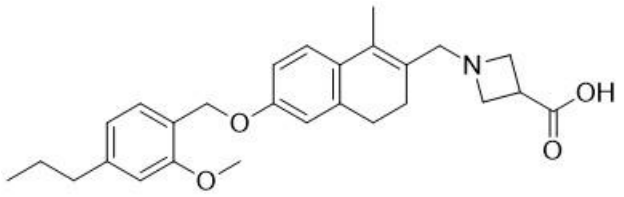
Product data sheet

MedKoo Cat#: 206453 Name: Ceralifimod CAS#: 891859-12-4 Chemical Formula: $C_{27}H_{33}NO_4$ Exact Mass: 435.24096 Molecular Weight: 435.56	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

Ceralifimod, also known as ONO-4641, is a next-generation sphingosine 1-phosphate (S1P) receptor agonist selective for S1P receptors 1 and 5. In vitro, ONO-4641 showed highly potent agonistic activities versus S1P receptors 1 and 5 [half maximal effective concentration (EC(50)) values of 0·0273 and 0·334 nM, respectively]. ONO-4641 decreased peripheral blood lymphocyte counts in rats by inhibiting lymphocyte egress from secondary lymphoid tissues. ONO-4641 prevented relapse of disease in a non-obese diabetic mouse model of relapsing-remitting EAE. ONO-4641 may provide therapeutic benefits in the treatment of multiple sclerosis.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	5.0	11.48

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.30	11.48	22.96
5 mM	0.46	2.30	4.59
10 mM	0.23	1.15	2.30
50 mM	0.05	0.23	0.46

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Komiya T, Sato K, Shioya H, Inagaki Y, Hagiya H, Kozaki R, Imai M, Takada Y, Maeda T, Kurata H, Kurono M, Suzuki R, Otsuki K, Habashita H, Nakade S. Efficacy and immunomodulatory actions of ONO-4641, a novel selective agonist for sphingosine 1-phosphate receptors 1 and 5, in preclinical models of multiple sclerosis. Clin Exp Immunol. 2013 Jan;171(1):54-62. doi: 10.1111/j.1365-2249.2012.04669.x. PMID: 23199323; PMCID: PMC3530095.

2. Ohno T, Hasegawa C, Nakade S, Kitagawa J, Honda N, Ogawa M. The prediction of human response to ONO-4641, a sphingosine 1-phosphate receptor modulator, from preclinical data based on pharmacokinetic-pharmacodynamic modeling. Biopharm Drug Dispos. 2010 Oct;31(7):396-406. doi: 10.1002/bdd.719. PMID: 20623701.

In vivo study

1. Komiya T, Gohda M, Shioya H, Katsumata S. Sphingosine 1-Phosphate Receptor Modulator ONO-4641 Regulates Trafficking of T Lymphocytes and Hematopoietic Stem Cells and Alleviates Immune-Mediated Aplastic Anemia in a Mouse Model. J Pharmacol Exp Ther. 2021 Feb;376(2):250-260. doi: 10.1124/jpet.120.000277. Epub 2020 Nov 30. PMID: 33257316.

2. Asakura T, Ishii M, Namkoong H, Suzuki S, Kagawa S, Yagi K, Komiya T, Hashimoto T, Okamori S, Kamata H, Tasaka S, Kihara A, Hegab AE, Hasegawa N, Betsuyaku T. Sphingosine 1-phosphate receptor modulator ONO-4641 stimulates CD11b+Gr-1+ cell expansion and inhibits lymphocyte infiltration in the lungs to ameliorate murine pulmonary emphysema. Mucosal Immunol. 2018 Nov;11(6):1606-1620. doi: 10.1038/s41385-018-0077-5. Epub 2018 Aug 16. PMID: 30116000.

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7. Bioactivity

Biological target:

Ceralifimod (ONO-4641) is selective, high potent agonist for sphingosine 1-phosphate receptors 1 and 5, with EC50s of 27.3, 334 pM for human S1P receptor 1 and 5, respectively.

In vitro activity

The objective of the study was to characterize the immunomodulatory effects of ONO-4641 using preclinical data. ONO-4641 was tested in-vitro pharmacological studies. In order to investigate the binding affinity of ONO-4641 for S1P receptors, competitive binding experiments of this substance were performed for the specific binding of [33P]-S1P to S1P receptors (Table 1). ONO-4641 inhibited the specific binding of [33P]-S1P to hS1P1 and hS1P5 in a concentration-dependent manner, with Ki values of 0·626 and 0·574 nM, respectively. ONO-4641 also inhibited the specific binding to hS1P4, but the Ki value of ONO-4641 was 28·8 nM, approximately 50 times higher than those for hS1P1 and hS1P5. Conversely, the inhibitory rate of ONO-4641 on the specific binding of [33P]-S1P to hS1P2 and hS1P3 was less than 50% even at a concentration of 10 μM. To investigate the species difference between human and rat, the binding affinity of ONO-4641 for rS1P1 was examined. The Ki value of ONO-4641 for rS1P1 was 0·772 nM, indicating that ONO-4641 has a high binding affinity for rS1P1 comparable to that for hS1P1 (Table 1). We examined whether ONO-4641 also induces S1P1 down-regulation on the cell membrane. Both the natural ligand S1P and S1P1-selective agonist SEW2871 were used as control. In cells expressing S1P1, ONO-4641 induced S1P1 down-regulation in a concentration-dependent manner and by approximately 90% at concentration of 25 nM (Fig. 1a). S1P and SEW2871 also decreased the expression of S1P1 receptors on the cell membrane. The EC50 values of ONO-4641, S1P, and SEW2871 were 0·778, 132 and 118 nM, respectively (Fig. 1b).

Clin Exp Immunol. 2013 Jan; 171(1): 54–62. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3530095/

In vivo activity

In this study, the S1P receptor modulator ONO-4641 induced the expansion of lung CD11b+Gr-1+ cells and lymphocytopenia was demonstrated in naive mice. ONO-4641-expanded CD11b+Gr-1+ cells showed higher arginase-1 activity, decreased T cell proliferation, and lower IFN-γ production in CD3+ T cells, similar to the features of myeloid-derived suppressor cells. ONO-4641 treatment decreased airspace enlargement in elastase-induced and cigarette smoke-induced emphysema models and attenuated emphysema exacerbation induced by post-elastase pneumococcal infection, which was also associated with an increased number of lung CD11b+Gr-1+ cells. Adoptive transfer of ONO-4641-expanded CD11b+Gr-1+ cells protected against elastase-induced emphysema. Lymphocytopenia observed in these models likely contributed to beneficial ONO-4641 effects. Thus, ONO-4641 attenuated murine pulmonary emphysema by expanding lung CD11b+Gr-1+ cell populations and inducing lymphocytopenia. The S1P receptor might be a promising target for strategies aimed at ameliorating pulmonary emphysema progression.

Mucosal Immunol. 2018 Nov;11(6):1606-1620. https://pubmed.ncbi.nlm.nih.gov/30116000/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.