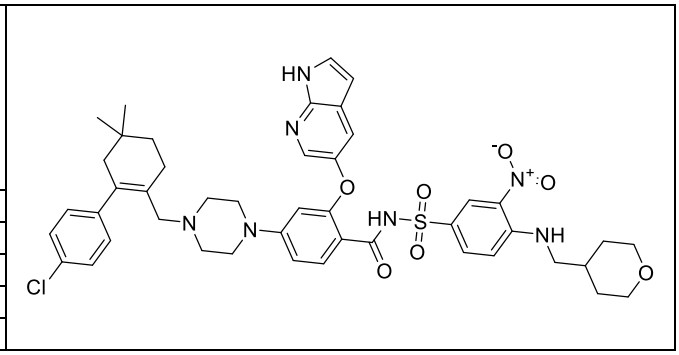
Product data sheet

MedKoo Cat#: 205807 Name: Venetoclax (ABT199) CAS#: 1257044-40-8 Chemical Formula: $C_{45}H_{50}ClN_7O_7S$ Exact Mass: 867.3181 Molecular Weight: 868.44	
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:
Venetoclax, also known as ABT-199 or GDC0199, is an orally bioavailable, selective small molecule inhibitor of the anti-apoptotic protein Bcl-2, with potential antineoplastic activity. Venetoclax mimics BH3-only proteins, the native ligands of Bcl-2 and apoptosis activators, by binding to the hydrophobic groove of Bcl-2 proteins thereby repressing Bcl-2 activity and restoring apoptotic processes in tumor cells.

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	70.0	80.6
Ethanol	0.1	0.12

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.15 mL	5.76 mL	11.51 mL
5 mM	0.23 mL	1.15 mL	2.30 mL
10 mM	0.12 mL	0.58 mL	1.15 mL
50 mM	0.02 mL	0.12 mL	0.23 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. Houshmand M, Garello F, Stefania R, Gaidano V, Cignetti A, Spinelli M, Fava C, Nikougoftar Zarif M, Galimberti S, Pungolino E, Annunziata M, Luciano L, Specchia G, Bocchia M, Binotto G, Bonifacio M, Martino B, Pregno P, Stagno F, Iurlo A, Russo S, Aime S, Circosta P, Saglio G. Targeting Chronic Myeloid Leukemia Stem/Progenitor Cells Using Venetoclax-Loaded Immunoliposome. Cancers (Basel). 2021 Mar 15;13(6):1311. doi: 10.3390/cancers13061311. PMID: 33804056; PMCID: PMC8000981.

In vivo study

1. Seyfried F, Demir S, Hörl RL, Stirnweiß FU, Ryan J, Scheffold A, Villalobos-Ortiz M, Boldrin E, Zinngrebe J, Enzenmüller S, Jenni S, Tsai YC, Bornhauser B, Fürstberger A, Kraus JM, Kestler HA, Bourquin JP, Stilgenbauer S, Letai A, Debatin KM, Meyer LH. Prediction of venetoclax activity in precursor B-ALL by functional assessment of apoptosis signaling. Cell Death Dis. 2019 Jul 29;10(8):571. doi: 10.1038/s41419-019-1801-0. PMID: 31358732; PMCID: PMC6662703.

7. Bioactivity
Biological target:

Bcl-2 inhibitor with a Ki of less than 0.01 nM

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In vitro activity

To study the selectivity of IL-VX (venetoclax-loaded immunoliposome) and to demonstrate the higher efficiency of the venetoclax-loaded liposome, the cells were also treated with free venetoclax at the same doses. Our results displayed that after 2 days of the treatment, free venetoclax did not have any apoptotic effect on CMLT1 cells even at the concentration of 1 µM, and a higher concentration was needed to observe the cytotoxic effect in this cell line (Figure 4A). However, it slightly reduced cell viability in HL60 cells. On the contrary, IL-VX induced its toxic effect on CD26+ CMLT1 cells starting from 100 nM, while its effect on CD26− HL60 cells was not significant (Figure 4B). These results confirmed the selectivity and efficiency of IL-VX and offered the opportunity to eliminate resistant cells even with a lower dose of the drug. As is clear in Figure 4C, TMRM percentage in CMLT1 was reduced following treatment with IL-VX. In healthy cells, TMRM accumulates in mitochondria and displays a bright signal. Reduction of TMRM signal may represent the reduction of mitochondria membrane potential and the start of apoptosis in treated cells.

Reference: Cancers (Basel). 2021 Mar; 13(6): 1311. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8000981/

In vivo activity

To address antileukemia activities of VEN (Venetoclax) in individual leukemia samples in a situation more similar to a potential clinical application, its antileukemia activities were investigated in a preclinical phase-II-like trial on different individual, patient-derived xenograft ALL samples in mice (N = 12). Three weeks after transplantation onto recipient mice, ALL-bearing animals were treated with VEN for 10 days and times to reoccurrence of full-blown, clinically apparent leukemia after treatment with VEN or vehicle were compared for each leukemia. Distinct in vivo antileukemia activities of VEN were observed and indicated by differences of survival times (‘delta survival’) ranging from minimal effects to prolonged survival without manifestation of ALL for more than 140 days (Fig.3a). This variation of in vivo responses is similar to the heterogeneity of VEN sensitivities observed ex vivo, and EC50 values analyzed ex vivo showed a moderate association with in vivo survival times (Table3,3, Supplementary Fig. 8). An analysis was then conducted to show whether the molecular markers associated with ex vivo VEN response would indicate in vivo antileukemia activity. No association of preclinical VEN activity with BCL-2 expression was found, neither alone nor relative to MCL-1 transcript levels ((Table3,3, Supplementary Fig. 8). However, direct VEN priming was associated with in vivo antileukemia activity of VEN (Table (Table33 and Fig. Fig.3b),3b), but not predictive for in vivo VEN activity (Fig.3c). Interestingly, functional dependence of the leukemia cells on BCL-2 (BAD-HRK priming) was strongly associated with in vivo VEN activity (Table33 and Fig.3d),3d), and importantly, showed high sensitivity and specificity in predicting preclinical in vivo antileukemia activity of VEN (Fig.3e3e).

Reference: Cell Death Dis. 2019 Aug; 10(8): 571. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6662703/