# Data Sheet

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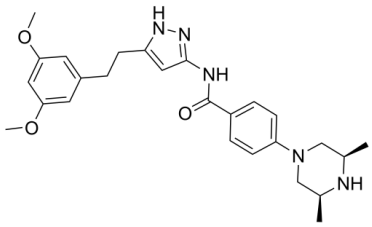
| **Product Name:** | Fexagratinib |
| **Cat. No.:** | CS-0971 |
| **CAS No.:** | 1035270-39-3 |
| **Molecular Formula:** | $C_{26}H_{33}N_5O_3$ |
| **Molecular Weight:** | 463.57 |
| **Target:** | FGFR |
| **Pathway:** | Protein Tyrosine Kinase/RTK |
| **Solubility:** | DMSO : 125 mg/mL (ultrasonic) |



## BIOLOGICAL ACTIVITY:

Fexagratinib (ADSK091) is a potent inhibitor of the **FGFR** family with **$IC_{50}$**s of 0.2 nM, 2.5 nM, 1.8 nM, and 165 nM for **FGFR1**, **FGFR2**, **FGFR3**, and **FGFR4**, respectively. IC50 & Target:IC50: 0.2 nM (FGFR1), 2.5 nM (FGFR2), 1.8 nM (FGFR3), 165 nM (FGFR4)[1] ***In Vitro:*** Fexagratinib also inhibits recombinant VEGFR2 (KDR) kinase activity with an $IC_{50}$ of 24 nM. In KG1a, Sum52-PE, MCF7, and KMS11 cell lines, Fexagratinib potently inhibits autophosphorylation of FGFR1, 2, and 3 tyrosine kinases ($IC_{50}$ values of 12, 2, and 40 nM, respectively) and displays weaker inhibition of FGFR4 cellular kinase activity ($IC_{50}$=142 nM). Significantly weaker inhibitory activity is observed versus cellular KDR and IGFR ligand-induced phosphorylation ($IC_{50}$ values of 258 and 828 nM, respectively), representing approximately 20- and 70-fold selectivity over cellular FGFR1. Besides, Fexagratinib potently inhibits FGFR phosphorylation and downstream signaling affected through FRS2, PLCγ, and MAPK at the cellular level[1]. ***In Vivo:*** Female SCID mice bearing KMS11 tumors are randomized and treated chronically with Fexagratinib at a range of well-tolerated doses. Oral Fexagratinib treatment results in dose-dependent tumor growth inhibition. Twice daily administration of Fexagratinib at 3 mg/kg gives statistically significant tumor growth inhibition of 53% (P<0.0005 by one-tailed t test) when compare with vehicle-treated controls, whereas doses of 12.5 mg/kg once daily and 6.25 mg/kg twice daily results in complete tumor stasis (P<0.0001). A further efficacy study in the KG1a model with 12.5 mg/kg once daily Fexagratinib results in 65% tumor growth inhibition (P=0.002)[1].

## PROTOCOL (Extracted from published papers and Only for reference)

**Cell Assay:** AZD4547 is prepared as a 10 mM stock solution, and then diluted in the relevant assay media before use[1].[1]Cell lines are incubated with fixed concentrations of AZD4547 for 72 hours. For fluorescence-activated cell sorting (FACS), cells are fixed with 70% ethanol and then incubated with propidium iodide/RNase A labeling solution. Cell-cycle profiles are assessed with a FACSCalibur instrument and CellQuest analysis software. For apoptotic analysis, cells and media are gently harvested and centrifuged, followed by washing of cell pellets. Cells are then processed for FITC staining and propidium iodide uptake. The proportion of cells staining positive for Annexin V are then assessed with a FACSCalibur instrument and quadrant sorting is done by CellQuest analysis software[1]. **Animal Administration:** [1]Mice[1]
Swiss derived nude (nu/nu) and severe combined immunodeficient mice (SCID) are used. Tumor xenografts are established by s.c. injection into the left flank with 0.1 mL tumor cells ($1\times10^6$ for LoVo, $1\times10^7$ for HCT-15, and $1\times10^7$ for Calu-6) or 0.2 mL ($2\times10^7$ for KMS11 and KG1a) mixed 1:1 with Matrigel, with the exception of LoVo and HCT-15, which do not include Matrigel. Mice are randomized into control and treatment groups (AZD4547, 1.5-50 mg/kg, once daily or twice daily by oral gavage) when tumors reach the determined size of more than 0.2 $cm^3$. Tumor volume (measured by caliper), animal body weight, and tumor condition are recorded twice weekly for the duration of the study. Tumor volume is calculated.

## References:

[1]. Gavine PR, et al. AZD4547: an orally bioavailable, potent, and selective inhibitor of the fibroblast growth factor receptor tyrosine kinase family. Cancer Res, 2012, 72(8), 2045-2056.

## CAIndexNames:

Benzamide, N-[5-[2-(3,5-dimethoxyphenyl)ethyl]-1H-pyrazol-3-yl]-4-[(3R,5S)-3,5-dimethyl-1-piperazinyl]-, rel-

## SMILES:

C[C@H](C1)N[C@@H](C)CN1C2=CC=C(C(NC3=NNC(CCC4=CC(OC)=CC(OC)=C4)=C3)=O)C=C2



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