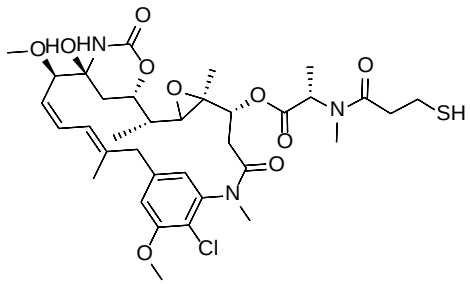
Product data sheet

MedKoo Cat#: 123212 Name: Mertansine (DM1) CAS#: 139504-50-0 Chemical Formula: $C_{35}H_{48}ClN_3O_{10}S$ Exact Mass: 737.2749 Molecular Weight: 738.29	
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:
Mertansine refers to the thiol-containing maytansinoid, DM1 (N2'-deacetyl-N2'-(3-mercapto-1-oxopropyl)maytansine) attached to a monoclonal antibody through reaction of the thiol group with an SPP (N-succinimidyl 4-(2-pyridyldithio)) linker to create an antibody-drug conjugate or ADC. Experimental ADCs with the SPP-DM1 design include lorvotuzumab mertansine. DM1 can also be linked to an antibody using the SMCC (4-(3-mercapto-2,5-dioxo-1-pyrrolidinylmethyl)-cylohexanecarboxylic acid) linker, in which case the International Nonproprietary Name of the conjugate formed contains the word emtansine. DM1 and its attachment via these linkers result from ImmunoGen Inc research. Trastuzumab emtansine (T-DM1) is an anti-HER2/neu antibody-drug conjugate.

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	60.0	81.26

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.35 mL	6.77 mL	13.54 mL
5 mM	0.27 mL	1.35 mL	2.71 mL
10 mM	0.14 mL	0.68 mL	1.35 mL
50 mM	0.03 mL	0.14 mL	0.27 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. Lopus M. Antibody-DM1 conjugates as cancer therapeutics. Cancer Lett. 2011 Aug 28;307(2):113-8. doi: 10.1016/j.canlet.2011.03.017. Epub 2011 Apr 9. PMID: 21481526; PMCID: PMC3105156.

In vivo study

1. Zhong P, Gu X, Cheng R, Deng C, Meng F, Zhong Z. αvβ3 integrin-targeted micellar mertansine prodrug effectively inhibits triple-negative breast cancer in vivo. Int J Nanomedicine. 2017 Oct 27;12:7913-7921. doi: 10.2147/IJN.S146505. PMID: 29138558; PMCID: PMC5667790.

7. Bioactivity
Biological target: Mertansine (DM1) is a microtubulin inhibitor and an antibody-conjugatable maytansinoid that is developed to overcome systemic toxicity associated with maytansine and to enhance tumor-specific delivery.

In vitro activity

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DM1 is a synthetic derivative of the tubulin-binding agent maytansine. Maytansine and the DM1 (S-methyl-DM1; ((N2'-deacetyl-N2'-(3-thiomethyl-1-oxopropyl)-maytansine; Fig. 1) suppress microtubule dynamics at very low drug concentrations. Maytansine as well as the DM1 derivative strongly suppress the dynamic instability parameters of microtubules assembled from MAP-free tubulin in vitro (Fig. 2). Maytansine and S-methyl-DM1 suppressed almost all dynamic instability parameters, including the growth rate, the shortening rate, the catastrophe frequency, and the rescue frequency, with the DM1 derivative showing stronger suppression of dynamics than the parent macrolide. The molecular mechanism of action of S-methyl-DM1 was found to be microtubule end poisoning. That is, S-methyl DM1 binds to the tips of microtubules and thereby inhibits the growth and the shortening of microtubules, leading to suppression of microtubule dynamics. Specifically, the maytansinoid showed high-affinity binding (KD, 0.1 μmol/L) to approximately 37 sites per microtubule.

Reference: Cancer Lett. 2011 Aug 28;307(2):113-8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3105156/

In vivo activity

cRGD-decorated, redox-activatable micellar mertansine prodrug (cRGD-MMP) can effectively target and deliver DM1 to αvβ3 integrin overexpressing MDA-MB-231 TNBC xenografts in nude mice, resulting in potent tumor growth inhibition. 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assays showed that cRGD-MMP had obvious targetability to MDA-MB-231 cells with a low half-maximal inhibitory concentration (IC50) of 0.18 μM, which was close to that of free DM1 and 2.2-fold lower than that of micellar mertansine prodrug (MMP; nontargeting control). The confocal microscopy studies demonstrated that cRGD-MMP mediated a clearly more efficient cellular uptake and intracellular release of doxorubicin (used as a fluorescent anticancer drug model) in MDA-MB-231 cells. Notably, cRGD-MMP loaded with 1,1'-dioctadecyltetramethyl indotricarbocyanine iodide (DiR; a hydrophobic near-infrared dye) was shown to quickly accumulate in the MDA-MB-231 tumor with strong DiR fluorescence from 2 to 24 h post injection. MMP loaded with DiR could also accumulate in the tumor, although significantly less than cRGD-MMP. The biodistribution studies revealed a high DM1 accumulation of 8.1%ID/g in the tumor for cRGD-MMP at 12 h post injection. The therapeutic results demonstrated that cRGD-MMP effectively suppressed MDA-MB-231 tumor growth at 1.6 mg DM1 equiv./kg without causing noticeable side effects, as shown by little body weight loss and histological analysis. This MMP has appeared as a promising platform for potent treatment of TNBCs.

Reference: Int J Nanomedicine. 2017 Oct 27;12:7913-7921. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5667790/