

LY-411575

Catalog No: tcsc0309



Available Sizes

Size: 5mg

Size: 10mg

Size: 50mg

Size: 100mg



Specifications

CAS No:

209984-57-6

Formula:

$C_{26}H_{23}F_2N_3O_4$

Pathway:

Stem Cell/Wnt;Neuronal Signaling;Stem Cell/Wnt

Target:

Apoptosis; Neuronal Signaling; Stem Cell/Wnt

Form:

White to off-white (Solid)

Purity / Grade:

≥98.0%

Solubility:

DMSO : 33.33 mg/mL (69.51 mM; Need ultrasonic)

Storage Instruction:

2-8°C

Observed Molecular Weight:

479.48

References

[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. *J Biol Chem*. 2004 Mar 26;279(13):12876-82. 2]. Curry CL, et al. Gamma secretase inhibitor blocks Notch activation and induces apoptosis in Kaposi's sarcoma tumor cells. *Oncogene*. 2005 Sep 22;24(42):6333-44. [3]. Hyde LA, et al. Studies to investigate the in vivo therapeutic window of the gamma-secretase inhibitor N2-[(2S)-2-(3,5-difluorophenyl)-2-hydroxyethanoyl]-N1-[(7S)-5-methyl-6-oxo-6,7-dihydro-5H-dibenzo[b,d]azepin-7-yl]-L-alaninamide (LY411,575) in the CRND8 mouse. *J Pharmacol Exp Ther*. 2006 Dec;319(3):1133-43. [4]. Otoguro T, et al. Inhibitory effect of presenilin inhibitor LY411575 on maturation of hepatitis C virus core protein, production of the viral particle and expression of host proteins involved in pathogenicity. *Microbiol Immunol*. 2016 Nov;60(11):740-753 [5]. Zhang J, et al. Notch signaling modulates proliferative vitreoretinopathy via regulating retinal pigment epithelial-to-mesenchymal transition. *Histochem Cell Biol*. 2017 Mar;147(3):367-375.

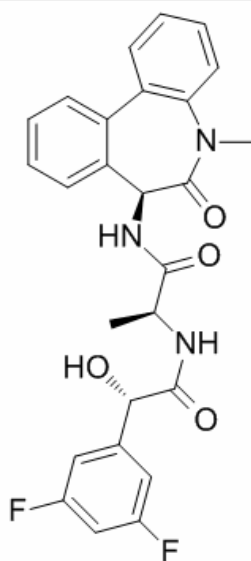
Product Description

LY-411575 is a potent **γ-secretase** inhibitor with **IC₅₀** of 0.078 nM/0.082 nM (membrane/cell-based), and also inhibits Notch S3 cleavage with **IC₅₀** of 0.39 nM.

IC50 & Target: IC50: 0.078 nM (γ-secretase in membrane), 0.082 nM (γ-secretase cell-based), 0.39 nM (Notch S3 cleavage cell-based) [1]

In Vitro: LY-411,575 blocks Notch activation, and results in apoptosis in primary and immortalized KS cells. LY-411,575 (500 μM) induces G2/M growth arrest SLK cells^[2]. LY411575 treatment significantly decreases the amounts of intracellular HCV RNA with IC₅₀ of 0.56 ± 0.20 μM and extracellular HCV particles. LY411575 (0-40 nM) alone or in combination with daclatasvir (0-40 pM) decreases supernatant infectious titers in a dose-dependent manner, and is synergistic regarding production of infectious virus. LY411575 (10 μM) treatment impairs ROS production in HCVcc-infected cells^[4]. LY411575 significantly attenuates EMT by inhibiting the Notch signaling activation in vitro^[5].

In Vivo: LY-411,575 (10 mg/kg) decreases brain and plasma Aβ40 and -42 robustly when chronically administered to TgCRND8 mice^[1]. LY411,575 reduces cortical Aβ40 in young transgenic CRND8 mice (ED₅₀ appr 0.6 mg/kg) and produces significant thymus atrophy and intestinal goblet cell hyperplasia at higher doses (>3 mg/kg). The extent of intestinal goblet cell hyperplasia induced by LY411,575 (10 mg/kg) is similar in young and aged mice^[3]. LY411575 inhibits mouse proliferative vitreoretinopathy (PVR) formation in vivo^[5].



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