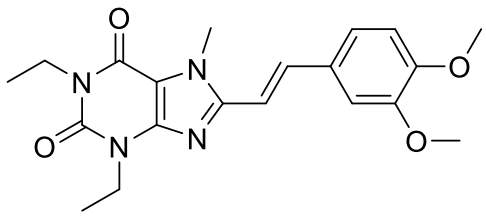
Product data sheet

MedKoo Cat#: 315137 Name: Istradefylline CAS#: 155270-99-8 Chemical Formula: $C_{20}H_{24}N_4O_4$ Exact Mass: 384.17976 Molecular Weight: 384.43	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Istradefylline (KW-6002) is a selective antagonist at the A2A receptor. It has been found to be useful in the treatment of Parkinson's disease. Istradefylline reduces dyskinesia resulting from long-term treatment with classical antiparkinson drugs such as levodopa. Istradefylline is an analog of caffeine.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	6	15.61

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.60 mL	13.01 mL	26.01 mL
5 mM	0.52 mL	2.60 mL	5.20 mL
10 mM	0.26 mL	1.30 mL	2.60 mL
50 mM	0.05 mL	0.26 mL	0.52 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Saki M, Yamada K, Koshimura E, Sasaki K, Kanda T. In vitro pharmacological profile of the A2A receptor antagonist istradefylline. Naunyn Schmiedebergs Arch Pharmacol. 2013 Nov;386(11):963-72. doi: 10.1007/s00210-013-0897-5. Epub 2013 Jun 29. PMID: 23812646.

In vivo study

1. Orr AG, Lo I, Schumacher H, Ho K, Gill M, Guo W, Kim DH, Knox A, Saito T, Saido TC, Simms J, Toddes C, Wang X, Yu GQ, Mucke L. Istradefylline reduces memory deficits in aging mice with amyloid pathology. Neurobiol Dis. 2018 Feb;110:29-36. doi: 10.1016/j.nbd.2017.10.014. Epub 2017 Oct 31. PMID: 29100987; PMCID: PMC5747997.

7. Bioactivity
Biological target:

Istradefylline is a very potent, selective and orally active adenosine A2A receptor antagonist with Ki of 2.2 nM in experimental models of Parkinson's disease.

In vitro activity

Product data sheet

Istradefylline exhibited high affinity for A2A receptors in humans, marmosets, dogs, rats, and mice. The affinities for the other subtypes of adenosine receptors (A1, A2B, and A3) were lower than that for A2A receptors in each species. Istradefylline demonstrated no significant affinity for other neurotransmitter receptors, including dopamine receptors (D1, D2, D3, D4, and D5). In addition, istradefylline hardly inhibited monoamine oxidase-A, monoamine oxidase-B, or catechol-O-methyl transferase. A kinetic analysis indicated that istradefylline reversibly binds to the human A2A receptors: The association reached equilibrium within 1 min, and the binding was also almost completely dissociated within 1 min. Istradefylline inhibited the A2A agonist CGS21680-induced accumulation of cAMP in the cultured cells and then shifted the concentration-response curve of CGS21680 to the right without affecting the maximal response of the agonist. These results indicate that istradefylline is a potent, selective, and competitive A2A receptor antagonist.

Reference: Naunyn Schmiedebergs Arch Pharmacol. 2013 Nov;386(11):963-72. https://dx.doi.org/10.1007/s00210-013-0897-5

In vivo activity

In 14–21-month-old wild-type (WT) nontransgenic mice and hAPP-J20 mice, administration of istradefylline in the drinking water caused dose-dependent increases of drug levels in plasma and brain (Suppl. Fig. 1). In pilot experiments, doses higher than 10 mg/kg/day increased total movements and rearing in both genotypes (Suppl. Fig. 2), consistent with reports that istradefylline enhances locomotion. To avoid this potential confound, mice were treated with 4 or 10 mg/kg/day. The effects of istradefylline on learning and memory were tested with the Morris water maze. hAPP mice treated with 4 or 10 mg/kg/day performed better than vehicle-treated hAPP mice during the first 20 seconds of the probe trial (Fig. 2E; Suppl. Fig. 3C). In a second probe trial 3 days after training, hAPP mice treated with 10 mg/kg/day again showed enhanced performance (Fig. 2G, H). Drug-treated hAPP mice also had faster swim speeds than vehicle-treated hAPP mice (Fig. 2F and I). At 15 mg/kg/day, istradefylline did not affect learning (Suppl. Fig. 5A) but impaired probe performance of WT mice and did not improve the performance in hAPP mice (Suppl. Fig. 5B–F). Thus, in aging mice with chronic plaque pathology, istradefylline enhances spatial memory primarily at low doses. Istradefylline at doses of 4, 10 and 15 mg/kg/day also improved learning of the cued navigation task in hAPP mice (Suppl. Fig. 6), possibly due to improvements in striatum-dependent navigation to the visible platform.

Reference: Neurobiol Dis. 2018 Feb;110:29-36. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/29100987/