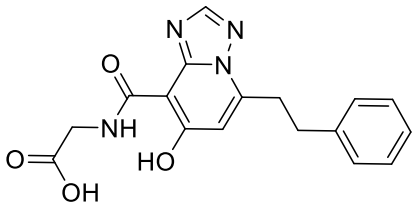
Product data sheet

MedKoo Cat#: 561113 Name: Enarodustat CAS#: 1262132-81-9 (free base) Chemical Formula: $C_{17}H_{16}N_4O_4$ Exact Mass: 340.1172 Molecular Weight: 340.34	
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:
Enarodustat, also known as JTZ-951, is a prolyl hydroxylase inhibitor. JTZ-951 (enarodustat) stabilizes HIF-α protein and induces erythropoiesis without effects on the function of vascular endothelial growth factor. Enarodustat increases endogenous erythropoietin levels in the treatment of anemia associated with chronic kidney disease (CKD). JTZ-951 induces erythropoiesis without affecting VEGF function. JTZ-951 may be a new oral candidate that increases and maintains hemoglobin concentrations in renal anemia patients.

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	60.44	177.59
DMSO:PBS (pH 7.2) (1:4)	0.20	0.59
DMF	30.0	88.15
Ethanol	25.0	73.46

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.94 mL	14.69 mL	29.38 mL
5 mM	0.59 mL	2.94 mL	5.88 mL
10 mM	0.29 mL	1.47 mL	2.94 mL
50 mM	0.06 mL	0.29 mL	0.59 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. Wakashima T, Tanaka T, Fukui K, Komoda Y, Shinozaki Y, Kobayashi H, Matsuo A, Nangaku M. JTZ-951, an HIF prolyl hydroxylase inhibitor, suppresses renal interstitial fibroblast transformation and expression of fibrosis-related factors. Am J Physiol Renal Physiol. 2020 Jan 1;318(1):F14-F24. doi: 10.1152/ajprenal.00323.2019. Epub 2019 Oct 21. PMID: 31630548.
2. Fukui K, Shinozaki Y, Kobayashi H, Deai K, Yoshiuchi H, Matsui T, Matsuo A, Matsushita M, Tanaka T, Nangaku M. JTZ-951 (enarodustat), a hypoxia-inducibe factor prolyl hydroxylase inhibitor, stabilizes HIF-α protein and induces erythropoiesis without effects on the function of vascular endothelial growth factor. Eur J Pharmacol. 2019 Sep 15;859:172532. doi: 10.1016/j.ejphar.2019.172532. Epub 2019 Jul 10. PMID: 31301309.

In vivo study

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1. Hasegawa S, Tanaka T, Saito T, Fukui K, Wakashima T, Susaki EA, Ueda HR, Nangaku M. The oral hypoxia-inducible factor prolyl hydroxylase inhibitor enarodustat counteracts alterations in renal energy metabolism in the early stages of diabetic kidney disease. Kidney Int. 2020 May;97(5):934-950. doi: 10.1016/j.kint.2019.12.007. Epub 2019 Dec 25. PMID: 32171449.
2. Sugahara M, Tanaka S, Tanaka T, Saito H, Ishimoto Y, Wakashima T, Ueda M, Fukui K, Shimizu A, Inagi R, Yamauchi T, Kadowaki T, Nangaku M. Prolyl Hydroxylase Domain Inhibitor Protects against Metabolic Disorders and Associated Kidney Disease in Obese Type 2 Diabetic Mice. J Am Soc Nephrol. 2020 Mar;31(3):560-577. doi: 10.1681/ASN.2019060582. Epub 2020 Jan 29. PMID: 31996409; PMCID: PMC7062217.

7. Bioactivity

Biological target:

Enarodustat is a potent and orally active factor prolyl hydroxylase inhibitor, with an EC50 of 0.22 μM.

In vitro activity

To evaluate the effect of JTZ-951 in this model, this study added JTZ-951 on day 0 and checked HIF-1α and HIF-2α protein stabilization, α-SMA expression, and hypoxic EPO upregulation. The addition of JTZ-951 stabilized HIF-1α and HIF-2α proteins (Fig. 2A), suppressed α-SMA expression (Fig. 2B), and maintained the hypoxic induction of EPO (Fig. 2C). Furthermore, JTZ-951 also reversed α-SMA upregulation on day 8 when added on day 6 (Fig. 2D).

Reference: Am J Physiol Renal Physiol. 2020 Jan 1;318(1):F14-F24. https://pubmed.ncbi.nlm.nih.gov/31630548/

In vivo activity

Glomerulomegaly was noticeable in group B compared with group A, which was reversed by enarodustat (Figure 9e). Transcriptome analysis of renal tissue in alloxan-induced diabetic mice showed symmetric metabolism alterations (diabetes vs. enarodustat) in the same way as in the STZ-induced diabetic rat model (Figure 10): fatty-acid metabolism was upregulated by diabetes, whereas glucose metabolism was upregulated by enarodustat. Furthermore, amino-acid metabolism was upregulated by diabetes and downregulated by enarodustat. Thus, enarodustat counteracted renal energy metabolism alterations occurring in the early stages of DKD in the alloxan-induced diabetic mouse model as well as in the STZ-induced diabetic rat model.

Reference: Kidney Int. 2020 May;97(5):934-950. https://pubmed.ncbi.nlm.nih.gov/32171449/