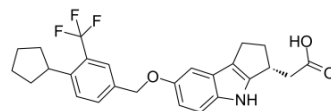


Etrasimod

Cat. No.:	HY-12789		
CAS No.:	1206123-37-6		
Molecular Formula:	C ₂₆ H ₂₆ F ₃ NO ₃		
Molecular Weight:	457.48		
Target:	LPL Receptor		
Pathway:	GPCR/G Protein		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 28 mg/mL (61.20 mM)
 * "≥" means soluble, but saturation unknown.

Concentration	Mass			
	1 mg	5 mg	10 mg	
1 mM	2.1859 mL	10.9294 mL	21.8589 mL	
5 mM	0.4372 mL	2.1859 mL	4.3718 mL	
10 mM	0.2186 mL	1.0929 mL	2.1859 mL	

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

Etrasimod (APD334) is a potent, selective and orally available antagonist of the sphingosine-1-phosphate-1 (S1P₁) receptor with an IC₅₀ value of 1.88 nM in CHO cells.

IC₅₀ & Target

IC₅₀: 1.88 nM (S1P₁)^[1]

In Vitro

APD334 is a structurally novel, selective, functional antagonist of S1P₁. In CHO cells expressing HA tagged S1P₁, APD334 is found to have an IC₅₀ value of 1.88 nM. Moderate agonism at human S1P₄ and S1P₅ is observed but is reduced relative to S1P₁, both in terms of potency and efficacy. APD334 is devoid of any agonism or antagonism at human S1P₂ and S1P₃. APD334 achieves good central exposure following oral dosing and possesses a favorable pharmacokinetic profile in multiple preclinical species. S1P₁ activity is maintained in mice (EC₅₀=0.44 nM), rats (EC₅₀=0.32 nM), dogs (EC₅₀=0.34 nM) and monkeys (EC₅₀=0.32 nM)^[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

APD334 has a relatively low systemic clearance (<4% of hepatic blood flow) and high C_{max} across all species. In both dog and

monkey a significant decrease in volume of distribution (V_{ss}) is observed relative to rodent. Oral bioavailability is in the range of 40–100%, and the terminal phase half-life varied from 6 h in monkey, to as long as 29 h in dog. Rat and monkey t_{1/2} values for siponimod (another S1P1 modulator currently in human trials) have been disclosed and are 6 and 19 h, respectively^[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration ^[1]

Rats: APD334 induced effects on blood lymphopenia are determined in male Sprague-Dawley rats. Briefly, male rats are given a 0 (vehicle only), 0.03 (mice only), 0.1, 0.3 or 1 mg/kg oral dose of APD334 formulated in 0.5% methylcellulose (MC) in water. Rat blood samples are collected at 0, 1, 3, 5, 8, 16, 24, 32, 48 and 72 hours post-dose^[1].

Mice: APD334 induced effects on blood lymphopenia are determined in male BALB/c mice. Briefly, male mice are given a 0 (vehicle only), 0.03 (mice only), 0.1, 0.3 or 1 mg/kg oral dose of APD334 formulated in 0.5% methylcellulose (MC) in water. Mouse blood samples are taken at 0, 1, 3, 5, 8, 16, 24 and 32 hours post-dose^[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Buzard DJ, et al. Discovery of APD334: Design of a Clinical Stage Functional Antagonist of the Sphingosine-1-phosphate-1 Receptor. ACS Med Chem Lett. 2014 Nov 4;5(12):1313-7.

Caution: Product has not been fully validated for medical applications. For research use only.

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