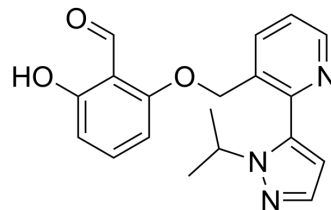


Voxelotor

Cat. No.:	HY-18681
CAS No.:	1446321-46-5
Molecular Formula:	C ₁₉ H ₁₉ N ₃ O 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	Solvent Concentration	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

- 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
- 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
- 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
- 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
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.08 mg/mL (6.17 mM); Clear solution
- 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].

IC₅₀ & 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] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.																
In Vivo	<p>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].</p> <p>?Voxelotor shows T_{1/2S} 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].</p> <p>?Voxelotor shows C_{maxS} 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].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <table border="1"> <tr> <td>Animal Model:</td> <td>HbSS Townes knock-in sickle mice (SS mice)^[1]</td> </tr> <tr> <td>Dosage:</td> <td>100 and 150 mg/kg</td> </tr> <tr> <td>Administration:</td> <td>Oral administration; twice a day; for 9-12 days</td> </tr> <tr> <td>Result:</td> <td>Reduced haemolysis.</td> </tr> </table> <table border="1"> <tr> <td>Animal Model:</td> <td>C57BL/6J mice, Sprague-Dawley rats, Beagle dogs and Cynomolgus monkeys^[1]</td> </tr> <tr> <td>Dosage:</td> <td>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</td> </tr> <tr> <td>Administration:</td> <td>Intravenous (IV: 70, 1.6, 1 and 1 mg/kg, respectively) Oral (PO: 30, 7.2, 2.5 and 4.3 mg/kg, respectively)</td> </tr> <tr> <td>Result:</td> <td>T_{1/2S} 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_{maxS} 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.</td> </tr> </table>	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 _{1/2S} 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 _{maxS} 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.
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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.

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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.

Caution: Product has not been fully validated for medical applications. For research use only.

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