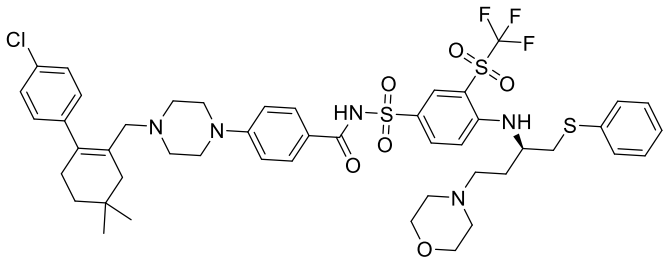
Product data sheet

MedKoo Cat#: 201970 Name: Navitoclax CAS#: 923564-51-6 Chemical Formula: $C_{47}H_{55}ClF_3N_5O_6S_3$ Exact Mass: 973.29551 Molecular Weight: 974.61	
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:
Navitoclax, also known as ABT-263, is an orally bioavailable, synthetic small-molecule antagonist of a subset of the B-cell leukemia 2 (Bcl-2) family of proteins with potential antineoplastic activity. ABT-263 selectively binds to apoptosis suppressor proteins Bcl-2, Bcl-XL, and Bcl-w and prevents their binding to the apoptotic effectors Bax and Bak proteins, which may trigger apoptosis in tumor cells overexpressing Bcl-2, Bcl-XL, and Bcl-w.

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	25.0	25.7

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.03 mL	5.13 mL	10.26 mL
5 mM	0.21 mL	1.03 mL	2.05 mL
10 mM	0.10 mL	0.51 mL	1.03 mL
50 mM	0.02 mL	0.10 mL	0.21 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. Chteinberg E, Wetzels S, Gerritsen W, Temmerman L, van den Oord J, Biessen E, Kurz AK, Winnepenninckx V, Zenke M, Speel EJ, Zur Hausen A. Navitoclax combined with Alpelisib effectively inhibits Merkel cell carcinoma cell growth in vitro. Ther Adv Med Oncol. 2020 Dec 14;12:1758835920975621. doi: 10.1177/1758835920975621. PMID: 33403016; PMCID: PMC7739210.

In vivo study

1. Zoeller JJ, Vagodny A, Daniels VW, Taneja K, Tan BY, DeRose YS, Fujita M, Welm AL, Letai A, Leverson JD, Blot V, Bronson RT, Dillon DA, Brugge JS. Navitoclax enhances the effectiveness of EGFR-targeted antibody-drug conjugates in PDX models of EGFR-expressing triple-negative breast cancer. Breast Cancer Res. 2020 Nov 30;22(1):132. doi: 10.1186/s13058-020-01374-8. PMID: 33256808; PMCID: PMC7708921.

7. Bioactivity
Biological target:

Bcl-xL, Bcl-2 and Bcl-w inhibitor with Ki of ≤ 0.5 nM, ≤1 nM and ≤1 nM in cell-free assays.

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In vitro activity

The MCC cell lines WaGa, MKL-1, MKL-2 and MCC13 as well as the B-ALL cell line REH were treated with different concentrations (range 1 nM to 1 μM) of the specific BCL-2 inhibitor Navitoclax (Figure 1I). With increasing concentrations, the cell viability decreased. For all cell lines except for BCL-2, negative MCC13 dose–response curves and IC50 values could be generated. MKL-1, WaGa and REH demonstrated similar high sensitivity towards Navitoclax treatment (IC50 around 100 nM). Surprisingly, MKL-2 was less sensitive (IC50 = 323.3 nM), although this cell line showed a high BCL-2 expression. Subsequently, BCL-2 inhibition was assessed to see if it promotes apoptosis in MCC cells, as assessed by the detection of cleaved PARP protein by apoptosis-activated caspases. Indeed, all cell lines except MCC13 (Figure 1L and andM)M) showed different levels of increase of cleaved PARP with incremental Navitoclax concentrations.

Reference: Ther Adv Med Oncol. 2020; 12: 1758835920975621. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7739210/

In vivo activity

Treatment with navitoclax plus ABT-414 caused a significant reduction in tumor growth in five of seven PDXs and significant tumor regression in the highest EGFR-expressing PDX. Navitoclax plus ABBV-321, an EGFR-targeted ADC that displays more effective wild-type EGFR-targeting, elicited more significant tumor growth inhibition and regressions in the two highest EGFR-expressing models evaluated. The level of mitochondrial apoptotic signaling induced by single or combined drug treatments, as measured by DBP, correlated with the treatment responses observed in vivo. Lastly, the majority of triple-negative patient tumors were found to express EGFR and co-express BCL-XL and/or BCL-2.

Reference: Breast Cancer Res. 2020; 22: 132. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7708921/