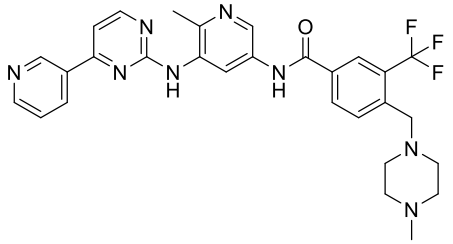
Product data sheet

MedKoo Cat#: 206184 Name: Flumatinib free base CAS#: 895519-90-1 (free base) Chemical Formula: $C_{29}H_{29}F_3N_8O$ Exact Mass: 562.24164 Molecular Weight: 562.59	
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:

Flumatinib, also known as HHGV678 , is a selective inhibitor of BCR-ABL/PDGFR/KIT. Flumatinib is currently in Phase I and II clinical trials in China for the treatment of chronic myelogenous leukemia (CML). Flumatinib effectively overcomes drug resistance of certain KIT mutants. Flumatinib mesylate can reduce the expression of C-MYC, HIF-1 α and VEGF in U266 cell line in a time- and dose-dependent manners.

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	100.0	177.75

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	1.78 mL	8.89 mL	17.77 mL
5 mM	0.36 mL	1.78 mL	3.55 mL
10 mM	0.18 mL	0.89 mL	1.78 mL
50 mM	0.04 mL	0.18 mL	0.36 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. Zhao J, Quan H, Xu Y, Kong X, Jin L, Lou L. Flumatinib, a selective inhibitor of BCR-ABL/PDGFR/KIT, effectively overcomes drug resistance of certain KIT mutants. Cancer Sci. 2014 Jan;105(1):117-25. doi: 10.1111/cas.12320. Epub 2014 Jan 4. PMID: 24205792; PMCID: PMC4317885.

In vivo study

1. Zhao J, Quan H, Xu Y, Kong X, Jin L, Lou L. Flumatinib, a selective inhibitor of BCR-ABL/PDGFR/KIT, effectively overcomes drug resistance of certain KIT mutants. Cancer Sci. 2014 Jan;105(1):117-25. doi: 10.1111/cas.12320. Epub 2014 Jan 4. PMID: 24205792; PMCID: PMC4317885.

7. Bioactivity

Biological target:

Flumatinib (HHGV678) is an orally available, selective inhibitor of Bcr-Abl. Flumatinib inhibits c-Abl, PDGFRβ and c-Kit with IC50s of 1.2 nM, 307.6 nM and 665.5 nM, respectively.

In vitro activity

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In 32D-V559D + Y823D cells, the phosphorylation levels of KIT, ERK1/2, and STAT3 were strongly inhibited by flumatinib, but not imatinib or sunitinib (Fig. 2). Similar findings were observed in 32D-V559D + N822K and 32D-V559D + A829P cells (Fig. S1). These results collectively show that flumatinib is capable of overcoming the imatinib and sunitinib resistance conferred by certain secondary activation loop mutations in vitro.

Reference: Cancer Sci. 2014 Jan; 105(1): 117–125. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4317885/

In vivo activity

In contrast, treatments with imatinib (150 mg/kg, b.i.d.) and flumatinib (75 mg/kg, q.d. and b.i.d.) extended the median survival to 23.5 ($P = 0.23$), 25.5 ($P = 0.061$), and 25.5 ($P < 0.05$) days, relative to the vehicle-treated group, respectively (Fig. 3). In addition, the survival of mice treated with flumatinib (75 mg/kg, b.i.d.) was significantly improved compared with mice treated with imatinib (150 mg/kg, q.d.; $P < 0.01$) or sunitinib (50 mg/kg, q.d.; $P < 0.01$).

Reference: Cancer Sci. 2014 Jan; 105(1): 117–125. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4317885/