor of hypoxia-inducible factor prolyl hydroxylase (HIF-PH; IC_{50}s = 1.4, 1.26, and 1.32 µM for HIF-PH1, HIF-PH2, and HIF-PH3, respectively).[1] It is selective for HIF-PH over other 2-oxoglutarate-dependent dioxygenases, including lysine-specific demethylase 5A (KDM5A), KDM5B, -5C, -5D, and -6B (IC_{50}s = >100 µM for all). Roxadustat (10-200 µM) stabilizes HIF-1α and HIF-2α in Hep3B hepatocellular carcinoma cells. It increases levels of secreted erythropoietin in Hep3B cells in a concentration-dependent manner and increases erythropoiesis in rats when administered at doses of 25 and 50 mg/kg.[2] Roxadustat reverses anemia in a rat model of chronic inflammation induced by peptidoglycan-polysaccharide, as well as a rat model of chronic kidney disease induced by 5/6 nephrectomy. It reduces tumor growth and increases survival in a murine Lewis lung carcinoma model when administered at a dose of 3 mg/animal.[3]

References

1. Yeh, T.-L., Leissing, T.M., Abboud, M.I., *et al*. Molecular and cellular mechanisms of HIF prolyl hydroxylase inhibitors in clinical trials. *Chem. Sci*. **8(11)**, 7651-7668 (2017).
2. Del Balzo, U., Signore, P.E., Walkinshaw, G., *et al*. Nonclinical characterization of the hypoxia-inducible factor prolyl hydroxylase inhibitor roxadustat, a novel treatment of anemia of chronic kidney disease. *J. Pharmacol. Exp. Ther*. **374(4)**, 342-353 (2020).
3. Nishide, S., Matsunaga, S., Shiota, M., *et al*. Controlling the phenotype of tumor-infiltrating macrophages via the PHD-HIF axis inhibits tumor growth in a mouse model. *iScience* **19**, 940-954 (2019).

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