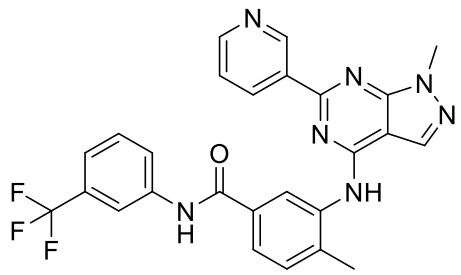
Product data sheet

MedKoo Cat#: 406172 Name: NVP-BHG712 CAS: 940310-85-0 Chemical Formula: $C_{26}H_{20}F_3N_7O$ Exact Mass: 503.1681 Molecular Weight: 503.4892	
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:
NVP-BHG712, also known as BHG-712, is a EphB4 kinase inhibitor and BCR-ABL inhibitor. NVP-BHG712 inhibits EphB4 kinase activity in the low nanomolar range in cellular assays showed high selectivity for targeting the EphB4 kinase when profiled against other kinases in biochemical as well as in cell based assays. BHG-712 shows excellent pharmacokinetic properties and potently inhibits EphB4 autophosphorylation in tissues after oral administration.

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
DMF	20.0	39.72
DMSO	50.75	100.80
DMSO:PBS (pH 7.2) (1:2)	0.33	0.66
Ethanol	2.5	4.97

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	1.99 mL	9.93 mL	19.86 mL
5 mM	0.40 mL	1.99 mL	3.97 mL
10 mM	0.20 mL	0.99 mL	1.99 mL
50 mM	0.04 mL	0.20 mL	0.40 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. Zhang Y, Yang C, Ge S, Wang L, Zhang J, Yang P. EphB4/ TNFR2/ERK/MAPK signaling pathway comprises a signaling axis to mediate the positive effect of TNF-α on osteogenic differentiation. BMC Mol Cell Biol. 2020 Apr 16;21(1):29. doi: 10.1186/s12860-020-00273-2. PMID: 32299362; PMCID: PMC7164363.
2. Rudzitis-Auth J, Fuß SA, Becker V, Menger MD, Laschke MW. Inhibition of erythropoietin-producing hepatoma receptor B4 (EphB4) signalling suppresses the vascularisation and growth of endometriotic lesions. Br J Pharmacol. 2020 Jul;177(14):3225-3239. doi: 10.1111/bph.15044. Epub 2020 Apr 12. PMID: 32144768; PMCID: PMC7312277.

In vivo study

1. Li L, Nan F, Guo Q, Guan D, Zhou C. Resistance to bevacizumab in ovarian cancer SKOV3 xenograft due to EphB4 overexpression. J Cancer Res Ther. 2019 Oct-Dec;15(6):1282-1287. doi: 10.4103/0973-1482.204896. PMID: 31898661.

Product data sheet

2. Martiny-Baron G, Holzer P, Billy E, Schnell C, Brueggen J, Ferretti M, Schmiedeberg N, Wood JM, Furet P, Imbach P. The small molecule specific EphB4 kinase inhibitor NVP-BHG712 inhibits VEGF driven angiogenesis. Angiogenesis. 2010 Sep;13(3):259-67. doi: 10.1007/s10456-010-9183-z. Epub 2010 Aug 29. PMID: 20803239; PMCID: PMC2941628.

7. Bioactivity

Biological target:

NVP-BHG712 is an oral active EphB4 kinase autophosphorylation inhibitor.

In vitro activity

Cells were then incubated in osteogenic induction medium supplemented with 200 nM NVP-BHG712 and/or 0.5 ng/ml TNF-α. MC3T3-E1 cells cultured in osteogenic induction medium served as controls. Seven days or 14 days after the treatment, this study found that NVP-BHG712 treatment significantly down-regulated TNF-α-stimulated ALP activity in MC3T3-E1 cells (Fig. 5a). Interestingly, 0.5 ng/ml TNF-α-stimulated TNFR2 expression was also partly reversed when EphB4 forward signaling was inhibited by NVP-BHG712 treatment (Figs. 5b-e), signifying that TNF-α-enhanced EphB4 signaling up-regulates TNFR2 expression.

Reference: BMC Mol Cell Biol. 2020 Apr 16;21(1):29. https://pubmed.ncbi.nlm.nih.gov/32299362/

In vivo activity

This study used ovarian xenograft mouse model to evaluate the underlying resistance mechanisms of BV (bevacizumab) in ovarian cancer treatment. The results showed that EphB4 was overexpressed in BV-resistant xenograft models instead of other common receptor tyrosine kinases. In addition, when coadministrated with EphB4 blocker NVP-BHG712, the antitumor effect of BV was significantly enhanced in the resistant model, further confirmed the role of EphB4 in BV-resistant ovarian cancer. These results indicate that NVP-BHG712 reverses EphB4 overexpression-mediated resistance to BV.

Reference: J Cancer Res Ther. 2019 Oct-Dec;15(6):1282-1287. https://pubmed.ncbi.nlm.nih.gov/31898661/