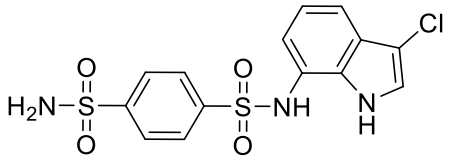
# Product data sheet

| | |
|---|---|
| MedKoo Cat#: 201540<br>Name: Indisulam<br>CAS#: 165668-41-7<br>Chemical Formula: $C_{14}H_{12}ClN_3O_4S_2$<br>Exact Mass: 384.99577<br>Molecular Weight: 385.84 |  |
| 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:**

Indisulam, also known as E7070, is a carbonic anhydrase inhbitor, is also a novel synthetic sulfonamide that targets the G1 phase of the cell cycle.. The potential antitumor activity of Indisulam was discovered through optimization of the structure-activity relationships of a series of sulfonamide structures. Indisulam causes a blockade in the G1/S transition through inhibition of the activation of both cyclin-dependent kinase 2 and cyclin E. Preclinical studies with Indisulam showed activity in multiple tumor types, most prominently in colon and lung cancer.

**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 | 30.0 | 77.75 |

**4. Stock solution preparation table:**

| Concentration / Solvent Volume / Mass | 1 mg | 5 mg | 10 mg |
|---|---|---|---|
| 1 mM | 2.59 mL | 12.96 mL | 25.92 mL |
| 5 mM | 0.52 mL | 2.59 mL | 5.18 mL |
| 10 mM | 0.26 mL | 1.30 mL | 2.59 mL |
| 50 mM | 0.05 mL | 0.26 mL | 0.52 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. Melnyk JE, Steri V, Nguyen HG, Hann B, Feng FY, Shokat KM. The splicing modulator sulfonamide indisulam reduces AR-V7 in prostate cancer cells. Bioorg Med Chem. 2020 Oct 15;28(20):115712. doi: 10.1016/j.bmc.2020.115712. Epub 2020 Aug 18. PMID: 33069070.
2. Ting TC, Goralski M, Klein K, Wang B, Kim J, Xie Y, Nijhawan D. Aryl Sulfonamides Degrade RBM39 and RBM23 by Recruitment to CRL4-DCAF15. Cell Rep. 2019 Nov 5;29(6):1499-1510.e6. doi: 10.1016/j.celrep.2019.09.079. PMID: 31693891; PMCID: PMC7950731.

In vivo study

1. Teixeira SA, Viapiano MS, Andrade AF, Nandhu MS, Pezuk JA, Bidinotto LT, Suazo VK, Neder L, Carlotti CG, Becker AP, Tone LG, Scrideli CA. The Carbonic Anhydrase Inhibitor E7070 Sensitizes Glioblastoma Cells to Radio- and Chemotherapy and Reduces Tumor Growth. Mol Neurobiol. 2021 Jun 3. doi: 10.1007/s12035-021-02437-3. Epub ahead of print. PMID: 34085182.
2. Melnyk JE, Steri V, Nguyen HG, Hann B, Feng FY, Shokat KM. The splicing modulator sulfonamide indisulam reduces AR-V7 in prostate cancer cells. Bioorg Med Chem. 2020 Oct 15;28(20):115712. doi: 10.1016/j.bmc.2020.115712. Epub 2020 Aug 18. PMID: 33069070.

# Product data sheet

**7. Bioactivity**

Biological target:

Indisulam (E 7070) is a carbonic anhydrase inhibitor with anticancer activity.

In vitro activity

Similar to this study's gene expression analysis, indisulam treatment resulted in multiple splicing events that were all dependent on RBM39. Indisulam treatment for 12 h resulted in 1,640 exon-skipping events, 132 intron retention events, and 22 alternative splice site events (Figure 6C). However, no RBM39-independent splicing changes occurred following indisulam treatment in cells expressing the RBM39 G268V allele. In addition, no RBM23-dependent splicing events were detected following auxin treatment in the RBM23-AID cell line (Figure 6C). Taken together, these results suggest that the observed effect of indisulam on splicing is mediated exclusively through RBM39 and not through degradation of RBM23 or any other substrate.

Reference: Cell Rep. 2019 Nov 5; 29(6): 1499–1510.e6. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7950731/

In vivo activity

Finally, this study established VCaP xenografts in castrated male mice to assess the effectiveness of combining indisulam and MDV in vivo relative to the monotherapies. The xenograft study was divided into four arms consisting of vehicle, MDV, indisulam and MDV + indisulam. Dosing for the monotherapies was established from literature precedent. Each arm was dosed on a repeating schedule of five days on then two days off for six weeks (Fig. 6A). Over the course of the study bi-weekly measurements were recorded to track tumor progression. The MDV arm of the study was minimally effective compared to vehicle due to AR-V7-driven growth of the xenografts. As expected, both the indisulam arm and MDV + indisulam arm of the study were significantly effective compared to the MDV arm (Fig. 6A and B). Interestingly, the indisulam arm (152.1 cc ± 20.3 cc at endpoint) was superior to the combination therapy (408.9 cc ± 37.4 cc) and the MDV monotherapy (698.9 cc ± 286.5 cc) (Fig. 6A and B).

Reference: Bioorg Med Chem. 2020 Oct 15;28(20):115712. https://pubmed.ncbi.nlm.nih.gov/33069070/