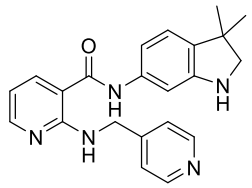
Product data sheet

MedKoo Cat#: 201934 Name: Motesanib CAS#: 453562-69-1 (free base) Chemical Formula: $C_{22}H_{23}N_5O$ Exact Mass: 373.1902 Molecular Weight: 373.46	
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:

Motesanib, also known as AMG-706, is the orally bioavailable multiple-receptor tyrosine kinase inhibitor with potential antineoplastic activity. Motesanib selectively targets and inhibits vascular endothelial growth factor (VEGFR), platelet-derived growth factor (PDGFR), kit, and Ret receptors, thereby inhibiting angiogenesis and cellular proliferation.

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	87.5	234.30
Ethanol	8.0	21.42

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.68 mL	13.39 mL	26.78 mL
5 mM	0.54 mL	2.68 mL	5.36 mL
10 mM	0.27 mL	1.34 mL	2.68 mL
50 mM	0.05 mL	0.27 mL	0.54 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. Wang YJ, Kathawala RJ, Zhang YK, Patel A, Kumar P, Shukla S, Fung KL, Ambudkar SV, Talele TT, Chen ZS. Motesanib (AMG706), a potent multikinase inhibitor, antagonizes multidrug resistance by inhibiting the efflux activity of the ABCB1. Biochem Pharmacol. 2014 Aug 15;90(4):367-78. doi: 10.1016/j.bcp.2014.06.006. Epub 2014 Jun 14. PMID: 24937702; PMCID: PMC4133117.
2. Caenepeel S, Renshaw-Gegg L, Baher A, Bush TL, Baron W, Juan T, Manoukian R, Tasker AS, Polverino A, Hughes PE. Motesanib inhibits Kit mutations associated with gastrointestinal stromal tumors. J Exp Clin Cancer Res. 2010 Jul 15;29(1):96. doi: 10.1186/1756-9966-29-96. PMID: 20633291; PMCID: PMC2912835.

In vivo study

1. Yamauchi F, Kamioka Y, Yano T, Matsuda M. In Vivo FRET Imaging of Tumor Endothelial Cells Highlights a Role of Low PKA Activity in Vascular Hyperpermeability. Cancer Res. 2016 Sep 15;76(18):5266-76. doi: 10.1158/0008-5472.CAN-15-3534. Epub 2016 Aug 3. PMID: 27488524.
2. Rho CR, Kang S, Park KC, Yang KJ, Choi H, Cho WK. Antiangiogenic effects of topically administered multiple kinase inhibitor, motesanib (AMG 706), on experimental choroidal neovascularization in mice. J Ocul Pharmacol Ther. 2015 Feb;31(1):25-31. doi: 10.1089/jop.2014.0023. PMID: 25255037; PMCID: PMC4286588.

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7. Bioactivity

Biological target:

Motesanib is a ATP-competitive inhibitor of VEGFR1/2/3 with IC50s of 2 nM/3 nM/6 nM, respectively.

In vitro activity

One of the major findings of this study was that motesanib significantly increased the sensitivity of ABCB1 overexpressing KB-C2 drug selected cell line to paclitaxel, colchicine and vincristine, which are substrates of ABCB1 transporter. The motesanib-induced enhancement in the sensitivity of KB-C2 cells to the substrates was represented by a significant decrease in the IC50 values for the aforementioned substrates in the presence of motesanib in the MTT assay, a measurement of cell survival (Table 1). The motesanib-induced potentiation was selective because at the concentrations used in this study (1 μM and 3 μM), motesanib (1) did not produce a significant toxic effect on the parental KB-3-1 cell (non-overexpressing) and (2) failed to potentiate the effect of the substrate drugs on the parental KB-3-1 cells.

Reference: Biochem Pharmacol. 2014 Aug 15; 90(4): 367–378. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4133117/

In vivo activity

Mice were injected intravenously with Evans blue dye and Motesanib (50 mg/kg) and subjected to the Miles assay. Motesanib reduced the extravasation of Evans blue in the tumor, but not the skin, indicating that Motesanib inhibited tumor vascular permeability (Fig. 6A). This finding is consistent with previous studies that demonstrated an inhibition of VEGF-induced vascular permeability by Motesanib administration. By immunohistochemistry, this study confirmed that Motesanib suppressed the VEGFR2 tyrosine kinase activity, but not the expression of VEGFR2 (Supplementary Fig. S3). This study next examined the response of endothelial PKA activity to Motesanib by in vivo FRET imaging. Motesanib robustly activated PKA in the endothelial cells of the tumors, but not in the endothelial cells of the subcutaneous tissues (Fig. 6B), indicating that VEGFR played a major role in the suppression of PKA. Notably, Motesanib had no effect on the ERK activities in tumor and normal endothelial cells (Fig. 6C). The lack of effect on ERK activity is probably due to the low basal ERK activity. In fact, when ERK activity in tumor endothelial cells was elevated by VEGF, Motesanib markedly decreased ERK activity (Supplementary Fig. S4A–S4C).

Reference: Cancer Res. 2016 Sep 15;76(18):5266-76. https://cancerres.aacrjournals.org/content/76/18/5266.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.