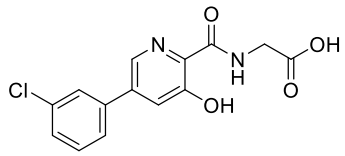
Product data sheet

MedKoo Cat#: 319561 Name: Vadadustat CAS#: 1000025-07-9 Chemical Formula: $C_{14}H_{11}ClN_2O_4$ Exact Mass: 306.0407 Molecular Weight: 306.7	
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:

Vadadustat, also known as AKB-6548 and PG-1016548, is a potent Hypoxia-inducible factor-proline dioxygenase inhibitor. AKB-6548 works by inhibiting hypoxia inducible factor-prolyl hydroxylase (HIP-PH), leading to stabilization and increased levels of HIFα. In turn HIFα improves production of hemoglobin and red blood cells (RBCs), while maintaining normal levels of erythropoietin (EPO) in patients. We believe this differentiated mechanism of action has the potential to be safer than that of injectable recombinant erythropoietin stimulating agents (rESAs), avoiding supra-physiological levels of EPO and saturation of EPO receptors for prolonged periods of time.

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	54.33	177.14
DMF	5.0	16.30
DMF:PBS (pH 7.2) (1:20)	0.04	0.13
Ethanol	5.5	17.93

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.26 mL	16.30 mL	32.61 mL
5 mM	0.65 mL	3.26 mL	6.52 mL
10 mM	0.33 mL	1.63 mL	3.26 mL
50 mM	0.07 mL	0.33 mL	0.65 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. Zielniok K, Burdzinska A, Kaleta B, Zagozdzon R, Paczek L. Vadadustat, a HIF Prolyl Hydroxylase Inhibitor, Improves Immunomodulatory Properties of Human Mesenchymal Stromal Cells. Cells. 2020 Nov 1;9(11):2396. doi: 10.3390/cells9112396. PMID: 33139632; PMCID: PMC7693843.

In vivo study

1. Hanudel MR, Wong S, Jung G, Qiao B, Gabayan V, Zuk A, Ganz T. Amelioration of chronic kidney disease-associated anemia by vadadustat in mice is not dependent on erythroferrone. Kidney Int. 2021 Jul;100(1):79-89. doi: 10.1016/j.kint.2021.03.019. Epub 2021 Mar 31. PMID: 33811979.

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7. Bioactivity

Biological target:

Vadadustat (PG-1016548) is a titratable, oral hypoxia-inducible factor prolyl hydroxylase (HIF-PH) inhibitor.

In vitro activity

This research has shown that Vadadustat pretreatment enhances the immunosuppressive potential of MSCs. Vadadustat significantly enhanced the suppressive effect of MSCs on PBMCs proliferation (MLR test), and this effect was partially associated with the modulation of MSCs secretome. However, the suppressive capacity of MSCs was higher in direct contact with PBMCs. This may indicate that changes in both, compounds secreted by MSCs and presented on their surface are responsible for enhancing the immunosuppressive effect of MSCs pretreated with Vadadustat. Moreover, Vadadustat significantly diminished the chemotactic properties of the MSCs secretome, as assessed by the monocyte-enriched PBMCs migration assay.

Reference: Cells. 2020 Nov; 9(11): 2396. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7693843/

In vivo activity

In the non-CKD model, in which the mice were not anemic, vadadustat induced similar increases in hemoglobin concentrations from pretreatment values in the WT and EKO groups (Supplementary Figure S1). In the CKD model, as expected, both WT and EKO groups developed moderate anemia (Figure 1a and b). Vadadustat normalized red blood cell counts and hemoglobin concentrations in both the WT and EKO CKD groups (Figure 1a and b). In the CKD models, whereas 3 weeks of vehicle treatment resulted in a mean 1.5 to 2.1 g/dl decrease in hemoglobin concentrations, 3 weeks of vadadustat treatment resulted in a mean 3.4 to 4.5 g/dl increase in hemoglobin concentrations (Figure 1c, Supplementary Figure S2). Vadadustat also increased hematocrit (Figure 1d), mean corpuscular volume (Figure 1e), mean corpuscular hemoglobin (Figure 1f), and red blood cell distribution width (Figure 1g) in both the WT and EKO CKD groups. Therefore, vadadustat ameliorated CKD-associated anemia in the presence or absence of ERFE, demonstrating ERFE-independent proerythropoietic effects.

Reference: Kidney Int. 2021 Jul;100(1):79-89. https://www.kidney-international.org/article/S0085-2538(21)00354-9/fulltext

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.