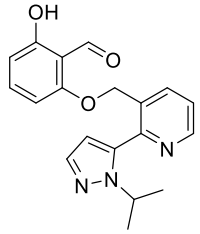
Product data sheet

MedKoo Cat#: 329516 Name: Voxelotor CAS#: 1446321-46-5 Chemical Formula: $C_{19}H_{19}N_3O_3$ Exact Mass: 337.1426 Molecular Weight: 337.379	
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:
Voxelotor, also known as GBT-440, is a hemoglobin S allosteric modulator. GBT440 Inhibits Sickling of Sickle Cell Trait Blood Under In Vitro Conditions Mimicking Strenuous Exercise. GBT440 increases haemoglobin oxygen affinity, reduces sickling and prolongs RBC half-life in a murine model of sickle cell 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	66.67	197.61
DMSO:PBS (pH 7.2) (1:5)	0.16	0.47
DMF	33.0	97.81
Ethanol	43.5	128.94

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.96 mL	14.82 mL	29.64 mL
5 mM	0.59 mL	2.96 mL	5.93 mL
10 mM	0.30 mL	1.48 mL	2.96 mL
50 mM	0.06 mL	0.30 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. Metcalf B, Chuang C, Dufu K, Patel MP, Silva-Garcia A, Johnson C, Lu Q, Partridge JR, Patskovska L, Patskovsky Y, Almo SC, Jacobson MP, Hua L, Xu Q, Gwaltney SL 2nd, Yee C, Harris J, Morgan BP, James J, Xu D, Hutchaleelaha A, Paulvannan K, Oksenberg D, Li Z. Discovery of GBT440, an Orally Bioavailable R-State Stabilizer of Sickle Cell Hemoglobin. ACS Med Chem Lett. 2017 Jan 23;8(3):321-326. doi: 10.1021/acsmedchemlett.6b00491. PMID: 28337324; PMCID: PMC5346980.
2. Dufu K, Lehrer-Graiwer J, Ramos E, Oksenberg D. GBT440 Inhibits Sickling of Sickle Cell Trait Blood Under In Vitro Conditions Mimicking Strenuous Exercise. Hematol Rep. 2016 Sep 28;8(3):6637. doi: 10.4081/hr.2016.6637. PMID: 27757216; PMCID: PMC5062624.

In vivo study

1. Gassner R, Schreier D, Hacker T, Tabima DM, Chesler N. GBT440 Increases Hematocrit and Improves Biventricular Function in Berkeley Sickle Cell Disease Mice. J Biomech Eng. 2021 Mar 1;143(3):034501. doi: 10.1115/1.4049079. PMID: 33175151; PMCID: PMC7871994.

2. Oksenberg D, Dufu K, Patel MP, Chuang C, Li Z, Xu Q, Silva-Garcia A, Zhou C, Hutchaleelaha A, Patskovska L, Patskovsky Y, Almo SC, Sinha U, Metcalf BW, Archer DR. GBT440 increases haemoglobin oxygen affinity, reduces sickling and prolongs RBC half-life in a murine model of sickle cell disease. Br J Haematol. 2016 Oct;175(1):141-53. doi: 10.1111/bjh.14214. Epub 2016 Jul 5. PMID: 27378309.

7. Bioactivity

Biological target:

Voxelotor (GBT 440) is an inhibitor of haemoglobin S (HbS) polymerization.

In vitro activity

GBT440 produced a concentration-dependent left shift in the OEC relative to untreated SCT blood in the hypertonic phosphate buffer (Figyre 5A) indicating a dose-dependent increase in Hb-O2 affinity. Most importantly, GBT440 dose-dependently decreased the number of sickled SCT RBCs in hypertonic phosphate buffer with pH 6.9 (Figure 5B). These results indicate that GBT440 inhibits in vitro sickling of SCT RBCs under conditions mimicking extreme hypoxia, dehydration and acidosis. Collectively, these results suggest that GBT440 may inhibit sickling of SCT blood in vivo under conditions that promote sickling such as during strenuous exerecise.

Reference: Hematol Rep. 2016 Sep 28; 8(3): 6637. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5062624/

In vivo activity

Compared to DMSO treated mice, three weeks of GBT440 significantly increased Hct (Fig. 1) such that the chronic anemia was effectively eliminated (Hct in age-matched C57BL/6 male mice, one of the 5 background strains of Berkeley mice, is 37%; Hct in 1 to 6 month old male and female littermate controls of the Berkeley mice is 42%). Echocardiography demonstrated that three weeks of treatment increased left ventricular ejection fraction (LVEF) and stroke volume index (stroke volume divided by body weight), as well as the pulmonary valve velocity time integral (PV VTI) (Fig. 2).

Reference: J Biomech Eng. 2021 Mar 1;143(3):034501. https://pubmed.ncbi.nlm.nih.gov/33175151/

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.