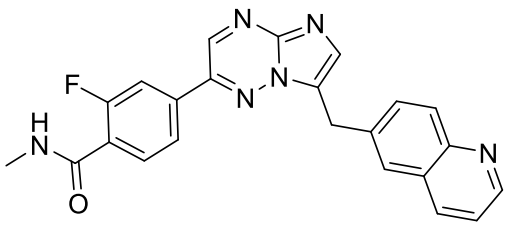
Product data sheet

MedKoo Cat#: 205494 Name: Capmatinib CAS#: 1029712-80-8 (free base) Chemical Formula: $C_{23}H_{17}FN_6O$ Exact Mass: 412.14479 Molecular Weight: 412.42	
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:
Capmatinib, also known as INCB28060 and INC280, is an orally bioavailable inhibitor of the proto-oncogene c-Met (hepatocyte growth factor receptor [HGFR]) with potential antineoplastic activity. c-Met inhibitor INC280 selectively binds to c-Met, thereby inhibiting c-Met phosphorylation and disrupting c-Met signal transduction pathways. This may induce cell death in tumor cells overexpressing c-Met protein or expressing constitutively activated c-Met protein. Capmatinib was approved in 2020.

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
DMF	1.0	2.42
DMF:PBS (pH 7.2) (1:3)	0.25	0.61
DMSO	9.1	22.06
Water	10.0	24.25

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.42 mL	12.12 mL	24.25 mL
5 mM	0.48 mL	2.42 mL	4.85 mL
10 mM	0.24 mL	1.21 mL	2.42 mL
50 mM	0.05 mL	0.24 mL	0.48 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. Brandes F, Schmidt K, Wagner C, Redekopf J, Schlitt HJ, Geissler EK, Lang SA. Targeting cMET with INC280 impairs tumour growth and improves efficacy of gemcitabine in a pancreatic cancer model. BMC Cancer. 2015 Feb 19;15:71. doi: 10.1186/s12885-015-1064-9. PMID: 25884642; PMCID: PMC4340491.

In vivo study

1. Bonan NF, Kowalski D, Kudlac K, Flaherty K, Gwilliam JC, Falkenberg LG, Maradiaga E, DeCicco-Skinner KL. Inhibition of HGF/MET signaling decreases overall tumor burden and blocks malignant conversion in Tpl2-related skin cancer. Oncogenesis. 2019 Jan 10;8(1):1. doi: 10.1038/s41389-018-0109-8. PMID: 30631034; PMCID: PMC6328619.

7. Bioactivity
Biological target:

ATP competitive c-Met kinase inhibitor (IC50=0.13 nM)

Product data sheet

In vitro activity

Pancreatic cancer is characterized by a strong stromal reaction. Therefore, the effects of cMET inhibition on ECs and VSMCs were examined. MTT assays in ECs under serum-starved conditions and stimulation with HGF, showed a slight but significant increase in growth that was diminished by INC280 (Capmatinib) (Additional file 3: Figure S3B). No effect upon constitutive conditions was observed (Additional file 3: Figure S3A). EC motility was significantly increased upon incubation with HGF, which was strongly reduced by INC280 (Figure 4A). Regarding activation of signaling pathways, treatment with INC280 strongly inhibited HGF-induced activation of Akt and ERK whereas no effects on constitutive Akt and ERK phosphorylation were found (Figure 4B). Taken together, these results show that INC280 affects ECs only when these cells are stimulated with HGF. Next we analyzed the impact of INC280 on VSMCs. MTT assays showed a dose-dependent inhibition of VSMC growth starting from INC280 (100nM) after 72 hours of incubation (Additional file 3: Figure S3C). In contrast to ECs, stimulation with HGF upon serum-starved conditions had no effect on VSMC growth and, accordingly, INC280 did not have a further growth inhibitory effect in MTT assays (Additional file 3: Figure S3D). Motility upon incubation with HGF in VSMCs was not induced, but targeting cMET with INC280 led to a significant inhibition of constitutive migration (Figure 4C). Finally, Western blotting did not show a substantial effect of INC280 on constitutive Akt phosphorylation and only a minor impact on ERK phosphorylation in VSMCs (Figure 4D). These results indicate that HGF does not affect VSMCs and cMET inhibition with INC280, therefore, has only minor effects on these cells.

Reference: BMC Cancer. 2015; 15: 71. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4340491/

In vivo activity

Tumors underwent a histological examination by a pathologist to determine phenotype and progression. Of the WT mice fed normal diet there were a total of 16 tumors. Twelve of the tumors were papillomas, with one converting to a squamous cell carcinoma (Fig.4d). Three additional tumors were cutaneous lipomas. This is in comparison to Tpl2 −/− mice which had a total of 61 tumors, 51 papillomas, four SCCs, three sebaceous adenomas, and three lipomas. In contrast, no Tpl2 −/− mice fed capmatinib diet had papillomas convert to SCCs (Fig. (Fig.4d).4d). Although Tpl2 −/− mice develop an overall higher tumor burder, there were no statistical differences in tumor size between genotypes and the rate of malignant conversion (7.8 vs. 8.3%) was similar between Tpl2 −/− and WT mice on normal diet. However, the rate of malignant conversion between Tpl2 −/− mice on normal diet (8.3%) vs. Tpl2 −/− mice on Capmatinib diet (0%) was significantly different ($p < 0.01$). In both genotypes male mice developed more tumors than female mice (Fig.4e; $p < 0.05$).

Reference: Oncogenesis. 2019 Jan; 8(1): 1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6328619/

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.