Istradefylline

Cat. No.: HY-10888
CAS No.: 155270-99-8
Molecular Formula: C$_{20}$H$_{24}$N$_4$O$_4$
Molecular Weight: 384.43
Target: Adenosine Receptor
Pathway: GPCR/G Protein
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 : 25.33 mg/mL (65.89 mM; Need ultrasonic and warming)

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent</th>
<th>Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mg</td>
<td>5 mg</td>
</tr>
<tr>
<td>1 mM</td>
<td>2.6013 mL</td>
<td>13.0063 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.5203 mL</td>
<td>2.6013 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2601 mL</td>
<td>1.3006 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: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.08 mg/mL (5.41 mM); Clear solution

**BIOLOGICAL ACTIVITY**

**Description**
Istradefylline is a very potent, selective and orally active adenosine A2A receptor antagonist with $K_i$ of 2.2 nM in experimental models of Parkinson’s disease.

**IC$_{50}$ & Target**
$K_i$: 2.2 nM (adenosine A2A receptor)

**In Vitro**
Istradefylline has 70-fold greater affinity for the A2AR than the A1 receptor with $K_i$ of 2.2 nM versus 150 nM$^1$. Istradefylline causes concentration-dependent abolition of bFGF induction of astrogliosis in primary rat striatal astrocytes$^4$.

Istradefylline binds to A1 receptor, A2A receptor, and A3 receptor in human with $K_i$s of >287 nM, 9.12 nM, and >681 nM, respectively, 50.9 nM and 1.57 nM for A1 receptor and A2A receptor in rat, 105.02 nM and 1.87 nM for A1 receptor and A2A receptor in mouse, respectively$^5$.

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

Istradefylline (3.3 mg/kg, i.p.) treatment before a single dose of MPTP attenuates the partial dopamine and DOPAC depletions measured in striata 1 week later[1]. Istradefylline reverses CGS21680-induced and reserpine-induced catalepsy with an ED50 of 0.05 mg/kg and 0.26 mg/kg, respectively. Istradefylline is over 10 times as potent in these models compared to other adenosine antagonists and dopamine agonist drugs. Istradefylline combined with L-dopa causes potent effects on haloperidol-induced and reserpine-induced catalepsy[2]. Istradefylline (10 mg/kg, p.o.) results in an increase in locomotor activity to approximately twice that of control and improves motor disability in MPTP-treated common marmosets. Istradefylline (10 mg/kg, p.o.) in combination with SKF80723, quinpirole, or L-DOPA produces a significant additive effect on locomotor activity and improvement of motor disability but not dyskinesia[3].

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### PROTOCOL

#### Cell Assay [5]

A CHO cell line permanently expressing the human adenosine A1 or A2A receptor is cultured in α-MEM supplemented with 10% (v/v) fetal bovine serum, 50 U/mL penicillin, and 50 μg/mL streptomycin. Cells are grown at 37°C in an environment of 5% CO2. These cells are seeded on black 96-well assay plates at a density of 15,000 cells/well, and then they are cultured for 24 h.

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#### Animal Administration [3]

The animals are housed either in pairs or alone under standard conditions at a temperature of 24-26°C and 50-60% relative humidity using a 12-h light-dark cycle. Diet consisted of standard food pellets, fresh fruit, and Mazuri marmoset jelly. The animals are treated with MPTP in a dose of 2.0 mg/kg sc daily for 5 days. Following MPTP treatment the animals are allowed to recover from the acute effects over a period of some 6-8 weeks. During MPTP treatment and throughout the following weeks, the animals are hand-fed with Mazuri marmoset jelly and fresh fruit puree until they are able to maintain themselves. Prior to behavioral testing, from 6-8 weeks to 8 months after exposure to MPTP, all animals show a marked reduction of basal locomotor activity, slower and less coordinated movements, abnormal postures of some parts of the body, and reduced checking movements and eye blinks. Istradefylline (KW-6002) is suspended in 0.3% Tween-80 and 10% sucrose solution and administered in a final volume of 2.0 mL/kg body weight by oral gavage.

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### CUSTOMER VALIDATION

- EMBO Rep. 2022 Apr 11;e53932.
- Neurochem Int. 2020 Dec 7;104935.

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### REFERENCES


