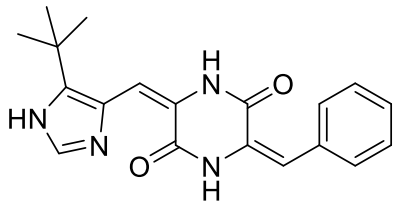
# Product data sheet

| | |
|---|---|
| MedKoo Cat#: 202040<br>Name: Plinabulin<br>CAS#: 714272-27-2<br>Chemical Formula: $C_{19}H_{20}N_4O_2$<br>Exact Mass: 336.15863<br>Molecular Weight: 336.39 |  |
| 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:**
Plinabulin is a VDA of novel structure in having been derived from a marine microbial source, as opposed to terrestrial sources for other VDAs. Plinabulin binds to the colchicine binding site of b-tubulin preventing polymerization and disrupting the cytoplasmic microtubule network. Plinabulin has been shown to produce anti-tumor activity in animal models as a single agent and synergistically with other chemotherapy agents including taxanes. Overall, preclinical studies indicated plinabulin had a favorable safety and activity profile leading to the initiation of clinical trials. Favorable data from early clinical studies lead to the initiation of a Phase 2 clinical trial program.

**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 | 20.0 | 59.5 |

**4. Stock solution preparation table:**

| Concentration / Solvent Volume / Mass | 1 mg | 5 mg | 10 mg |
|---|---|---|---|
| 1 mM | 2.97 mL | 14.86 mL | 29.73 mL |
| 5 mM | 0.59 mL | 2.97 mL | 5.95 mL |
| 10 mM | 0.30 mL | 1.49 mL | 2.97 mL |
| 50 mM | 0.06 mL | 0.30 mL | 0.59 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. Cimino PJ, Huang L, Du L, Wu Y, Bishop J, Dalsing-Hernandez J, Kotlarczyk K, Gonzales P, Carew J, Nawrocki S, Jordan MA, Wilson L, Lloyd GK, Wirsching HG. Plinabulin, an inhibitor of tubulin polymerization, targets KRAS signaling through disruption of endosomal recycling. Biomed Rep. 2019 Apr;10(4):218-224. doi: 10.3892/br.2019.1196. Epub 2019 Mar 5. PMID: 30972217; PMCID: PMC6439430.
2. Singh AV, Bandi M, Raje N, Richardson P, Palladino MA, Chauhan D, Anderson KC. A novel vascular disrupting agent plinabulin triggers JNK-mediated apoptosis and inhibits angiogenesis in multiple myeloma cells. Blood. 2011 May 26;117(21):5692-700. doi: 10.1182/blood-2010-12-323857. Epub 2011 Mar 31. PMID: 21454451; PMCID: PMC3110026.

In vivo study

1. Cimino PJ, Huang L, Du L, Wu Y, Bishop J, Dalsing-Hernandez J, Kotlarczyk K, Gonzales P, Carew J, Nawrocki S, Jordan MA, Wilson L, Lloyd GK, Wirsching HG. Plinabulin, an inhibitor of tubulin polymerization, targets KRAS signaling through disruption of endosomal recycling. Biomed Rep. 2019 Apr;10(4):218-224. doi: 10.3892/br.2019.1196. Epub 2019 Mar 5. PMID: 30972217; PMCID: PMC6439430.

2. Singh AV, Bandi M, Raje N, Richardson P, Palladino MA, Chauhan D, Anderson KC. A novel vascular disrupting agent plinabulin triggers JNK-mediated apoptosis and inhibits angiogenesis in multiple myeloma cells. Blood. 2011 May 26;117(21):5692-700. doi: 10.1182/blood-2010-12-323857. Epub 2011 Mar 31. PMID: 21454451; PMCID: PMC3110026.

**7. Bioactivity**

Biological target:

Plinabulin (NPI-2358) is a vascular disrupting agent (VDA) against β-tubulin -depolymerizing with an IC50 of 9.8 nM against HT-29 cells.

In vitro activity

To examine the antivascular activity of plinabulin, capillary tubule formation assays were performed with the use of HUVECs. Even low concentrations of plinabulin (5nM treatment for 12 hours) triggered significantly decreased tubule formation in HUVECs (Figure 3A; 70%-80% decrease; $P < .05$; $n = 3$). To further confirm the antivascular activity of plinabulin, the effects of plinabulin on the chemotactic motility of both MM and endothelial cells were examined with the use of trans-well insert assays. A marked reduction was observed in serum-dependent migration in plinabulin-treated MM cells (Figure 3B; 58% ± 2.1% inhibition in plinabulin-treated vs control; $P < .05$). At this concentration 5nM plinabulin for 12 hours did not affect survival of MM cells (> 95% viable cells). Similar effects of plinabulin were noted against HUVECs (Figure 3C; 48% ± 1.7% decrease in migration; $P < .05$). Together, these data suggest that plinabulin disrupts tumor vasculature by inhibiting both cell migration and endothelial cell tubule formation.

Blood. 2011 May 26; 117(21): 5692–5700. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3110026/

In vivo activity

MM.1S tumor-bearing mice were treated with plinabulin (7.5 mg/kg intraperitoneally) or vehicle alone twice a week for 3 weeks. Plinabulin treatment inhibited tumor growth and prolonged survival in mice (Figure 7A,C; $P < .05$). Plinabulin treatment was well tolerated, without significant weight loss (Figure 7B). Importantly, increased survival was noted in mice receiving plinabulin versus vehicle alone ($P = .0041$); median survival in the control group was 15 days versus 35 days in the plinabulin treatment group (Figure 7C). Tumors from plinabulin-treated compared with control mice were next examined, and immunostaining for cleaved caspase-3 and vasculature-related marker such as factor VIII was performed. As shown in Figure 7D, increase in cleaved caspase-3 was observed in tumor sections from the plinabulin-treated group versus the control group (Figure 7D bottom). Moreover, antivascular activity of plinabulin was evidenced by a significant reduction in factor VIII expression (Figure 7D top). These results show that in vivo anti-MM activity of plinabulin is associated with disruption of tumor vasculature and proapoptotic activity.

Blood. 2011 May 26; 117(21): 5692–5700. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3110026/