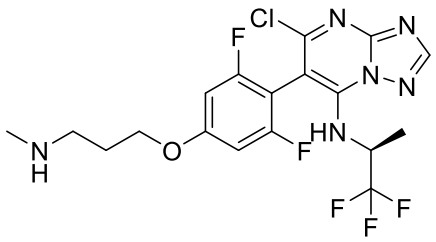
Product data sheet

MedKoo Cat#: 200730 Name: Cevipabulin (free base) CAS#: 849550-05-6 (free base) Chemical Formula: $C_{18}H_{18}ClF_5N_6O$ Exact Mass: 464.11508 Molecular Weight: 464.82	
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:
Cevipabulin (free base), also known as TTI-237, an antimicrotubule agent, is a small synthetic molecule of triazolopyrimidine derivative with potential antitumor activity. With a novel mechanism of action distinct from the action of other vinca alkaloid compounds, TTI-237 specifically binds to tubulin at the vinca site, and promotes the polymerization of tubulin into microtubules. TTI-237 stabilizes tubulin and inhibits microtubule disassembly. This results in cell cycle arrest at the G2/M phase, and leading to cell death.

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	16.0	34.4

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.15 mL	10.76 mL	21.51 mL
5 mM	0.43 mL	2.15 mL	4.30 mL
10 mM	0.22 mL	1.08 mL	2.15 mL
50 mM	0.04 mL	0.22 mL	0.43 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. Yang J, Yu Y, Li Y, Yan W, Ye H, Niu L, Tang M, Wang Z, Yang Z, Pei H, Wei H, Zhao M, Wen J, Yang L, Ouyang L, Wei Y, Chen Q, Li W, Chen L. Cevipabulin-tubulin complex reveals a novel agent binding site on α-tubulin with tubulin degradation effect. Sci Adv. 2021 May 19;7(21):eabg4168. doi: 10.1126/sciadv.abg4168. PMID: 34138737; PMCID: PMC8133757.
2. Beyer CF, Zhang N, Hernandez R, Vitale D, Lucas J, Nguyen T, Discafani C, Ayral-Kaloustian S, Gibbons JJ. TTI-237: a novel microtubule-active compound with in vivo antitumor activity. Cancer Res. 2008 Apr 1;68(7):2292-300. doi: 10.1158/0008-5472.CAN-07-1420. PMID: 18381436.

In vivo study

1. Beyer CF, Zhang N, Hernandez R, Vitale D, Lucas J, Nguyen T, Discafani C, Ayral-Kaloustian S, Gibbons JJ. TTI-237: a novel microtubule-active compound with in vivo antitumor activity. Cancer Res. 2008 Apr 1;68(7):2292-300. doi: 10.1158/0008-5472.CAN-07-1420. PMID: 18381436.

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7. Bioactivity

Biological target:

Cevipabulin (TTI-237) is a, microtubule-active antitumor compound and inhibits the binding of [^{3}H] vinblastine to tubulin, with an IC50 of 18-40 nM for cytotoxicity in human tumor cell line.

In vitro activity

To elucidate the cellular effect of cevipabulin at an early time point, a label-free quantitative proteomic analysis was carried out on a 6-hour cevipabulin-treated human cervical adenocarcinoma cell line HeLa. Cevipabulin significantly down-regulated the protein level of α-tubulin, β-tubulin, and their isoforms with high selectivity (Fig. 1A). Immunoblotting study confirmed that cevipabulin decreased tubulin proteins in HeLa, human colon colorectal carcinoma cell line Hct116, human large cell lung carcinoma cell line H460, and human B cell lymphoma cell SU-DHL-6 in a dose-dependent (Fig. 1B) and time-dependent manner in HeLa cells (Fig. 1C), demonstrating that the reduction of tubulin was a common biochemical consequence of cevipabulin treatment in cancer cells. The quantitative PCR assay showed that cevipabulin had no effect on α- and β-tubulin mRNA levels (Fig. 1D), indicating that the down-regulation of tubulin protein treated by cevipabulin was posttranscriptional. N-carbobenzyloxy-L-leucyl-L-leucyl-L-leucinal (MG132), a proteasome inhibitor, could completely block cevipabulin-induced tubulin degradation (Fig. 1E). All these proved that cevipabulin promotes tubulin degradation in a proteasome-dependent pathway.

Reference: Sci Adv. 2021 May 19;7(21):eabg4168. https://advances.sciencemag.org/content/7/21/eabg4168

In vivo activity

TTI-237 was tested for antitumor efficacy in two mouse xenograft models. In the first, the compound, which has excellent solubility in water, was formulated in 0.9% saline and given i.v. to athymic mice bearing staged tumors of LoVo human colon adenocarcinoma. The compound was given every 4 days for four cycles at doses of 5, 10, 15, and 20 mg/kg/dose. The compound showed dose-dependent effects, with good antitumor activity at 20 and 15 mg/kg (Fig. 6A). In the second model, U87-MG human glioblastoma, TTI-237 was given both i.v. and p.o. at a single dose of 25 mg/kg to tumor-bearing mice. The compound was about equally effective by the two routes (Fig. 6B).

Reference: Cancer Res. 2008 Apr 1;68(7):2292-300. https://cancerres.aacrjournals.org/content/68/7/2292.long

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.