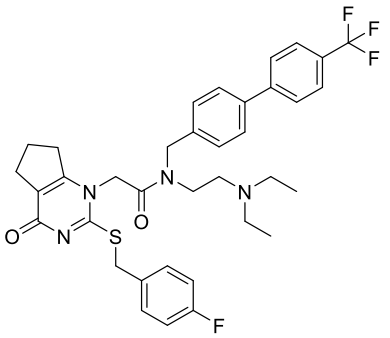
Product data sheet

MedKoo Cat#: 319502 Name: Darapladib CAS#: 356057-34-6 Chemical Formula: $C_{36}H_{38}F_4N_4O_2S$ Exact Mass: 666.26516 Molecular Weight: 666.77961	
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:

Darapladib, also known as SB-480848, is a reversible lipoprotein-associated phospholipase A2 (Lp-PLA2) inhibitor with IC50 of 0.25 nM, which is in Phase 3 trials. Recent studies showed that risk of major coronary events not reduced by darapladib therapy. In patients with stable coronary heart disease, darapladib did not significantly reduce the risk of the primary composite end point of cardiovascular death, myocardial infarction, or stroke.

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	72.0	107.98
Ethanol	62.0	92.98

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.50 mL	7.50 mL	15.00 mL
5 mM	0.30 mL	1.50 mL	3.00 mL
10 mM	0.15 mL	0.75 mL	1.50 mL
50 mM	0.03 mL	0.15 mL	0.30 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. Wang YJ, Chang SB, Wang CY, Huang HT, Tzeng SF. The selective lipoprotein-associated phospholipase A2 inhibitor darapladib triggers irreversible actions on glioma cell apoptosis and mitochondrial dysfunction. Toxicol Appl Pharmacol. 2020 Sep 1;402:115133. doi: 10.1016/j.taap.2020.115133. Epub 2020 Jul 12. PMID: 32668280.

In vivo study

1. Zhang J, Xu DL, Liu XB, Bi SJ, Zhao T, Sui SJ, Ji XP, Lu QH. Darapladib, a Lipoprotein-Associated Phospholipase A2 Inhibitor, Reduces Rho Kinase Activity in Atherosclerosis. Yonsei Med J. 2016 Mar;57(2):321-7. doi: 10.3349/ymj.2016.57.2.321. PMID: 26847282; PMCID: PMC4740522.
2. Wihastuti TA, Heriansyah T, Hanifa H, Andarini S, Sholichah Z, Sulfia YH, Adam AA, Refialdinata J, Lutfiana NC. Darapladib inhibits atherosclerosis development in type 2 diabetes mellitus Sprague-Dawley rat model. Endocr Regul. 2018 Apr 1;52(2):69-75. doi: 10.2478/enr-2018-0008. PMID: 29715185.

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7. Bioactivity

Biological target:

Darapladib is a potent inhibitor of lipoprotein-associated phospholipase A2 (Lp-PLA2) with IC50 of 0.25 nM.

In vitro activity

In this study, we evaluated the anti-glioma effects of darapladib, a selective reversible inhibitor of lipoprotein-associated phospholipase A2 (Lp-PLA2) that is encoded by the PLA2G7 gene and serves as a predictive biomarker of sub-clinical inflammation in cardiovascular diseases. The three glioma cell lines (rat C6 glioma cell line, human U87MG, and human U251MG) and an ex vivo brain tissue slice-glioma cell co-culture system were used to validate the inhibitory effect of darapladib on the expansion of glioma cells. Exposure to darapladib at doses higher than 5 μM induced profound cytotoxicity in C6, U87MG, and U251MG. Moreover, the colony formation ability of the glioma cell lines was significantly repressed after the addition of darapladib. Although darapladib did not reduce the generation of the Lp-PLA2 downstream molecule, arachidonic acid (AA), in the glioma cells, this small compound triggered mitochondrial membrane depolarization and cell apoptosis in these glioma cells. In addition, transient exposure to darapladib induced the upregulation of phosphorylated extracellular signal-regulated kinase 1/2 (ERK1/2) levels, but reduced phosphorylation of AKT/PKB (protein kinase B).

Reference: Toxicol Appl Pharmacol. 2020 Sep 1;402:115133. https://pubmed.ncbi.nlm.nih.gov/32668280/

In vivo activity

The principal aim of this study was to examine whether darapladib (a selective Lp-PLA2 inhibitor) could reduce the elevated Lp-PLA2 and Rho kinase activity in atherosclerosis. Studies were performed in male Sprague-Dawley rats. The atherosclerosis rats were prepared by feeding them with a high-cholesterol diet for 10 weeks. Levels of TC, LDL-C, CRP, Lp-PLA2, and Rho kinase activity were respectively reduced in darapladib groups, whereas NO production was enhanced. When compared to the low-dose darapladib group, the reduction of the levels of TC, LDL-C, CRP, and Lp-PLA2 was more prominent in the high-dose darapladib group ($p<0.05$), and the increase of NO production was more prominent ($p<0.05$). Cardiomyocyte apoptosis of the high-dose darapladib group was also significantly reduced compared to the low-dose darapladib group ($p<0.05$). However, there was no significant difference in Rho kinase activity between the low-dose darapladib group and the high-dose darapladib group ($p>0.05$). In conclusion, darapladib, a Lp-PLA2 inhibitor, leads to cardiovascular protection that might be mediated by its inhibition of both Rho kinase and Lp-PLA2 in atherosclerosis.

Reference: Yonsei Med J. 2016 Mar;57(2):321-7. https://pubmed.ncbi.nlm.nih.gov/26847282/

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.