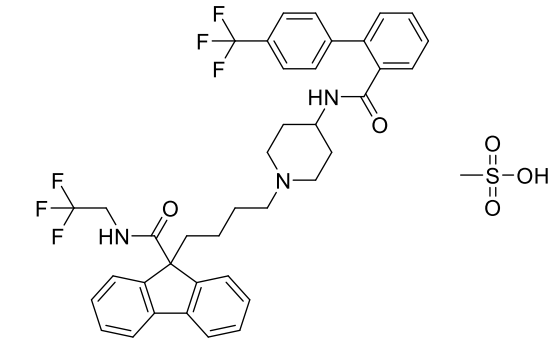
Product data sheet

MedKoo Cat#: 314228 Name: Lomitapide mesylate CAS#: 202914-84-9 (mesylate) Chemical Formula: $C_{40}H_{41}F_6N_3O_5S$ Molecular Weight: 789.83	
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:

Lomitapide is a MTP inhibitor. Lomitapid is a novel agent for the treatment of homozygous familial hypercholesterolemia. Lomitapide is an orally active inhibitor of microsomal triglyceride transfer protein that is indicated as an adjunct to a low-fat diet and other lipid-lowering treatments, including LDL apheresis where available for the reduction of LDL-C, total cholesterol, apolipoprotein B, and non-high-density lipoprotein cholesterol in adult patients with HoFH.

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	100.0	126.61
Ethanol	100.0	126.61

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.27 mL	6.33 mL	12.66 mL
5 mM	0.25 mL	1.27 mL	2.53 mL
10 mM	0.13 mL	0.63 mL	1.27 mL
50 mM	0.03 mL	0.13 mL	0.25 mL

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. de Sousa ACC, Maepa K, Combrinck JM, Egan TJ. Lapatinib, Nilotinib and Lomitapide Inhibit Haemozoin Formation in Malaria Parasites. Molecules. 2020 Mar 29;25(7):1571. doi: 10.3390/molecules25071571. PMID: 32235391; PMCID: PMC7180468.

In vivo study

1. Liu C, Kim YS, Kim J, Pattison J, Kamaid A, Miller YI. Modeling hypercholesterolemia and vascular lipid accumulation in LDL receptor mutant zebrafish. J Lipid Res. 2018 Feb;59(2):391-399. doi: 10.1194/jlr.D081521. Epub 2017 Nov 29. PMID: 29187523; PMCID: PMC5794413.

7. Bioactivity

Biological target:

Lomitapide mesylate(AEGR-733; BMS-201038) is an inhibitor of microsomal triglyceride-transfer protein (MTP) wtih in vitro IC50 of 8 nM.

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In vitro activity

Bayesian statistics was previously used as a tool to virtually screen USFDA approved drugs for predicted β-haematin (synthetic haemozoin) inhibition and in vitro antimalarial activity. Here, the experimental evaluation of nine of the highest ranked drugs, is reported, confirming the accuracy of the model by showing an overall 93% hit rate. Lapatinib, nilotinib, and lomitapide showed the best activity for inhibition of β-haematin formation and parasite growth and were found to inhibit haemozoin formation in the parasite, providing mechanistic insights into their mode of antimalarial action. Furthermore, the SBVS method correctly identified the three most important β-haematin inhibiting drugs identified in the USFDA set using the Bayesian model, namely lapatinib, nilotinib, and lomitapide. Lapatinib, nilotinib, and lomitapide were all found to increase the freely exchangeable haem, and decrease haemozoin in a dose dependent manner confirmed by an unpaired two tailed t-test relative to control, therefore confirming that these drugs inhibit cellular haemozoin formation (Figure 2).

Reference: Molecules. 2020 Apr; 25(7): 1571. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7180468/

In vivo activity

To evaluate whether the new animal model in which ldlr mutant zebrafish are subjected to short-term (5 days) HCD feeding can be useful for drug screening, the effects of probucol, an antioxidant, and lomitapide, an MTP inhibitor, were tested on vascular lipid accumulation. Both probucol and lomitapide have been shown to exert antioxidant and MTP inhibitor properties, respectively, in zebrafish. As was expected, lomitapide decreased the plasma lipid levels in ldlr mutants, as assessed by ORO staining (Fig. 5A), by blocking their absorption in the intestine. Vascular lipid deposits were not decreased by probucol treatment but were significantly decreased by the treatment with lomitapide (Fig. 5B, C), suggesting that lipid levels, but not lipid oxidation, play a dominant role in early vascular lipid accumulation event in loss-of-function ldlr mutant larvae.

Reference: J Lipid Res. 2018 Feb; 59(2): 391–399. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5794413/