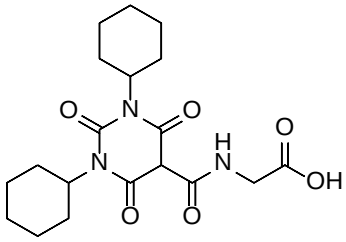
Product data sheet

MedKoo Cat#: 206434 Name: Daprodustat CAS#: 960539-70-2 Chemical Formula: $C_{19}H_{27}N_3O_6$ Exact Mass: 393.1890 Molecular Weight: 393.44	
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:
Daprodustat, also known as GSK1278863, is a novel HIF-prolyl hydroxylase inhibitor. Hypoxia inducible factor (HIF) stabilization by HIF-prolyl hydroxylase (PHD) inhibitors may improve ischemic conditions such as peripheral artery disease (PAD). Short-term treatment with a novel HIF-prolyl hydroxylase inhibitor (GSK1278863) failed to improve measures of performance in subjects with claudication-limited peripheral artery 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
DMF	3.0	7.63
DMSO	14.17	36.02
DMSO:PBS (pH 7.2) (1:1)	0.50	1.27
Ethanol	1.0	2.54

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.54 mL	12.71 mL	25.42 mL
5 mM	0.51 mL	2.54 mL	5.08 mL
10 mM	0.25 mL	1.27 mL	2.54 mL
50 mM	0.05 mL	0.25 mL	0.51 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. Ariazi JL, Duffy KJ, Adams DF, Fitch DM, Luo L, Pappalardi M, Biju M, DiFilippo EH, Shaw T, Wiggall K, Erickson-Miller C. Discovery and Preclinical Characterization of GSK1278863 (Daprodustat), a Small Molecule Hypoxia Inducible Factor-Prolyl Hydroxylase Inhibitor for Anemia. J Pharmacol Exp Ther. 2017 Dec;363(3):336-347. doi: 10.1124/jpet.117.242503. Epub 2017 Sep 19. PMID: 28928122.

In vivo study

1. Ariazi JL, Duffy KJ, Adams DF, Fitch DM, Luo L, Pappalardi M, Biju M, DiFilippo EH, Shaw T, Wiggall K, Erickson-Miller C. Discovery and Preclinical Characterization of GSK1278863 (Daprodustat), a Small Molecule Hypoxia Inducible Factor-Prolyl Hydroxylase Inhibitor for Anemia. J Pharmacol Exp Ther. 2017 Dec;363(3):336-347. doi: 10.1124/jpet.117.242503. Epub 2017 Sep 19. PMID: 28928122.

7. Bioactivity

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Biological target: Daprodustat (GSK1278863) is a hypoxia-inducible factor prolyl hydroxylase (HIF-PH) inhibitor.

In vitro activity

The immediate downstream effect of PHD (a family of HIF-prolyl hydroxylases) inhibition in a cellular context is HIFα subunit accumulation. Stabilization of HIF1α and HIF2α was determined by Western blot analysis of nuclear protein extracts after GSK1278863 treatment of Hep3B cells. Western blot analysis demonstrated that neither HIF1α nor HIF2α was detected in the vehicle-treated cells, and both HIF1α and HIF2α were visualized in the control-treated cells. Treatment with either 25 or 50 μM GSK1278863 for 6 hours resulted in the accumulation of both HIF1α and HIF2α subunits (Fig. 5). These results demonstrate that prolyl hydroxylase inhibition by GSK1278863 treatment of cells results in the immediate downstream effect of HIFα subunit stabilization.

Reference: J Pharmacol Exp Ther. 2017 Dec;363(3):336-347. https://jpet.aspetjournals.org/content/363/3/336.long

In vivo activity

In vivo, normal female B6D2F1 mice were administered a single oral dose of GSK1278863 at 60 mg/kg, and blood samples were collected at intervals between 4 and 30 hours after dosing (n = 6 mice/time point for GSK1278863-treated mice; vehicle-treated mice were sampled at 6 hours only). After the treatment with GSK1278863, the EPO (erythropoietin) protein levels peaked at 12 hours after dosing (Fig. 6), representing an 11.2-fold increase with a mean plasma concentration of 1303 pg/ml. Additionally, the EPO values at all other time points remained elevated by 1.9- to 2.9-fold relative to the vehicle-treated mice. The VEGF (vascular endothelial growth factor) concentrations remained generally unchanged across the time course and were only slightly higher than those of vehicle-treated mice. These data indicate that a single 60 mg/kg dose of GSK1278863 results in a significant but transient increase in circulating levels of EPO, with minimal impact on VEGF concentrations.

Reference: J Pharmacol Exp Ther. 2017 Dec;363(3):336-347. https://jpet.aspetjournals.org/content/363/3/336.long