# Voxelotor

**Cat. No.:** HY-18681

**CAS No.:** 1446321-46-5

**Molecular Formula:** $C_{19}H_{19}N_3O_3$

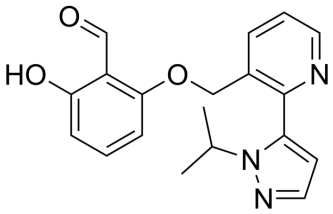
**Molecular Weight:** 337.37

**Target:** Others

**Pathway:** Others

**Storage:** 4°C, stored under nitrogen

* In solvent : -80°C, 1 year; -20°C, 6 months (stored under nitrogen)



## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : 100 mg/mL (296.41 mM; Need ultrasonic)

| Preparing Stock Solutions | Concentration / Solvent / 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 |

Please refer to the solubility information to select the appropriate solvent.

**In Vivo**

1. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (7.41 mM); Clear solution
2. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.41 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (6.17 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (6.17 mM); Clear solution
5. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (6.17 mM); Clear solution
6. Add each solvent one by one: 1% DMSO >> 99% saline
   Solubility: 0.5 mg/mL (1.48 mM); Suspended solution; Need ultrasonic

## BIOLOGICAL ACTIVITY

**Description**

Voxelotor (GBT 440) is a potent inhibitor of haemoglobin S (HbS) polymerization. Voxelotor has the potential for sickle cell disease (SCD) treatment[1].

| | |
|---|---|
| **$IC_{50}$ & Target** | HbS polymerization[1] |
| **In Vitro** | Voxelotor (GBT440) binds to the N-terminal a chain of haemoglobin (Hb), increases haemoglobin S (HbS) affinity for oxygen, delays in vitro HbS polymerization and prevents sickling of red blood cells (RBCs)[1].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **In Vivo** | Voxelotor (GBT440; 100-150 mg/kg; administered twice a day by oral gavage for 9-12 days) reduces ex vivo sickling and prolongs red blood cells (RBCs) half-life in a murine model of sickle cell disease (SCD)[1].<br>?Voxelotor shows $T_{1/2}$s of 11.7, 19.1±1.5, 66.0±11, 28.8±4.0 hours for mouse (70 mg/kg; i.v.), rat (1.6 mg/kg; i.v.), dog (1 mg/kg; i.v.), and momkey (1 mg/kg; i.v.), respectively[1].<br>?Voxelotor shows $C_{max}$s of 81.9, 71.2±6.0, 5.56±1.6, and 25.2±5.5 μg/mL for mouse (30 mg/kg; p.o.), rat (7.2 mg/kg; p.o.), dog (2.5 mg/kg; p.o.), and momkey (4.25 mg/kg; p.o.), respectively[1].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

| | |
|---|---|
| Animal Model: | HbSS Townes knock-in sickle mice (SS mice)[1] |
| Dosage: | 100 and 150 mg/kg |
| Administration: | Oral administration; twice a day; for 9-12 days |
| Result: | Reduced haemolysis. |

| | |
|---|---|
| Animal Model: | C57BL/6J mice, Sprague-Dawley rats, Beagle dogs and Cynomolgus monkeys[1] |
| Dosage: | 70, 1.6, 1 and 1 mg/kg for mice, rats, dogs and monkeys, respectively<br>30, 7.2, 2.5 and 4.25 mg/kg for mice, rats, dogs and monkeys, respectively |
| Administration: | Intravenous (IV: 70, 1 6, 1 and 1 mg/kg, respectively)<br>Oral (PO: 30, 7 2, 2 5 and 4 3 mg/kg, respectively) |
| Result: | $T_{1/2}$s of 11.7, 19.1±1.5, 66.0±11, 28.8±4.0 hours for mouse (70 mg/kg; i.v.), rat (1.6 mg/kg; i.v.), dog (1 mg/kg; i.v.), and momkey (1 mg/kg; i.v.), respectively.<br>$C_{max}$s of 81.9, 71.2±6.0, 5.56±1.6, and 25.2±5.5 μg/mL for mouse (30 mg/kg; p.o.), rat (7.2 mg/kg; p.o.), dog (2.5 mg/kg; p.o.), and momkey (4.25 mg/kg; p.o.), respectively. |

## CUSTOMER VALIDATION

- Am J Hematol. 2019 May;94(5):575-584.
- Pharmaceutics. 2021, 13(9), 1388.
- Sci Rep. 2020 Nov 20;10(1):20277.
- Am J Clin Pathol. 2020 Oct 13;154(5):627-634.
- J Pharm Biomed Anal. 2022: 115152.

See more customer validations on www.MedChemExpress.com

## REFERENCES

[1]. Metcalf B, Chuang C, Dufu K, et al. Discovery of GBT440, an Orally Bioavailable R-State Stabilizer of Sickle Cell Hemoglobin. ACS Med Chem Lett. 2017;8(3):321-326.

[2]. Oksenberg D, et al. 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.



Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA