Voxelotor

Cat. No.: HY-18681
CAS No.: 1446321-46-5
Molecular Formula: C₁₉H₁₉N₃O₃
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)

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Concentration</th>
<th>Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mg</td>
<td>5 mg</td>
</tr>
<tr>
<td></td>
<td>1 mM</td>
<td>2.9641 mL</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>0.5928 mL</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td>0.2964 mL</td>
</tr>
</tbody>
</table>

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].
### 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.

<table>
<thead>
<tr>
<th>Animal Model:</th>
<th>HbSS Townes knock-in sickle mice (SS mice)(^1)</th>
</tr>
</thead>
<tbody>
<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>
</tbody>
</table>

### 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)\(^1\).

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\(^1\).

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\(^1\).

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

<table>
<thead>
<tr>
<th>Animal Model:</th>
<th>C57BL/6J mice, Sprague-Dawley rats, Beagle dogs and Cynomolgus monkeys(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosage:</td>
<td>70, 1.6, 1 and 1 mg/kg for mice, rats, dogs and monkeys, respectively</td>
</tr>
<tr>
<td>Administration:</td>
<td>30, 7.2, 2.5 and 4.25 mg/kg for mice, rats, dogs and monkeys, respectively</td>
</tr>
<tr>
<td>Result:</td>
<td>(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.), 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.</td>
</tr>
</tbody>
</table>

### CUSTOMER VALIDATION

- Pharmaceutics. 2021, 13(9), 1388.

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### REFERENCES
