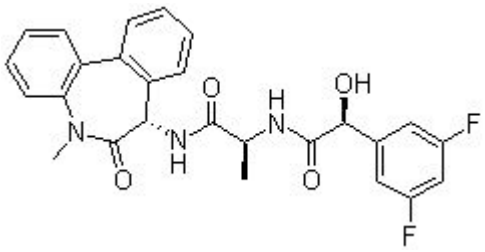
Product Introduction

LY411575

LY411575 is a potent **γ-secretase** inhibitor with **IC50** of 0.078 nM/0.082 nM (membrane/cell-based), also inhibits Notch clevage with with**IC50** of 0.39 nM.

Technical Data:

Molecular Weight (MW):	479.48	
Formula:	C26H23F2N3O4	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 96 mg/mL	
	Water <1 mg/mL	
	Ethanol 96 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	209984-57-6	

Biological Activity

LY-411575 inhibits γ-secretase which can be assessed by the substrates like amyloid precursor protein (APP) and Notch S3 cleavage. [1] LY-411575, which blocks Notch activation, results in apoptosis in primary and immortalized KS cells. [2]

10 mg/kg oral dose of LY-411575 decreases brain and plasma Aβ40 and -42 dose-dependently. [1] LY-411575 reduces cortical Aβ40 in young (preplaque) transgenic CRND8 mice (ED50 ≈ 0.6 mg/kg) and

produces significant thymus atrophy and intestinal goblet cell hyperplasia at higher doses (>3 mg/kg). The therapeutic window is similar after oral and subcutaneous administration and in young and aged CRND8 mice. Both the thymus and intestinal side effects are reversible after a 2-week washout period. Three-week treatment with 1 mg/kg LY411575 reduces cortical Aβ40 by 69% without inducing intestinal effects, although a previously unreported change in coat color is observed. [3]

References

[1] Wong GT, et al, J Biol Chem, 2004, 279(13), 12876-12882.

[2] Curry CL, et al, Oncogene, 2005, 24(42), 6333-6344.

[2] Hyde LA, et al, J Pharmacol Exp Ther, 2006, 319(3), 1133-1143.

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