Ponesimod

Cat. No.: HY-10569

CAS No.: 854107-55-4

Molecular Formula: $C_{23}H_{25}ClN_2O_4S$

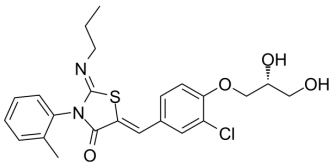
Molecular Weight: 460.97

Target: LPL Receptor

Pathway: GPCR/G Protein

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (216.93 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1693 mL	10.8467 mL	21.6934 mL
5 mM	0.4339 mL	2.1693 mL	4.3387 mL
10 mM	0.2169 mL	1.0847 mL	2.1693 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.42 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.42 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Ponesimod (ACT-128800) is a potent, selective and orally active agonist of $S1P_1$, with an IC_{50} of 6 nM in a radioligand binding assay. Ponesimod activates $S1P_1$-mediated signal transduction with high potency (EC_{50}=5.7 nM). Ponesimod can protect against lymphocyte-mediated tissue inflammation[1][2][3].

IC_{50} & Target

S1PR1	S1PR5	S1PR4	S1PR3
6 nM (IC_{50})	142 nM (IC_{50})	1956 nM (IC_{50})	2068 nM (IC_{50})

In Vitro

Ponesimod activates human $S1P_{1-5}$ receptors with EC_{50}s of 5.7, >10000, 105, 1108 and 59.1 nM respectively in GTPγS binding assay[2].

?Ponesimod activates $S1P_1$ receptors with EC_{50}s of 5.7, 1.9, and 1.4 nM for human, rat, and mouse S1P receptors respectively [2].

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

In Vivo

Ponesimod (30 and 175 mg/kg; once daily p.o. for 8 d) prevents delayed-type hypersensitivity in mice[2].

?Ponesimod (30 mg/kg by gavage 3 h before and 6 h after adjuvant injection followed by 100 mg/kg/day by administration as food admix for 18 days) prevents adjuvant-induced arthritis in rats[2].

?Ponesimod (0.3-100 mg/kg; a single oral gavage) causes a dose-dependent reduction in lymphocyte count, with a plateau effect being reached at 3 mg/kg in rats[2].

?Ponesimod (100 mg/kg; once daily oral gavage for 7 d) results in a lymphocyte count reduction to 1900 lymphocytes/μL, and this effect is maintained over the entire 7 days studies. Lymphocyte count returned to baseline levels within 48 h after discontinuation of dosing[2].

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

Animal Model:	Female BALB/c mice (15-25 g) sensitized with DNFB[2]
Dosage:	30 and 175 mg/kg
Administration:	Gavage (30 mg/kg) 19 and 3 h before sensitization, followed by administration as food admix (175 mg/kg/day) for 8 days
Result:	Caused a 60 to 90% reduction of delayed-type hypersensitivity (DTH) parameters of the skin, such as edema, protein extravasation, and neutrophil myeloperoxidase (MPO) activity. Reduced skin levels of proinflammatory cytokines, such as IL-1β, IL-6, IFNγ, TNFα, and several chemokines to different degrees ranging from -27 to -100%.

CUSTOMER VALIDATION

- J Neuroimmunol. 2021, 577583.
- Research Square Preprint. 2023 Aug 29.

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REFERENCES

[1]. Piali L, et al. The selective sphingosine 1-phosphate receptor 1 agonist ponesimod protects against lymphocyte-mediated tissue inflammation. J Pharmacol Exp Ther. 2011 May;337(2):547-56.

[2]. Bolli MH, et al. 2-imino-thiazolidin-4-one derivatives as potent, orally active S1P1 receptor agonists. J Med Chem. 2010 May 27;53(10):4198-211.

[3]. Brossard P, et al. Pharmacokinetics and pharmacodynamics of ponesimod, a selective S1P1 receptor modulator, in the first-in-human study. Br J Clin Pharmacol. 2013 Dec;76(6):888-96.

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