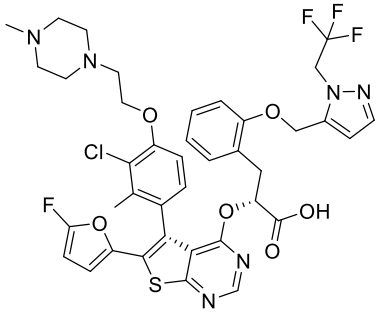
Product data sheet

MedKoo Cat#: 406849 Name: S63845 CAS#: 1799633-27-4 Chemical Formula: $C_{39}H_{37}ClF_4N_6O_6S$ Exact Mass: 828.2120 Molecular Weight: 829.26	
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:
S63845 is a potent and selective myeloid cell leukemia 1 (MCL1) inhibitor. In vivo, S63845 shows potent anti-tumour activity with an acceptable safety margin as a single agent in several cancers. MCL1 inhibition proved effective against several solid cancer-derived cell lines.

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
DMF	30.0	36.18
DMSO	54.44	65.65
Ethanol	65.0	78.38

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.21 mL	6.03 mL	12.06 mL
5 mM	0.24 mL	1.21 mL	2.41 mL
10 mM	0.12 mL	0.60 mL	1.21 mL
50 mM	0.02 mL	0.12 mL	0.24 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. Sumarni U, Zhu J, Sinnberg T, Eberle J. Sensitivity of Cutaneous T-Cell Lymphoma Cells to the Mcl-1 Inhibitor S63845 Correlates with the Lack of Bcl-w Expression. Int J Mol Sci. 2022 Oct 18;23(20):12471. doi: 10.3390/ijms232012471. PMID: 36293331; PMCID: PMC9604298.
2. Kotschy A, Szlavik Z, Murray J, Davidson J, Maragno AL, Le Toumelin-Braizat G, Chanrion M, Kelly GL, Gong JN, Moujalled DM, Bruno A, Csekei M, Paczal A, Szabo ZB, Sipos S, Radics G, Proszenyak A, Balint B, Ondi L, Blasko G, Robertson A, Surgenor A, Dokurno P, Chen I, Matassova N, Smith J, Pedder C, Graham C, Studeny A, Lysiak-Auvity G, Girard AM, Gravé F, Segal D, Riffkin CD, Pomilio G, Galbraith LC, Aubrey BJ, Brennan MS, Herold MJ, Chang C, Guasconi G, Cauquil N, Melchiore F, Guigal-Stephan N, Lockhart B, Colland F, Hickman JA, Roberts AW, Huang DC, Wei AH, Strasser A, Lessene G, Geneste O. The MCL1 inhibitor S63845 is tolerable and effective in diverse cancer models. Nature. 2016 Oct 27;538(7626):477-482. doi: 10.1038/nature19830. Epub 2016 Oct 19. PMID: 27760111.

In vivo study

Product data sheet

1. Zhang H, Li F, Yang M, Zhang W, He M, Xu H, Wang C, Zhang Y, Wang W, Gao Y, Du X, Li Y. MCL-1 Inhibitor S63845 Distinctively Affects Intramedullary and Extramedullary Hematopoiesis. Pharmaceutics. 2023 Mar 28;15(4):1085. doi: 10.3390/pharmaceutics15041085. PMID: 37111571; PMCID: PMC10144179.
2. Azad AI, Krishnan A, Troop L, Li Y, Katsumi T, Pavelko K, Kostallari E, Guicciardi ME, Gores GJ. Targeted Apoptosis of Ductular Reactive Cells Reduces Hepatic Fibrosis in a Mouse Model of Cholestasis. Hepatology. 2020 Sep;72(3):1013-1028. doi: 10.1002/hep.31211. PMID: 32128842; PMCID: PMC7774262.

7. Bioactivity

Biological target:

S63845 is a potent and selective MCL1 inhibitor (Ki (MCL1, FP) < 1.2 nM; Kd (MCL1, SPR) = 0.19 nM; Ki (BCL2, FP) > 10.000 1.2 nM; Ki (BCL-XL, FP) > 10.000 1.2 nM). S63845 binds with high affinity to the BH3-binding groove of MCL1. S63845 potently kills MCL1-dependent cancer cells, including multiple myeloma, leukaemia and lymphoma cells, by activating the BAX/BAK-dependent mitochondrial apoptotic pathway.

In vitro activity

This study investigated the effects of S63845 on several cutaneous T-cell lymphoma (CTCL) cell lines. S63845 induced significant apoptosis, reduced cell viability, disrupted mitochondrial function, and activated caspases in two CTCL cell lines (HH and HuT-78). However, two other cell lines (MyLa and SeAx) remained completely resistant to S63845. Cells resistant to S63845 were sensitive to inhibitors of Bcl-2, Bcl-xL, and Bcl-w, such as ABT-263 and ABT-737.

Reference: Int J Mol Sci. 2022 Oct 18;23(20):12471. https://pubmed.ncbi.nlm.nih.gov/36293331/

In vivo activity

In a mouse model of hematopoietic injury, S63845 affected the hematopoiesis of various lineages in the early stage of action, causing extramedullary compensatory hematopoiesis in the myeloid and megakaryocytic lineages. The maturation of the erythroid lineage in the intramedullary and extramedullary segments was blocked to varying degrees, and both the intramedullary and extramedullary lymphoid lineages were inhibited.

Reference: Pharmaceutics. 2023 Mar 28;15(4):1085. https://pubmed.ncbi.nlm.nih.gov/37111571/

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.