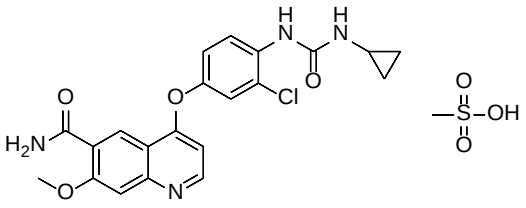
Product data sheet

MedKoo Cat#: 201080 Name: Lenvatinib mesylate CAS#: 857890-39-2 (mesylate) Chemical Formula: $C_{22}H_{23}ClN_4O_7S$ Molecular Weight: 522.96	
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:
Lenvatinib, also known as E7080, is a synthetic, orally available inhibitor of vascular endothelial growth factor receptor 2 (VEGFR2, also known as KDR/FLK-1) tyrosine kinase with potential antineoplastic activity. E7080 blocks VEGFR2 activation by VEGF, resulting in inhibition of the VEGF receptor signal transduction pathway, decreased vascular endothelial cell migration and proliferation, and vascular endothelial cell apoptosis.

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	5.78	11.05
DMSO:PBS (pH 7.2) (1:5)	0.16	0.31

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	1.91 mL	9.56 mL	19.12 mL
5 mM	0.38 mL	1.91 mL	3.82 mL
10 mM	0.19 mL	0.96 mL	1.91 mL
50 mM	0.04 mL	0.19 mL	0.38 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. Ogasawara S, Mihara Y, Kondo R, Kusano H, Akiba J, Yano H. Antiproliferative Effect of Lenvatinib on Human Liver Cancer Cell Lines In Vitro and In Vivo. Anticancer Res. 2019 Nov;39(11):5973-5982. doi: 10.21873/anticanres.13802. PMID: 31704822.
2. Matsuki M, Hoshi T, Yamamoto Y, Ikemori-Kawada M, Minoshima Y, Funahashi Y, Matsui J. Lenvatinib inhibits angiogenesis and tumor fibroblast growth factor signaling pathways in human hepatocellular carcinoma models. Cancer Med. 2018 Jun;7(6):2641-2653. doi: 10.1002/cam4.1517. Epub 2018 May 7. PMID: 29733511; PMCID: PMC6010799.

In vivo study

1. Ogasawara S, Mihara Y, Kondo R, Kusano H, Akiba J, Yano H. Antiproliferative Effect of Lenvatinib on Human Liver Cancer Cell Lines In Vitro and In Vivo. Anticancer Res. 2019 Nov;39(11):5973-5982. doi: 10.21873/anticanres.13802. PMID: 31704822.
2. Matsuki M, Hoshi T, Yamamoto Y, Ikemori-Kawada M, Minoshima Y, Funahashi Y, Matsui J. Lenvatinib inhibits angiogenesis and tumor fibroblast growth factor signaling pathways in human hepatocellular carcinoma models. Cancer Med. 2018 Jun;7(6):2641-2653. doi: 10.1002/cam4.1517. Epub 2018 May 7. PMID: 29733511; PMCID: PMC6010799.

7. Bioactivity

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Biological target: Lenvatinib mesylate (E7080 mesylate) is a tyrosine kinase inhibitor that inhibits VEGFR1-3, FGFR1-4, PDGFR, KIT, and RET.

In vitro activity

The antiproliferative activity of lenvatinib against nine HCC cell lines was examined in vitro. Lenvatinib showed selective and potent antiproliferative activity against the HCC cell lines Hep3B2.1 - 7, HuH - 7, and JHH - 7, with IC50 values of 0.23, 0.42, and 0.64 μ mol/L, respectively (Fig. 1A and B). Immunoblotting analysis showed that FGF19, FGFR4, and β - Klotho were highly expressed in these three cell lines, indicating that the FGF19 – FGFR4 axis was activated (Fig. 1C), consistent with previous reports. Lenvatinib also showed moderate inhibitory effects on the proliferation of SNU - 398, Li - 7, and HuH - 1 cells, with IC50 values of 1.56, 1.65, and 2.59 μ mol/L, respectively (Fig. 1A and B). Although FGF19 protein was not expressed, some members of the FGFR family were detected in these cells (Fig. 1C). Because these cell lines are modestly sensitive to pan - FGFR inhibitors such as BGJ398, lenvatinib might inhibit proliferation of the cells by targeting an activated FGF signaling pathway. Lenvatinib did not show clear antiproliferative activity against SK - HEP - 1, SNU - 449, or PLC/PRF/5 cells (IC50 >5 μ mol/L; Fig. 1A and B), which were also insensitive to pan - FGFR inhibitors.

Reference: Cancer Med. 2018 Jun;7(6):2641-2653. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6010799/

In vivo activity

The in vivo antitumor activity of lenvatinib against HCC (human hepatocellular carcinoma) xenografts with activated FGF signaling pathways in the Hep3B2.1 - 7 and SNU - 398 models was evaluated. In vivo growth of xenograft tumors was significantly inhibited by lenvatinib at doses of 3 – 30 mg/kg in the Hep3B2.1 - 7 model and 10, 30 mg/kg in the SNU - 398 model (Fig. 3A). BWL (body weight loss) of the treatment group was similar to that of the corresponding vehicle control group, although cachexia - induced BWL was observed in each control group (Fig. S5). To examine whether lenvatinib inhibited FGF signaling pathways within the Hep3B2.1 - 7 and SNU - 398 xenograft tumors, tumor samples were collected 2 h after a single lenvatinib treatment, and phosphorylation levels of FRS2 and another downstream molecule of FGFR, Erk1/2, were evaluated. Lenvatinib at 10 and 30 mg/kg inhibited phosphorylation of FRS2 and Erk1/2 in the Hep3B2.1 - 7 model (Fig. 3C); lenvatinib at 3 – 30 mg/kg inhibited FRS2 phosphorylation in the SNU - 398 model (Fig. 3E); and lenvatinib at 30 mg/kg inhibited Erk1/2 phosphorylation in the SNU - 398 model (Fig. 3E). These results suggest that targeting FGFR of HCC cells underlies the antitumor activity of lenvatinib in preclinical HCC models with activated FGF signaling pathways.

Reference: Cancer Med. 2018 Jun;7(6):2641-2653. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6010799/