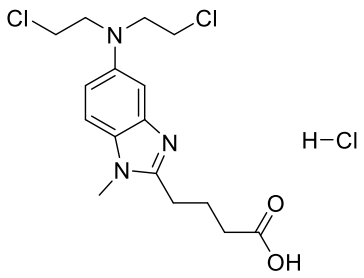
Product data sheet

MedKoo Cat#: 200470 Name: Bendamustine HCl CAS#: 3543-75-7 (HCl) Chemical Formula: $C_{16}H_{22}Cl_3N_3O_2$ Molecular Weight: 394.72	
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:

Bendamustine hydrochloride is the hydrochloride salt of bendamustine, a bifunctional mechlorethamine derivative with alkylator and antimetabolite activities. Bendamustine possesses three active moieties: an alkylating group; a benzimidazole ring, which may act as a purine analogue; and a butyric acid side chain. Although its exact mechanism of action is unknown, this agent appears to act primarily as an alkylator. Bendamustine metabolites alkylate and crosslink macromolecules, resulting in DNA, RNA and protein synthesis inhibition, and, subsequently, apoptosis. In October 2008, the FDA granted further approval to market Treanda for the treatment of indolent B-cell non-Hodgkin's lymphoma (NHL) that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen.

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	72.49	183.65
Ethanol	78.0	197.61
Water	43.94	111.32

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.53 mL	12.67 mL	25.33 mL
5 mM	0.51 mL	2.53 mL	5.07 mL
10 mM	0.25 mL	1.27 mL	2.53 mL
50 mM	0.05 mL	0.25 mL	0.51 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. Stokes J, Hoffman EA, Zeng Y, Larmonier N, Katsanis E. Post-transplant bendamustine reduces GvHD while preserving GvL in experimental haploidentical bone marrow transplantation. Br J Haematol. 2016 Jul;174(1):102-16. doi: 10.1111/bjh.14034. Epub 2016 Mar 31. PMID: 27030315; PMCID: PMC4917459.
2. Leoni LM, Bailey B, Reifert J, Bendall HH, Zeller RW, Corbeil J, Elliott G, Niemeyer CC. Bendamustine (Treanda) displays a distinct pattern of cytotoxicity and unique mechanistic features compared with other alkylating agents. Clin Cancer Res. 2008 Jan 1;14(1):309-17. doi: 10.1158/1078-0432.CCR-07-1061. PMID: 18172283.

In vivo study

1. Molina MS, Stokes J, Hoffman EA, Eremija J, Zeng Y, Simpson RJ, Katsanis E. Bendamustine Conditioning Skews Murine Host DCs Toward Pre-cDC1s and Reduces GvHD Independently of Batf3. Front Immunol. 2020 Jul 16;11:1410. doi: 10.3389/fimmu.2020.01410. PMID: 32765499; PMCID: PMC7378358.

2. Stokes J, Hoffman EA, Molina MS, Kummet N, Simpson RJ, Zeng Y, Katsanis E. Bendamustine with total body irradiation conditioning yields tolerant T-cells while preserving T-cell-dependent graft-versus-leukemia. Oncoimmunology. 2020 Apr 30;9(1):1758011. doi: 10.1080/2162402X.2020.1758011. PMID: 32391190; PMCID: PMC7199810.

7. Bioactivity

Biological target:

Bendamustine hydrochloride (SDX-105), a purine analogue, is a DNA cross-linking agent.

In vitro activity

PT-BEN (post-transplant bendamustine) is lymphodepleting, relatively spares the myeloid compartment and significantly increases MDSCs. This study therefore further investigated the differential effects of BEN on these subsets in vitro. MDSCs were generated from naïve BM in the presence of increasing concentrations of BEN. After 3 days in culture, >90% of cells were CD11b+Gr-1+ (Supplemental Figure 7), with no significant differences between groups. MDSCs generated with higher concentrations of BEN were significantly more suppressive than those generated with lower concentrations (Figure 7A).

Reference: Br J Haematol. 2016 Jul; 174(1): 102–116. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4917459/

In vivo activity

Therefore, this study evaluated the two host cDC subsets in BEN+TBI (bendamustine combined with total body irradiation) vs. CY+TBI (cyclophosphamide with total body irradiation) conditioning. Representative flow plots of cDC1 and cDC2 populations on day 0 are depicted in Figure 3A, demonstrating differences between BEN+TBI and CY+TBI. The CD8α-SIRPα- DCs are considered pre-cDCs that have not yet committed to either of the two cDC lineages. Quantification of these flow cytometry plots shows significantly more CD8α+ cDC1s with BEN+TBI conditioning than with CY+TBI (Figure 3B), and significantly fewer SIRPα+ cDC2s (Figure 3D) on day +1. The absolute numbers of CD8α+ cDC1s (Figure 3C) and SIRPα+ cDC2s (Figure 3E) were not different on day 0. Given that total cDCs have been reported to exacerbate GvHD, whereas CD8α+ cDC1s are highly effective suppressors of GvHD, this study evaluated the ratio of CD8α+cDC1 to SIRPα+cDC2 in each mouse conditioned with BEN+TBI or CY+TBI. This study found that the ratio of favorable cDC1s to unfavorable cDC2s was significantly higher in BEN+TBI mice on days 0 and +1 (Figure 3F).

Reference: Front Immunol. 2020; 11: 1410. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7378358/