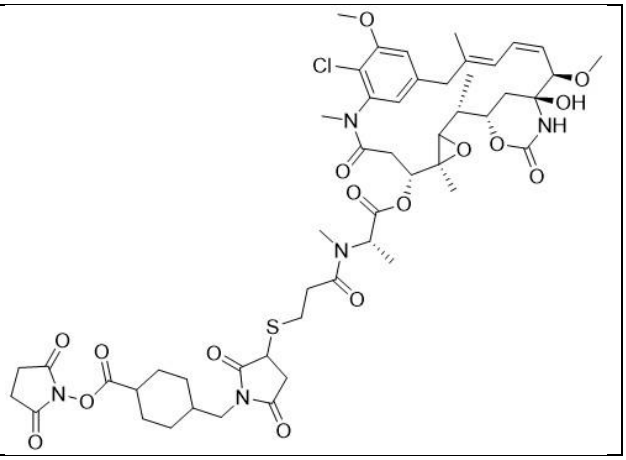
Product data sheet

MedKoo Cat#: 407202 Name: DM1-SMCC CAS#: 1228105-51-8 Chemical Formula: $C_{51}H_{66}ClN_5O_{16}S$ Exact Mass: 1071.39138 Molecular Weight: 1072.62	
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:

DM1-SMCC is DM1 with a reactive linker SMCC, which can react with antibody to make antibody drug conjugate. DM1 is an antibody-conjugatable maytansinoid that was developed to overcome systemic toxicity associated with maytansine and to enhance tumor-specific delivery. DM1 binds at the tips of microtubules and suppresses the dynamicity of microtubules.

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	93.23

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	0.93	4.66	9.32
5 mM	0.19	0.93	1.86
10 mM	0.09	0.47	0.93
50 mM	0.02	0.09	0.19

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. Ikeda H, Hideshima T, Fulciniti M, Lutz RJ, Yasui H, Okawa Y, Kiziltepe T, Vallet S, Pozzi S, Santo L, Perrone G, Tai YT, Cirstea D, Raje NS, Uherek C, Dälken B, Aigner S, Osterroth F, Munshi N, Richardson P, Anderson KC. The monoclonal antibody nBT062 conjugated to cytotoxic Maytansinoids has selective cytotoxicity against CD138-positive multiple myeloma cells in vitro and in vivo. Clin Cancer Res. 2009 Jun 15;15(12):4028-37. doi: 10.1158/1078-0432.CCR-08-2867. Epub 2009 Jun 9. PMID: 19509164.
2. Erickson HK, Park PU, Widdison WC, Kovtun YV, Garrett LM, Hoffman K, Lutz RJ, Goldmacher VS, Blättler WA. Antibody-maytansinoid conjugates are activated in targeted cancer cells by lysosomal degradation and linker-dependent intracellular processing. Cancer Res. 2006 Apr 15;66(8):4426-33. doi: 10.1158/0008-5472.CAN-05-4489. PMID: 16618769.

In vivo study

1. Erickson HK, Widdison WC, Mayo MF, Whiteman K, Audette C, Wilhelm SD, Singh R. Tumor delivery and in vivo processing of disulfide-linked and thioether-linked antibody-maytansinoid conjugates. Bioconjug Chem. 2010 Jan;21(1):84-92. doi: 10.1021/bc900315y. PMID: 19891424.
2. Ikeda H, Hideshima T, Fulciniti M, Lutz RJ, Yasui H, Okawa Y, Kiziltepe T, Vallet S, Pozzi S, Santo L, Perrone G, Tai YT, Cirstea D, Raje NS, Uherek C, Dälken B, Aigner S, Osterroth F, Munshi N, Richardson P, Anderson KC. The monoclonal antibody nBT062

conjugated to cytotoxic Maytansinoids has selective cytotoxicity against CD138-positive multiple myeloma cells in vitro and in vivo. Clin Cancer Res. 2009 Jun 15;15(12):4028-37. doi: 10.1158/1078-0432.CCR-08-2867. Epub 2009 Jun 9. PMID: 19509164.

7. Bioactivity

Biological target:

SMCC-DM1 (DM1-SMCC) is a drug-linker conjugate composed of a potent microtubule-disrupting agent DM1 and a linker SMCC to make antibody drug conjugate (ADC).

In vitro activity

In particular, the metabolic fate in cells of huC242-maytansinoid conjugates containing either a disulfide linker (huC242-SPDB-DM4) or a thioether linker (huC242-SMCC-DM1) was examined. The disulfide-linked antibody-maytansinoid conjugate, huC242-SPDB-DM4, and the thioether-linked conjugate, huC242-SMCC-DM1, were first assayed for their cytotoxic potency against antigen-positive COLO 205 cells and antigen-negative Namalwa cells (both sensitive to maytansine with IC50 values of ~30 to 60 pmol/L for both cell lines) using an 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT)–based assay. The conjugates displayed similar potencies with IC50 values of 40 pmol/L against COLO 205 cells and 20 to 80 nmol/L against Namalwa cells upon a 4-day exposure of the cells to the conjugates (Fig. 1A). To examine the fate of the maytansinoid drug upon incubation of target cells with an antibody-maytansinoid conjugate, conjugates with maytansinoids were prepared that were 3H-labeled at the C-20 methoxy group (see Fig. 5). Radiolabeled maytansinoid conjugates, huC242-SPDB-[3H]DM4 (250 mCi/mmol) and huC242-SMCC-[3H]DM1 (214 mCi/mmol), exhibit in vitro cytotoxicities similar to nonradiolabeled conjugate samples (data not shown). The two major metabolites, S-methyl-DM4 and lysine-Nε-SMCC-DM1, were synthesized and tested for their in vitro cytotoxicity against COLO 205 cells and Namalwa cells. Lysine-Nε-SMCC-DM1 was ~105-fold less potent against both cell lines with an IC50 value of 0.1 μmol/L (data not shown). Accumulation of the lysine-Nε-SMCC-DM1 metabolite from the noncleavable conjugate is coincident with the observed formation of the potent S-methyl-DM4, DM4, and lysine-Nε-SPDB-DM4 from the cleavable conjugate. This suggests that the lysine-Nε-SMCC-DM1 metabolite is as potent as the metabolites from the cleavable conjugate when delivered intracellularly and that all of the maytansinoid metabolites are active when produced in the cell.

Cancer Res. 2006 Apr 15;66(8):4426-33. https://pubmed.ncbi.nlm.nih.gov/16618769/

In vivo activity

The antitumor effect of murine/human chimeric CD138-specific monoclonal antibody nBT062 conjugated with highly cytotoxic maytansinoid derivatives against multiple myeloma (MM) cells were investigated in vitro and in vivo. The in vivo activity of BT062-SPDB-DM4, BT062-SMCC-DM1, and BT062-SPP-DM was examined in murine MM cell xenograft model of human and severe combined immunodeficient (SCID) mice bearing implant bone chips injected with human MM cells (SCID-hu model). The in vivo efficacy of nBT062-SPDB-DM4, nBT062-SMCC-DM1, and nBT062-SPP-DM1 was next evaluated in SCID mice bearing established CD138-positive MOLP-8 human MM cells. A single i.v. administration of the immunoconjugates caused significant dose-dependent tumor growth inhibition and tumor regression at concentrations that were well tolerated, evidenced by stable body weight. nBT062-SPDB-DM4 was the most active conjugate tested in this model (Fig. 6A). In addition, weekly dosing of the nBT062-SMCC-DM1 (six doses of 13.8 μg/kg) completely blocked tumor growth during the dosing period (Supplementary Fig. S6A). In summary, nBT062-SMCC-DM1, nBT062-SPDB-DM4, and nBT062-SPP-DM1 have in vitro and in vivo antitumor activity against CD138-positive MM cells and can overcome the protective effects of cytokines and BMSCs

Clin Cancer Res. 2009 Jun 15;15(12):4028-37. https://pubmed.ncbi.nlm.nih.gov/19509164/