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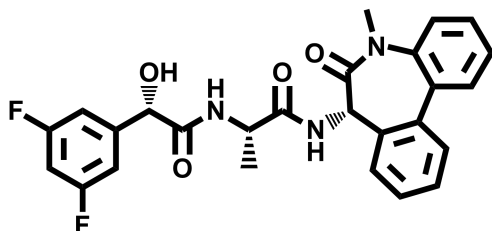
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## $\gamma$ -secretase Inhibitor LY411575

**Chemical Name:** (S)-2-((S)-2-(3,5-difluorophenyl)-2-hydroxyacetamido)-N-((S)-5-methyl-6-oxo-6,7-dihydro-5H-dibenzo[b,d]azepin-7-yl)propanamide



Molecular Weight:	479.48
Formula:	C <sub>26</sub> H <sub>23</sub> F <sub>2</sub> N <sub>3</sub> O <sub>4</sub>
Purity:	≥ 98%
CAS#:	209984-57-6
Solubility:	DMSO up to 100mM
Storage	Powder: 4°C 1 year DMSO: 4°C 3 month -20°C 1 year

### Biological Activity:

LY411575 is a highly potent, selective, and orally bioavailable inhibitor of gamma secretase with an IC<sub>50</sub> of ~0.1 nM for APP23 and APP51/16 in primary neurons. It has been shown to promote goblet cell differentiation in mouse intestine. LY411575 has also been observed to promote neural differentiation of mouse embryonic stem (ES) cells. In recent studies, LY411575 increased hair cell number in organ of Corti explants. Systemic LY411575 administration increased hair cell number and promoted hearing recovery in a noise-damaged cochlea, but local LY411575 administration promoted hearing recovery through transdifferentiation of supporting cells into hair cells after noise-induced hearing loss in the mature cochlea.

### How to Use:

**In vitro:** LY411575 was usually used at 10  $\mu$ M final concentration in vitro and in cellular assays.

**In vivo:** LY411575 was orally dosed to mice at 10-50mg/kg once per day or intraperitoneally dosed to mice at 5 mg/kg once per day.

### Reference:

1. Wong GT, et al. Chronic treatment with the gamma-secretase inhibitor LY-411,575 inhibits beta-amyloid peptide production and alters lymphopoiesis and intestinal cell differentiation. (2004) *J Biol Chem.* 279(13):12876-82.
2. Dev KK, et al. Signal peptide peptidase dependent cleavage of type II transmembrane substrates releases intracellular and extracellular signals. (2006) *Eur J Pharmacol.* 540(1-3):10-7.
3. Fuwa H, et al. Divergent synthesis of multifunctional molecular probes to elucidate the enzyme specificity of dipeptidic gamma-secretase inhibitors. (2007) *ACS Chem Biol.* 2(6):408-18.
4. Spilman P, et al. A gamma-secretase inhibitor and quinacrine reduce prions and prevent dendritic degeneration in murine brains. (2008) *Proc Natl Acad Sci U S A.* 105(30):10595-600.
5. Abranches E, et al. Neural differentiation of embryonic stem cells in vitro: a road map to neurogenesis in the embryo. (2009) *PLoS One.* 4(7):e6286.
6. Mizutari K, et al. Notch inhibition induces cochlear hair cell regeneration and recovery of hearing after acoustic trauma. (2013) *Neuron.* 77(1):58-69.

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