Voxelotor

Cat. No.: HY-18681

CAS No.: 1446321-46-5

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

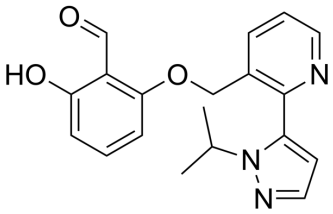
Molecular Weight: 337.37

Target: Others

Pathway: Others

Storage: 4°C, stored under nitrogen

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



SOLVENT & SOLUBILITY

In Vitro

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

Preparing Stock Solutions	Solvent / Mass / Concentration	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) ▯▯ N ▯▯▯▯▯▯ (Hb) ▯▯▯▯▯▯▯▯▯ S (HbS) ▯▯▯▯▯▯▯▯▯▯▯▯▯ HbS ▯▯▯▯▯▯▯▯▯ (RBC) ▯▯▯▯[1]▯ MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Voxelotor (GBT440▯100-150 mg/kg▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯ 9-12 ▯) ▯▯▯▯▯▯▯ (SCD) ▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯ (RBC) ▯ ▯▯▯▯[1]▯ Voxelotor ▯▯▯▯▯▯ $T_{1/2}$ ▯ 11.7▯19.1±1.5▯66.0±11▯28.8±4.0 ▯▯ (70 mg/kg▯iv)▯▯▯▯ (1.6 mg/kg▯iv)▯▯ (1 mg/kg▯iv)▯▯ momkey (1 mg/kg▯iv)▯▯▯▯[1]▯ Voxelotor ▯▯▯▯ (30 mg/kg▯po)▯▯▯▯ (7.2 mg/kg▯po)▯▯ (2.5 mg/kg▯po) ▯ momkey (4.25 mg/kg▯po) C_{max}s ▯ 81.9, 71.2±6.0, 5.56±1.6, and 25.2±5.5 μg/mL[1]▯ 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 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) 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. 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.
- J Pharm Biomed Anal. 2022: 115152.
- Am J Clin Pathol. 2020 Oct 13;154(5):627-634.

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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.

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