Macitentan

Cat. No.: HY-14184
CAS No.: 441798-33-0
Molecular Formula: $C_{19}H_{20}Br_2N_6O_4S$
Molecular Weight: 588.27
Target: Endothelin Receptor; Apoptosis
Pathway: GPCR/G Protein; Apoptosis
Storage:
- Powder: -20°C for 3 years, 4°C for 2 years
- In solvent: -80°C for 2 years, -20°C for 1 year

SOLVENT & SOLUBILITY

In Vitro

DMSO: $\geq 50$ mg/mL (84.99 mM)

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Mass (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>1.6999 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>8.4995 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>16.9990 mL</td>
</tr>
</tbody>
</table>

* "$\geq$" means soluble, but saturation unknown.

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
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<td></td>
</tr>
<tr>
<td>5 mM</td>
<td>0.3400 mL</td>
<td>1.6999 mL</td>
<td>3.3998 mL</td>
<td></td>
</tr>
<tr>
<td>10 mM</td>
<td>0.1700 mL</td>
<td>0.8499 mL</td>
<td>1.6999 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: $\geq 2.5$ mg/mL (4.25 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: $\geq 2.5$ mg/mL (4.25 mM); Clear solution
3. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: $\geq 2.5$ mg/mL (4.25 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Macitentan (ACT-064992) is an orally active, non-peptide dual ETA and ETB (endothelin receptor) antagonist. Macitentan has the potential for idiopathic pulmonary fibrosis (IPF) and pulmonary arterial hypertension (PAH)[1].

$IC_{50}$ & Target
<table>
<thead>
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<th>$IC_{50}$</th>
<th>Target</th>
</tr>
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<tbody>
<tr>
<td>ET$_A$</td>
<td>ET$_B$</td>
</tr>
</tbody>
</table>

In Vitro
Tube formation ability is restored when microvascular endothelial cells are preincubated with BOS or macitentan (ACT-
064992), also reducing the expression of mesenchymal markers and restoring CD31 expression and the imbalance between VEGF-A and VEGF-A165b[1].

Macitentan inhibits OATP1B1-mediated uptake of atorvastatin and OATP1B3-mediated uptake of estrone-3-sulfate with IC$_{50}$ ± SE values of 6.3 ± 0.7 and 11.8 ± 5.0μM, respectively[3].

Treatment with macitentan or with ACT-132577 does not lead to intracellular accumulation of R123 in HeyA8-MDR, showing that these compounds are not P-gp inhibitors[4].

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

<table>
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<th>In Vivo</th>
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</thead>
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| Macitentan (ACT-064992; 25 mg/kg/day, p.o.) prevents increased production of vasoactive and fibrogenic factors, NF-κB activation, structural and functional changes, and increases extracellular matrix protein production in type 2 diabetes in type 2 diabetes[2].
| Macitentan (10 mg/kg, p.o.) coupled with once-per-week 5 mg/kg taxol, significantly reduces the weight (size) of HeyA8-MDR tumors in mice. Combination therapy with macitentan (10 or 50 mg/kg, but not 5 mg/kg) and taxol or macitentan (10 mg/kg) and cisplatinum significantly reduces the number of proliferating Ki-67-positive cells[4].
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### PROTOCOL

#### Animal Administration [2]

Male db/db mice and age and sex-matched controls (27-32 g) are used for the assay. Randomly selected diabetic animals are monitored for either 2 months or for 4 months after onset of diabetes. Groups (n=7/group) of the diabetic mice are subjected to oral macitentan treatment for the same period (25 mg/kg/day, food admix). The animals are monitored through assessment of body weight and blood glucose.

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

### CUSTOMER VALIDATION

- Cells. 2021, 10(11), 3072.

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### REFERENCES


