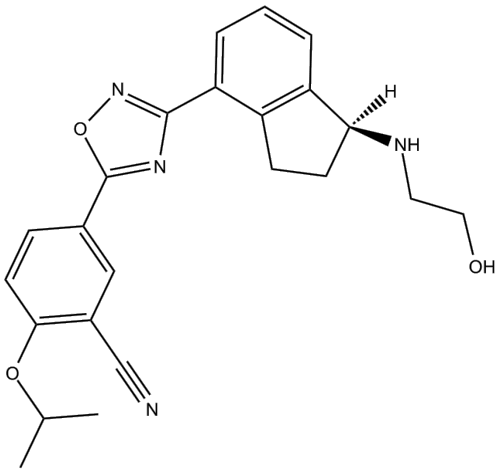
Product Data Sheet

Product Name: Ozanimod (RPC1063)
Cat. No.: GC14360

Chemical Properties

Cas. No.	1306760-87-1		
Chemical Name	(S)-5-(3-(1-((2-hydroxyethyl)amino)-2,3-dihydro-1H-inden-4-yl)-1,2,4-oxadiazol-5-yl)-2-isopropoxybenzonitrile		
SMILES	CC(OC1=C(C#N)C=C(C2=NC(C3=CC=CC4=C3CC[C@]4([H])NCCO)=NO2)C=C1)C		
Formula	$C_{23}H_{24}N_4O_3$	M.Wt	404.46
Solubility	≥ 40.4mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment [1]:

Cell lines	501Mel cells, 1205LU cells, and M249R cells (human melanoma cell lines)

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Preparation Method	Melanoma cell lines were transduced with NucLight Red lentivirus reagent and selected with puromycin (1mg/ml). Cells were treated with different concentrations of Ozanimod (0.5, 1.6, 5.5, 18, and 60μM) using clinical doses for in vitro cell cultures.
Reaction Conditions	0.5-60μM; 6 days
Applications	Ozanimod significantly increased median confluence overall for all lineages. Ozanimod-treated cells increased confluency in 501Mel, 1205LU, and M249R cell lines.

Animal experiment [2]:

Animal models	C57BL/6J mice (8-10 weeks old)
Preparation Method	The collagenase-induced intracerebral hemorrhage (ICH) model was established by injecting collagenase type VII (0.075U in 0.5μL saline) into the basal ganglia. Ozanimod was administered by gavage 2h after surgery and once a day thereafter until sacrifice at 3 days post-ICH.
Dosage form	1mg/kg; oral gavage; once daily for 4 days

Caution: Product has not been fully validated for medical applications. For research use only.
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Applications	Ozanimod treatment improved neurobehavioral deficits and decreased weight loss after ICH. Ozanimod significantly reduced hematoma volume and brain water content. Ozanimod reduced the density of activated microglia and infiltrated neutrophils in the perihematoma region. Ozanimod mitigated brain cell death and reduced Evans blue dye leakage, indicating improved blood-brain barrier integrity.

References:
[1] Ruetsch-Chelli C, Okuda DT, Rocher F, et al. Sphingosine-1 Phosphate Receptor Modulators Increase In Vitro Melanoma Cell Line Proliferation at Therapeutic Doses Used in Patients with Multiple Sclerosis. Neurol Ther. 2023 Feb;12(1):289-302.
[2] Wang F, Zhang X, Liu Y, et al. Neuroprotection by Ozanimod Following Intracerebral Hemorrhage in Mice. Front Mol Neurosci. 2022 Jun 15;15:927150.

Background

Ozanimod (RPC1063) is a sphingosine-1-phosphate (S1P) receptor modulator that can cross the blood-brain barrier. Ozanimod selectively binds to S1P1 (EC_{50}=1.03nM) and S1P5 (EC_{50}=8.6nM) receptors. Ozanimod is used for the treatment of relapsing multiple sclerosis and ulcerative colitis[1-4].

In vitro, Ozanimod (0.5-60μM) treated 501Mel, 1205LU, and M249R melanoma cell lines for 6 days. Ozanimod significantly increased cell confluency and promoted cell proliferation[5]. Ozanimod (1nM-1mM) treated HUVEC cells for 60 minutes, followed by stimulation with S1P (80nM) for 60 minutes. Ozanimod produced a rapid and concentration-dependent increase in baseline normalized cell index and was able to desensitize the S1P1 receptor[6].

In vivo, Ozanimod (1mg/kg; once daily) was administered by oral gavage to intracerebral hemorrhage model C57BL/6J mice (8-10 weeks old) for 4 consecutive days. Ozanimod significantly improved neurobehavioral deficits and reduced weight loss in the mice[7]. Ozanimod (0.3-3.0mg/kg; once daily) was administered by oral gavage to systemic lupus erythematosus NZBWF1 mice for 20 weeks. Ozanimod significantly improved renal pathological damage in the mice[8].

Product Data Sheet

References:

[1] Selkirk JV, Dines KC, Yan YG, et al. Deconstructing the Pharmacological Contribution of Sphingosine-1 Phosphate Receptors to Mouse Models of Multiple Sclerosis Using the Species Selectivity of Ozanimod, a Dual Modulator of Human Sphingosine 1-Phosphate Receptor Subtypes 1 and 5. J Pharmacol Exp Ther. 2021 Dec;379(3):386-399.
[2] Sandborn WJ, Feagan BG, D'Haens G, et al. Ozanimod as Induction and Maintenance Therapy for Ulcerative Colitis. N Engl J Med. 2021 Sep 30;385(14):1280-1291.
[3] Lamb YN. Ozanimod: First Approval. Drugs. 2020 Jun;80(8):841-848.
[4] Paik J. Ozanimod: A Review in Ulcerative Colitis. Drugs. 2022 Aug;82(12):1303-1313.
[5] Ruetsch-Chelli C, Okuda DT, Rocher F, et al. Sphingosine-1 Phosphate Receptor Modulators Increase In Vitro Melanoma Cell Line Proliferation at Therapeutic Doses Used in Patients with Multiple Sclerosis. Neurol Ther. 2023 Feb;12(1):289-302.
[6] Grailhe P, Boutarfa-Madec A, Beauverger P, et al. A label-free impedance assay in endothelial cells differentiates the activation and desensitization properties of clinical S1P1 agonists. FEBS Open Bio. 2020 Oct;10(10):2010-2020.
[7] Wang F, Zhang X, Liu Y, et al. Neuroprotection by Ozanimod Following Intracerebral Hemorrhage in Mice. Front Mol Neurosci. 2022 Jun 15;15:927150.
[8] Taylor Meadows KR, Steinberg MW, Clemons B, et al. Ozanimod (RPC1063), a selective S1PR1 and S1PR5 modulator, reduces chronic inflammation and alleviates kidney pathology in murine systemic lupus erythematosus. PLoS One. 2018 Apr 2;13(4):e0193236.

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