# Product data sheet

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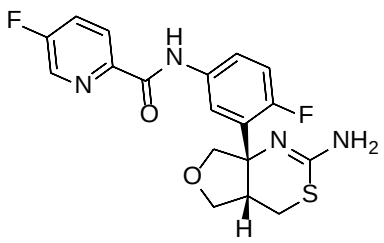
|---|---|
| MedKoo Cat#: 522472<br>Name: LY2886721<br>CAS#: 1262036-50-9 (free base)<br>Chemical Formula: $C_{18}H_{16}F_2N_4O_2S$<br>Exact Mass: 390.0962<br>Molecular Weight: 390.41 |  |
| Product supplied as: | Powder |
| Purity (by HPLC): | ≥ 98% |
| Shipping conditions | Ambient temperature |
| Storage conditions: | Powder: -20°C 3 years; 4°C 2 years. |
| | In solvent: -80°C 3 months; -20°C 2 weeks. |

**1. Product description:**
LY2886721 is a potent and selective BACE1 inhibitor. LY2886721 elicits robust central Aβ pharmacodynamic responses in mice, dogs, and humans. LY2886721 has high selectivity against key off-target proteases, which efficiently translates in vitro activity into robust in vivo amyloid β lowering in nonclinical animal models. Similar potent and persistent amyloid β lowering was observed in plasma and lumbar CSF when single and multiple doses of LY2886721 were administered to healthy human subjects. BACE1 is a key protease controlling the formation of amyloid β, a peptide hypothesized to play a significant role in the pathogenesis of Alzheimer's disease (AD).

**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 | 26.67 | 68.31 |

**4. Stock solution preparation table:**

| Concentration / Solvent Volume / Mass | 1 mg | 5 mg | 10 mg |
|---|---|---|---|
| 1 mM | 2.56 mL | 12.81 mL | 25.61 mL |
| 5 mM | 0.51 mL | 2.56 mL | 5.12 mL |
| 10 mM | 0.26 mL | 1.28 mL | 2.56 mL |
| 50 mM | 0.05 mL | 0.26 mL | 0.51 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. May PC, Willis BA, Lowe SL, Dean RA, Monk SA, Cocke PJ, Audia JE, Boggs LN, Borders AR, Brier RA, Calligaro DO, Day TA, Ereshefsky L, Erickson JA, Gevorkyan H, Gonzales CR, James DE, Jhee SS, Komjathy SF, Li L, Lindstrom TD, Mathes BM, Martényi F, Sheehan SM, Stout SL, Timm DE, Vaught GM, Watson BM, Winneroski LL, Yang Z, Mergott DJ. The potent BACE1 inhibitor LY2886721 elicits robust central Aβ pharmacodynamic responses in mice, dogs, and humans. J Neurosci. 2015 Jan 21;35(3):1199-210. doi: 10.1523/JNEUROSCI.4129-14.2015. PMID: 25609634; PMCID: PMC6605527.

In vivo study

1. Dekeryte R, Franklin Z, Hull C, Croce L, Kamli-Salino S, Helk O, Hoffmann PA, Yang Z, Riedel G, Delibegovic M, Platt B. The BACE1 inhibitor LY2886721 improves diabetic phenotypes of BACE1 knock-in mice. Biochim Biophys Acta Mol Basis Dis. 2021 Jul 1;1867(7):166149. doi: 10.1016/j.bbadis.2021.166149. Epub 2021 Apr 20. PMID: 33892080.
2. May PC, Willis BA, Lowe SL, Dean RA, Monk SA, Cocke PJ, Audia JE, Boggs LN, Borders AR, Brier RA, Calligaro DO, Day TA, Ereshefsky L, Erickson JA, Gevorkyan H, Gonzales CR, James DE, Jhee SS, Komjathy SF, Li L, Lindstrom TD, Mathes BM, Martényi F, Sheehan SM, Stout SL, Timm DE, Vaught GM, Watson BM, Winneroski LL, Yang Z, Mergott DJ. The potent BACE1

inhibitor LY2886721 elicits robust central Aβ pharmacodynamic responses in mice, dogs, and humans. J Neurosci. 2015 Jan 21;35(3):1199-210. doi: 10.1523/JNEUROSCI.4129-14.2015. PMID: 25609634; PMCID: PMC6605527.

**7. Bioactivity**

Biological target: LY2886721 is a beta-site amyloid precursor protein cleaving enzyme 1 (BACE1) inhibitor with an IC50 of 20.3 nM.

In vitro activity

The in vitro cellular activity of LY2886721 was assessed (Table 2). The HEK293Swe model consisted of a human embryonic kidney cell stably expressing a cDNA encoding human APP harboring a Swedish mutation. Overnight exposure of HEK293Swe cells to increasing concentrations of LY2886721 showed a concentration-dependent decrease in the amount of Aβ secreted into the condition medium. Consistent with a mechanism of BACE inhibition, the EC50s for inhibition of Aβ1–40 and Aβ1–42 were essentially identical, 18.5 and 19.7 nm, respectively. These results were achieved in the absence of any overt cytotoxicity.

Reference: J Neurosci. 2015 Jan 21;35(3):1199-210. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6605527/

In vivo activity

LY2886721 treatment improved glucose homeostasis and hepatic gluconeogenesis in diabetic PLB4 mice, as determined by improvements in basal glucose and glucose/pyruvate tolerance tests. Furthermore, LY2886721 improved hepatic insulin sensitivity, as indicated by enhanced basal hyperphosphorylation of insulin receptors. In PLB4 brains, altered basal conditions of APP expression and processing were detected, with beneficial effects on APP processing achieved by LY2886721 treatment.

Reference: Biochim Biophys Acta Mol Basis Dis. 2021 Jul 1;1867(7):166149.
https://www.sciencedirect.com/science/article/abs/pii/S092544392100082X?via%3Dihub

*Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.*