Vadadustat

Cat. No.: HY-101277
CAS No.: 1000025-07-9
Molecular Formula: C₁₄H₁₁ClN₂O₄
Molecular Weight: 306.7
Target: HIF/HIF Prolyl-Hydroxylase
Pathway: Metabolic Enzyme/Protease
Storage: Powder -20°C 3 years
        4°C 2 years
        In solvent -80°C 6 months
        -20°C 1 month

SOLVENT & SOLUBILITY

In Vitro
DMSO: 100 mg/mL (326.05 mM; Need ultrasonic)

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Mass Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>3.2605 mL</td>
<td>16.3026 mL</td>
<td>32.6051 mL</td>
<td></td>
</tr>
<tr>
<td>5 mM</td>
<td>0.6521 mL</td>
<td>3.2605 mL</td>
<td>6.5210 mL</td>
<td></td>
</tr>
<tr>
<td>10 mM</td>
<td>0.3261 mL</td>
<td>1.6303 mL</td>
<td>3.2605 mL</td>
<td></td>
</tr>
</tbody>
</table>

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

In Vivo
1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (8.15 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (8.15 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (8.15 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Vadadustat (PG-1016548) is a titratable, oral hypoxia-inducible factor prolyl hydroxylase (HIF-PH) inhibitor. Vadadustat is an erythropoiesis-stimulating agent and has the potential for anemia treatment in chronic kidney disease in vivo.

IC₅₀ & Target
IC₅₀: HIF-PH

In Vitro
Vadadustat induces endogenous erythropoietin synthesis and enhances iron mobilization. Vadadustat is well-tolerated in healthy volunteers and patients with chronic kidney disease, where it increases reticulocytes, plasma EPO, and Hb levels in a
dose-dependent manner. The increase in plasma EPO levels seen with vadadustat is comparable in magnitude to that occurring physiologically at moderate altitude and shows a normal diurnal pattern with a return to baseline levels prior to the next dose. Vadadustat improves iron homeostasis by decreasing hepcidin and increasing transferrin levels. Once-daily oral administration of vadadustat, titrated to increase and maintain Hb in the target range, may provide multiple advantages over conventional ESAs[1]. Vadadustat is observed to have a half-life of approximately 4.5 hours. Overall, patients demonstrate an increase in Hb levels, from 9.91 g/dL at baseline to 10.54 g/dL by day 29. Ferritin levels decrease from 334.1 ng/mL at baseline to 271.7 ng/mL by day 29[2].

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

REFERENCES


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