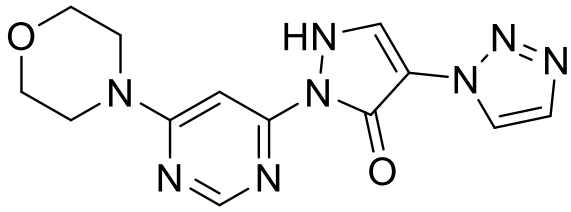
Product data sheet

MedKoo Cat#: 525715 Name: Molidustat CAS#: 1154028-82-6 Chemical Formula: $C_{13}H_{14}N_8O_2$ Exact Mass: 314.12397 Molecular Weight: 314.3	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Molidustat, also known as BAY 85-3934, is a novel inhibitor of hypoxia-inducible factor (HIF) prolyl hydroxylase (PH) which stimulates erythropoietin (EPO) production and the formation of red blood cells. Phase I data have shown that inhibition of HIF-PH by Molidustat results in an increase in endogenous production of EPO. Molidustat is currently clinical trials at Bayer for the treatment of patients suffering from renal anemia due to chronic kidney disease.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	5.0	15.91
5% TFA	1.67	5.31

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.18 mL	15.91 mL	31.82 mL
5 mM	0.64 mL	3.18 mL	6.36 mL
10 mM	0.32 mL	1.59 mL	3.18 mL
50 mM	0.06 mL	0.32 mL	0.64 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Kachamakova-Trojanowska N, Podkalicka P, Bogacz T, Barwacz S, Józkowicz A, Dulak J, Łoboda A. HIF-1 stabilization exerts anticancer effects in breast cancer cells in vitro and in vivo. Biochem Pharmacol. 2020 May;175:113922. doi: 10.1016/j.bcp.2020.113922. Epub 2020 Mar 20. PMID: 32205093.

2. Coyle RC, Barrs RW, Richards DJ, Ladd EP, Menick DR, Mei Y. Targeting HIF-α for robust prevascularization of human cardiac organoids. J Tissue Eng Regen Med. 2021 Feb;15(2):189-202. doi: 10.1002/term.3165. Epub 2020 Dec 8. PMID: 33868541; PMCID: PMC8049092.

In vivo study

1. Flamme I, Oehme F, Ellinghaus P, Jeske M, Keldenich J, Thuss U. Mimicking hypoxia to treat anemia: HIF-stabilizer BAY 85-3934 (Molidustat) stimulates erythropoietin production without hypertensive effects. PLoS One. 2014 Nov 13;9(11):e111838. doi: 10.1371/journal.pone.0111838. PMID: 25392999; PMCID: PMC4230943.

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2. Zhang A, Nakano D, Morisawa N, Kitada K, Kittikulsuth W, Rahman A, Morikawa T, Konishi Y, Nishiyama A. Effects of molidustat, a hypoxia-inducible factor prolyl hydroxylase inhibitor, on sodium dynamics in hypertensive subtotally nephrectomized rats. J Pharmacol Sci. 2021 Jun;146(2):98-104. doi: 10.1016/j.jphs.2021.03.007. Epub 2021 Mar 31. PMID: 33941326.

7. Bioactivity

Biological target: Stabilizes HIF-1α and inhibits prolyl hydroxylase. The mean IC50 values of Molidustat for PHD1, PHD2, and PHD3 are 480 nM, 280 nM, and 450 nM, respectively.

In vitro activity

Using this cell model Molidustat was observed to stabilize HIF-1α in the case of the highest (50 μM) concentration of the compound (Fig. 1A), however, the expression of VEGF, a known HIF-1-dependent gene, was increased already by 10 μM molidustat after 24 h treatment. Both VEGF mRNA expression and protein release to the media were increased after 24 h and 48 h (Fig. 1 B, C). his compound enhanced VEGF expression to a similar or even higher level as hypoxia (Fig. 1 B, C). At the highest dose (50 μM), a nearly two-fold decrease in cell survival was observed after 72 h as compared to 48 h (Fig. 2A). Additionally, the clonogenic potential of MDA-MB-231 cells in response to molidustat was tested. The ability of cells to form colonies was slightly impaired after 10 μM molidustat (Fig. 2B). However, the number of colonies was greatly diminished in the wells with 25 μM inhibitor added. At the highest concentration, cell survival was dramatically affected to the level, where no colonies could be observed. To check whether molidustat induces cell apoptosis, flow cytometry analysis using double staining with Hoechst/7-AAD was performed. There was an increase in the apoptotic fraction after 72 h of the treatment only at the highest inhibitor concentration in comparison to untreated cells (Fig. 2C). However, the percentage of apoptotic cells was rather small (up to 8%) pointing at other pathways implemented in the decreased breast cancer cell viability.

Reference: Biochem Pharmacol. 2020 May;175:113922.
https://www.sciencedirect.com/science/article/pii/S0006295220301507?via%3Dihub

In vivo activity

HIF stabilization by oral administration of the HIF-PH inhibitor BAY 85-3934 (molidustat) results in dose-dependent production of EPO in healthy Wistar rats and cynomolgus monkeys. Molidustat therapy is aldo effective in the treatment of renal anemia in rats with impaired kidney function and, unlike treatment with rhEPO, resulted in normalization of hypertensive blood pressure in a rat model of CKD

Reference: PLoS One. 2014 Nov 13;9(11):e111838. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4230943/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.