Product Datasheet

Technical Data

Formula	$C_{19}H_{19}N_3O_3$					
Molecular Weight	337.37	**CAS No.**	1446321-46-5			
Solubility (25°C)*	In vitro	DMSO	67 mg/mL (198.59 mM)			
		Ethanol	5 mg/mL (14.82 mM)			
		Water	Insoluble			
	In vivo (Add solvents to the product individually and in order)	Oral Administration	Homogeneous suspension	CMC-NA	≥5mg/ml	Taking the 1 mL working solution as an example, add 5 mg of this product to 1 ml of CMC-Na solution, mix evenly to obtain a homogeneous suspension with a final concentration of 5 mg/ml.
		Injection	Clear solution	5%DMSO [1]→ 40%PEG300 [2]→ 5%Tween80 [3]→ 50%ddH2O Validated by Capsid Bio labs. Should you need adjustments to this formulation, contact our sales team for custom testing.	3.350mg/ml (9.93mM)	Taking the 1 mL working solution as an example, add 50 μL of 67 mg/ml clarified DMSO stock solution to 400 μL of PEG300, mix evenly to clarify it; add 50 μL of Tween80 to the above system, mix evenly to clarify; then continue to add 500 μL of ddH2O to adjust the volume to 1 mL. The mixed solution should be used immediately for optimal results.
			Clear solution	5% DMSO [1]→ 95% Corn oil Validated by Capsid Bio labs. Should you need adjustments to this formulation, contact our sales team for custom testing.	0.830mg/ml (2.46mM)	Taking the 1 mL working solution as an example, add 50 μL of 16.6 mg/ml clear DMSO stock solution to 950 μL of corn oil and mix evenly. The mixed solution should be used immediately for optimal results.

* <1 mg/ml means slightly soluble or insoluble.
* Please note that Capsid Bio tests the solubility of all compounds in-house, and the actual solubility may differ slightly from published values. This is normal and is due to slight batch-to-batch variations.
* Room temperature shipping (Stability testing shows this product can be shipped at 2-8°C for storage purposes.)

Preparing Stock Solutions

Concentration \ Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.9641 mL	14.8205 mL	29.6410 mL
5 mM	0.5928 mL	2.9641 mL	5.9282 mL
10 mM	0.2964 mL	1.4821 mL	2.9641 mL
50 mM	0.0593 mL	0.2964 mL	0.5928 mL

Biological Activity

Description	Voxelotor is a novel small molecule **hemoglobin modifier** which increases hemoglobin oxygen affinity.
In vitro	GBT440 is a new potent allosteric effector of sickle cell hemoglobin that increases the affinity of hemoglobin for oxygen and consequently inhibits its polymerization when subjected to hypoxic conditions. GBT440 inhibits these isozymes(CYP 1A2, 2C8, 2C9, 2C19, 2D6, and 3A4) with IC50 ranging from 7.9 to 148 μM. It is not a substrate for either P-gp or BCRP transporters[1]. It binds to the N-terminal a chain of Hb[2].
In vivo	GBT440 has favorable oral bioavailability of 60, 37, and 36% in rats, dogs, and monkeys, respectively, with similar blood and plasma half-lives of approximately 20 h each. T1/2 value of GBT440 in all animal species is significantly shorter than the T1/2 of red blood cells (~20 days), which supports that binding of GBT440 to hemoglobin is a reversible process. GBT440 is currently in Phase 3 clinical trials (NCT03036813) in SCD patients[1]. GBT440 increases haemoglobin oxygen affinity, reduces sickling and prolongs RBC half-life in a murine model of sickle cell disease. In a murine model of SCD, GBT440 extends the half-life of RBCs, reduces reticulocyte counts and prevents ex vivo RBC sickling. Importantly, oral dosing of GBT440 in animals demonstrates suitability for once daily dosing in humans and a highly selective partitioning into RBCs, which is a key therapeutic safety attribute. GBT440 shows dose proportional PK, a terminal half-life of 1.5-3 d[2].

Protocol (from reference)

Cell Assay:[2]

- **Cell lines**
  sickle RBCs
- **Concentrations**
  0, 300, 600, 1000 μM
- **Incubation Time**
  1 h
- **Method**
  whole blood (20% Hct) from SCD patients who has been transfusion free for 2 to 3 months (HbS > 70%) is incubated with various concentrations of GBT440 for 1 h at 37°C, diluted 100-fold in TES/saline buffer and deoxygenated in a Hemox Analyser

Animal Study:[1]

- **Animal Models**
  Sprague-Dawley rats
- **Dosages**
  7.2 to 120 mg/kg
- **Administration**
  oral administration

References

https://pubmed.ncbi.nlm.nih.gov/28337324/ https://pubmed.ncbi.nlm.nih.gov/27378309/

RETURN POLICY

Capsid Bio's Unconditional Return Policy ensures a smooth online shopping experience for our customers. If you are in any way unsatisfied with your purchase, you may return any item(s) within 7 days of receiving it. In the event of product quality issues, either protocol related or product related problems, you may return any item(s) within 365 days from the original purchase date. Please follow the instructions below when returning products.

SHIPPING & STORAGE

Capsid Bio products are transported at room temperature. If you receive the product at room temperature, please rest assured, the Capsid Bio Quality Inspection Department has conducted experiments to verify that the normal temperature placement of one month will not affect the biological activity of powder products. After collecting, please store the product according to the requirements described in the datasheet. Most Capsid Bio products are stable under the recommended conditions.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

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