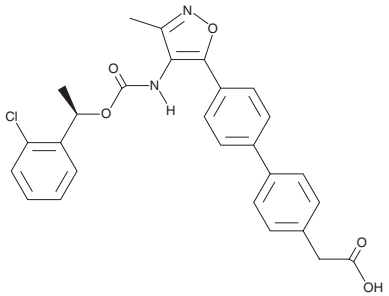
PRODUCT INFORMATION

AM966

Item No. 22048

CAS Registry No.:	1228690-19-4
Formal Name:	4'-[4-[[[(1R)-1-(2-chlorophenyl)ethoxy] carbonyl]amino]-3-methyl-5-isoxazolyl]-[1,1'-biphenyl]-4-acetic acid
MF:	$C_{27}H_{23}ClN_2O_5$
FW:	490.9
Purity:	≥98%
UV/Vis.:	λ_{max}: 296 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥2 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

AM966 is supplied as a crystalline solid. A stock solution may be made by dissolving the AM966 in the solvent of choice. AM966 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of AM966 in ethanol is approximately 2.5 mg/ml and approximately 30 mg/ml in DMSO and DMF.

AM966 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, AM966 should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. AM966 has a solubility of approximately 0.2 mg/ml in a 1:4 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

AM966 is an orally bioavailable, potent, and selective antagonist of the lysophosphatidic acid receptor 1 (LPA_1) that has an IC_{50} value of 17 nM in a calcium assay using CHO cells transfected with the human LPA_1 receptor.[1] It is selective for LPA_1 over the LPA_2, LPA_3, LPA_4, and LPA_5 receptors (IC_{50}s = 1,700, 1,600, 7,700, and 8,600 nM for $LPA_{2\text{-}5}$, respectively). *In vitro*, AM966 inhibits LPA-induced lung fibroblast cell chemotaxis (IC_{50} = 181 nM), increases barrier permeability, activates RhoA, and induces phosphorylation of myosin light chain and vascular endothelium cadherin (VE-cadherin).[2,3] At a dose of 30 mg/kg in mice, it reduces inflammation, tissue fibrosis, and vascular permeability following bleomycin-induced lung injury. AM966 also blocks amitriptyline-induced ERK1/2, CREB, and insulin growth factor-1 receptor (IGF-IR) phosphorylation *in vitro*.[2]

References

1. Swaney, J.S., Chapman, C., Correa, L.D., *et al.* A novel, orally active LPA_1 receptor antagonist inhibits lung fibrosis in the mouse bleomycin model. *Br. J. Pharmacol.* **160(7)**, 1699-1713 (2010).
2. Olianas, M.C., Dedoni, S., and Onali, P. Antidepressants activate the lysophosphatidic acid receptor LPA_1 to induce insulin-like growth factor-I receptor transactivation, stimulation of ERK1/2 signaling and cell proliferation in CHO-K1 fibroblasts. *Biochem. Pharmacol.* **95(4)**, 311-323 (2015).
3. Cai, J., Wei, J., Li, S., *et al.* AM966, an antagonist of lysophosphatidic acid receptor 1, increases lung microvascular endothelial permeability through activation of Rho signaling pathway and phosphorylation of VE-cadherin. *Mediators Inflamm.* **2017**, 6893560 (2017).

CAYMAN CHEMICAL
1180 EAST ELLSWORTH RD
ANN ARBOR, MI 48108 · USA
PHONE: [800] 364-9897
[734] 971-3335
FAX: [734] 971-3640
CUSTSERV@CAYMANCHEM.COM
WWW.**CAYMANCHEM**.COM