Etrasimod

Cat. No.: HY-12789

CAS No.: 1206123-37-6

Molecular Formula: $C_{26}H_{26}F_3NO_3$

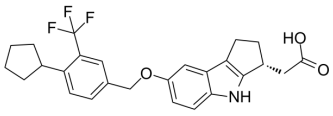
Molecular Weight: 457.48

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.

Preparing Stock Solutions

Concentration \ Solvent \ 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 ($S1P_1$) receptor with an IC_{50} value of 1.88 nM in CHO cells.

IC_{50} & Target

IC50: 1.88 nM (S1P1)[1]

In Vitro

APD334 is a structurally novel, selective, functional antagonist of $S1P_1$. In CHO cells expressing HA tagged $S1P_1$, APD334 is found to have an IC_{50} value of 1.88 nM. Moderate agonism at human $S1P_4$ and $S1P_5$ is observed but is reduced relative to $S1P_1$, both in terms of potency and efficacy. APD334 is devoid of any agonism or antagonism at human $S1P_2$ and $S1P_3$. APD334 achieves good central exposure following oral dosing and possesses a favorable pharmacokinetic profile in multiple preclinical species. $S1P_1$ activity is maintained in mice (EC_{50}=0.44 nM), rats (EC_{50}=0.32 nM), dogs (EC_{50}=0.34 nM) and monkeys (EC_{50}=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 (Vss) 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].

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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.

India Contact:
Life Technologies (India) Pvt. Ltd.
306, Aggarwal City Mall, Opposite M2K Pitampura, Delhi – 110034 (INDIA). Ph: +91-11-42208000, 42208111, 42208222, Mobile: +91-9810521400, Fax: +91-11-42208444
Email: customerservice@lifetechindia.com Website: www.lifetechindia.com