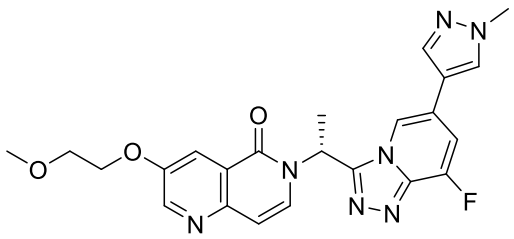
Product data sheet

MedKoo Cat#: 204320 Name: AMG-337 CAS#: 1173699-31-4 Chemical Formula: $C_{23}H_{22}FN_7O_3$ Exact Mass: 463.1768 Molecular Weight: 463.4734	
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:
AMG 337 is an orally bioavailable inhibitor of the proto-oncogene c-Met with potential antineoplastic activity. c-Met inhibitor AMG 337 selectively binds to c-Met, thereby 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.

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	50	107.88
Ethanol	50	107.88

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.16 mL	10.79 mL	21.58 mL
5 mM	0.43 mL	2.16 mL	4.32 mL
10 mM	0.22 mL	1.08 mL	2.16 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. Hughes PE, Rex K, Caenepeel S, Yang Y, Zhang Y, Broome MA, Kha HT, Burgess TL, Amore B, Kaplan-Lefko PJ, Moriguchi J, Werner J, Damore MA, Baker D, Choquette DM, Harmange JC, Radinsky R, Kendall R, Dussault I, Coxon A. In Vitro and In Vivo Activity of AMG 337, a Potent and Selective MET Kinase Inhibitor, in MET-Dependent Cancer Models. Mol Cancer Ther. 2016 Jul;15(7):1568-79. doi: 10.1158/1535-7163.MCT-15-0871. Epub 2016 Apr 19. PMID: 27196782.

2. Du Z, Caenepeel S, Shen Y, Rex K, Zhang Y, He Y, Tang ET, Wang O, Zhong W, Zhou H, Huang J, Huang E, Hu L, Coxon A, Zhang M. Preclinical Evaluation of AMG 337, a Highly Selective Small Molecule MET Inhibitor, in Hepatocellular Carcinoma. Mol Cancer Ther. 2016 Jun;15(6):1227-37. doi: 10.1158/1535-7163.MCT-15-0745. Epub 2016 Mar 29. PMID: 27196749.

In vivo study

1. Du Z, Caenepeel S, Shen Y, Rex K, Zhang Y, He Y, Tang ET, Wang O, Zhong W, Zhou H, Huang J, Huang E, Hu L, Coxon A, Zhang M. Preclinical Evaluation of AMG 337, a Highly Selective Small Molecule MET Inhibitor, in Hepatocellular Carcinoma. Mol Cancer Ther. 2016 Jun;15(6):1227-37. doi: 10.1158/1535-7163.MCT-15-0745. Epub 2016 Mar 29. PMID: 27196749.

2. Hughes PE, Rex K, Caenepeel S, Yang Y, Zhang Y, Broome MA, Kha HT, Burgess TL, Amore B, Kaplan-Lefko PJ, Moriguchi J, Werner J, Damore MA, Baker D, Choquette DM, Harmange JC, Radinsky R, Kendall R, Dussault I, Coxon A. In Vitro and In Vivo Activity of AMG 337, a Potent and Selective MET Kinase Inhibitor, in MET-Dependent Cancer Models. Mol Cancer Ther. 2016 Jul;15(7):1568-79. doi: 10.1158/1535-7163.MCT-15-0871. Epub 2016 Apr 19. PMID: 27196782.

7. Bioactivity

Biological target:

AMG-337 is a potent and highly selective small molecule ATP-competitive MET kinase inhibitor with an IC50 of < 5nM in enzymatic assays.

In vitro activity

The effect of AMG 337 on cell proliferation was examined in a panel of 22 cancer cell lines that were reported to have elevated MET gene copy number, only 2 of which, SNU-5 and Hs746T, overlapped with the larger 260 cell line panel profiled with Compound 5 (Supplementary Table S2; ref. 27). Growth conditions for each cell line were optimized and cell viability was assessed following 72 hours of treatment with AMG 337. In addition, array CGH analysis was performed to quantify and confirm MET gene copy number, and cell lysates were generated to measure levels of total and phosphorylated MET protein. Nine cell lines exhibited sensitivity to AMG 337, (IC50 < 50 nmol/L; Fig. 1B and C), whereas the remaining cell lines were insensitive (IC50 > 3 μmol/L). A strong correlation was observed between high-level focal amplification of MET [aCGH log2 ratio of >2.5 (copy number >12), amplicon size <q-arm chromosome 7] and sensitivity to AMG 337, with seven of eight focally amplified cell lines demonstrating sensitivity to AMG 337 (Fig. 1C). The lack of sensitivity to AMG 337 in the remaining focally amplified cell line, NCI-H1573 (Fig. 1D), was presumably driven by a downstream activating mutation in KRAS (G12A) that promoted MAPK and PI3K signaling in the presence of MET inhibition (Supplementary Fig. S3).

Reference: Mol Cancer Ther. 2016 Jul;15(7):1568-79. http://mct.aacrjournals.org/cgi/pmidlookup?view=long&pmid=27196782

In vivo activity

Daily oral administration was used to evaluate the in vivo antitumor activity of AMG 337 in two patient-derived xenograft (PDX) models of hepatocellular carcinoma (LI0612 and LI1078). AMG 337 exerted potent antiproliferative activity against 2 of 40 hepatocellular carcinoma cell lines, namely, MHCC97H (IC50, 0.015 μmol/L) and HCCLM3 (IC50, 0.025 μmol/L). Both sensitive cell lines showed MET amplification (MET/CEN-7 >2.0) assessed by FISH, and high MET expression (3+ IHC) assessed by IHC. AMG 337 potently inhibited p-MET in all cell lines with detectable levels of total MET. However, the dose-dependent inhibition of downstream effectors of HGF/MET signaling, including p-GAB1, p-AKT, and p-ERK, was limited to those cell lines sensitive to AMG 337 in a viability assay (MHCC97H and HCCLM3). AMG 337 significantly inhibited tumor growth at all doses tested in the MET-amplified and MET-high-expressing hepatocellular carcinoma PDX model LI0612 and had no effect on tumor growth in the non-MET-amplified and MET-low-expressing hepatocellular carcinoma PDX model LI1078.

Reference: Mol Cancer Ther. 2016 Jun;15(6):1227-37. http://mct.aacrjournals.org/cgi/pmidlookup?view=long&pmid=27196749

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.