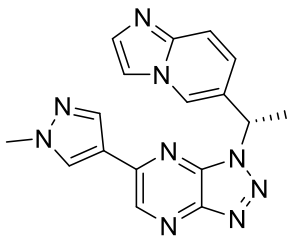
Product data sheet

MedKoo Cat#: 206080 Name: Savolitinib CAS#: 1313725-88-0 Chemical Formula: $C_{17}H_{15}N_9$ Exact Mass: 345.14504 Molecular Weight: 345.36	
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:

Savolitinib, also known as Volitinib, AZD6094 or HMPL-504, is an orally bioavailable inhibitor of the c-Met receptor tyrosine kinase with potential antineoplastic activity. Volitinib selectively binds to and inhibits the activation of c-Met in an ATP-competitive manner, and disrupts c-Met signal transduction pathways. This may result in cell growth inhibition in tumors that overexpress the 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	25.0	72.4

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.90 mL	14.48 mL	28.96 mL
5 mM	0.58 mL	2.90 mL	5.79 mL
10 mM	0.29 mL	1.45 mL	2.90 mL
50 mM	0.06 mL	0.29 mL	0.58 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. Jia H, Dai G, Weng J, Zhang Z, Wang Q, Zhou F, Jiao L, Cui Y, Ren Y, Fan S, Zhou J, Qing W, Gu Y, Wang J, Sai Y, Su W. Discovery of (S)-1-(1-(Imidazo[1,2-a]pyridin-6-yl)ethyl)-6-(1-methyl-1H-pyrazol-4-yl)-1H-[1,2,3]triazolo[4,5-b]pyrazine (volitinib) as a highly potent and selective mesenchymal-epithelial transition factor (c-Met) inhibitor in clinical development for treatment of cancer. J Med Chem. 2014 Sep 25;57(18):7577-89. doi: 10.1021/jm500510f. Epub 2014 Sep 15. PMID: 25148209.

In vivo study

1. Hosonuma M, Sakai N, Furuya H, Kurotaki Y, Sato Y, Handa K, Dodo Y, Ishikawa K, Tsubokura Y, Negishi-Koga T, Tsuji M, Kasama T, Kiuchi Y, Takami M, Isozaki T. Inhibition of hepatocyte growth factor/c-Met signalling abrogates joint destruction by suppressing monocyte migration in rheumatoid arthritis. Rheumatology (Oxford). 2021 Jan 5;60(1):408-419. doi: 10.1093/rheumatology/keaa310. PMID: 32770199.
2. Schuller AG, Barry ER, Jones RD, Henry RE, Frigault MM, Beran G, Linsenmayer D, Hattersley M, Smith A, Wilson J, Cairo S, Déas O, Nicolle D, Adam A, Zinda M, Reimer C, Fawell SE, Clark EA, D'Cruz CM. The MET Inhibitor AZD6094 (Savolitinib, HMPL-504) Induces Regression in Papillary Renal Cell Carcinoma Patient-Derived Xenograft Models. Clin Cancer Res. 2015 Jun 15;21(12):2811-9. doi: 10.1158/1078-0432.CCR-14-2685. Epub 2015 Mar 16. PMID: 25779944.

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7. Bioactivity

Biological target:

Savolitinib (AZD-6094) is a c-Met inhibitor with IC50s of 5 nM and 3 nM for c-Met and p-Met, respectively.

In vitro activity

As shown in Table 5, after introduction of a methyl, enantiomerically pure compounds 28 (Savolitinib)–31 demonstrated good inhibition of c-Met activity. Compared with unbranched compounds 16 and 23C, compounds 28 and 30, respectively, had equal activities against c-Met kinase and slightly better potency in cellular assays. More significantly, their abilities to inhibit HGF-induced proliferation were improved. Especially compound 28 inhibited proliferation 12-fold more potently than compound 16.

Reference: J Med Chem. 2014 Sep 25;57(18):7577-89. https://pubmed.ncbi.nlm.nih.gov/25148209/

In vivo activity

AZD6094 dosed at 0.5, 2.5, 10, and 25 mg/kg daily induced dose dependent antitumor activity in RCC-47 resulting in approximately 63% TGI, ~89% TGI, ~64% regression, and ~96% regression, respectively (Fig. 3B). RCC-47 is a fast growing model, with animals in the vehicle group requiring sacrifice as early as 10 days after initiation of treatment. Tumors grew back in 9 of 10 mice within 3 weeks after treatment was stopped; one mouse remained tumor free for 3 months (final measurement, results not shown). In RCC-43b, AZD6094 again showed a dose-dependent antitumor activity ranging from approximately 85% TGI when dosed at 2.5 mg/kg daily, stasis when dosed 10 mg/kg daily, and approximately 20% regression when dosed at 25 mg/kg daily.

Reference: Clin Cancer Res. 2015 Jun 15;21(12):2811-9. https://clincancerres.aacrjournals.org/content/21/12/2811.long