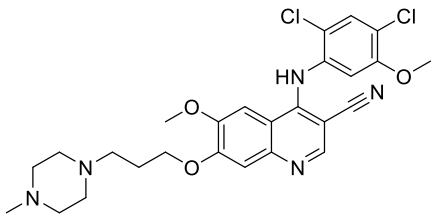
Product data sheet

MedKoo Cat#: 200560 Name: Bosutinib CAS#: 380843-75-4 Chemical Formula: $C_{26}H_{29}Cl_2N_5O_3$ Exact Mass: 529.16475 Molecular Weight: 530.44	
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:

Bosutinib, also known as SKI-606, is a synthetic quinolone derivative and dual kinase inhibitor that targets both Abl and Src kinases with potential antineoplastic activity. Unlike imatinib, bosutinib inhibits the autophosphorylation of both Abl and Src kinases, resulting in inhibition of cell growth and apoptosis. Because of the dual mechanism of action, this agent may have activity in resistant CML disease, other myeloid malignancies and solid tumors. Abl kinase is upregulated in the presence of the abnormal Bcr-abl fusion protein which is commonly associated with chronic myeloid leukemia (CML). Overexpression of specific Src kinases is also associated with the imatinib-resistant CML phenotype. Bosutinib received US FDA and EU European Medicines Agency approval on September 4, 2012 and 27 March, 2013 respectively for the treatment of adult patients with Philadelphia chromosome-positive (Ph+) chronic myelogenous leukemia (CML) with resistance, or intolerance to prior therapy.

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	54.76	103.24
Ethanol	14.09	26.56

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.89 mL	9.43 mL	18.85 mL
5 mM	0.38 mL	1.89 mL	3.77 mL
10 mM	0.19 mL	0.94 mL	1.89 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, Yu L, Guo W, Liu L, Zhang G, Zhang F, Qu Y, Liu Y, Li H, Li H. Bosutinib Acts as a Tumor Inhibitor via Downregulating Src/NF-κB/Survivin Expression in HeLa Cells. Anat Rec (Hoboken). 2019 Dec;302(12):2193-2200. doi: 10.1002/ar.24269. Epub 2019 Oct 9. PMID: 31569304.

2. Segrelles C, Contreras D, Navarro EM, Gutiérrez-Muñoz C, García-Escudero R, Paramio JM, Lorz C. Bosutinib Inhibits EGFR Activation in Head and Neck Cancer. Int J Mol Sci. 2018 Jun 21;19(7):1824. doi: 10.3390/ijms19071824. PMID: 29933569; PMCID: PMC6073167.

In vivo study

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1. Kleinveld DJB, Botros L, Maas MAW, Kers J, Aman J, Hollmann MW, Juffermans NP. Bosutinib reduces endothelial permeability and organ failure in a rat polytrauma transfusion model. Br J Anaesth. 2021 May;126(5):958-966. doi: 10.1016/j.bja.2021.01.032. Epub 2021 Mar 6. PMID: 33685634.
2. Botros L, Pronk MCA, Juschten J, Liddle J, Morsing SKH, van Buul JD, Bates RH, Tuinman PR, van Bezu JSM, Huveneers S, Bogaard HJ, van Hinsbergh VWM, Hordijk PL, Aman J. Bosutinib prevents vascular leakage by reducing focal adhesion turnover and reinforcing junctional integrity. J Cell Sci. 2020 May 14;133(9):jcs240077. doi: 10.1242/jcs.240077. PMID: 32198280.

7. Bioactivity

Biological target:

Bosutinib is a dual Src/Abl inhibitor with IC50s of 1.2 nM and 1 nM, respectively.

In vitro activity

This study examined the effects of bosutinib on colony formation and migration of HeLa cells, and determined whether bosutinib could induce HeLa cells apoptosis. The results showed that bosutinib inhibited HeLa cells proliferation and migration. Bosutinib significantly changed cell morphology, which indicated bosutinib-induced cytotoxicity in HeLa cells. But, the cytotoxic effects of bosutinib on HeLa cells were attenuated in the presence of over-expressed survivin, which indicated that bosutinib suppressed the viability of HeLa cells in a survivin-dependent manner. In addition, bosutinib increased the rate of apoptosis, suggesting that Src inhibition may also play a role in the process of apoptosis in HeLa cells. The results of Western blot revealed decreased expression of phospho-Src, Src, phospho-NF-κBp65, and survivin. Moreover, phospho-NF-κBp65 and survivin, but not phospho-Src and Src were upregulated in the survivin over-expressed group, suggesting that phospho-NF-κBp65 and survivin may play a role in bosutinib-induced HeLa cells apoptosis.

Reference: Anat Rec (Hoboken). 2019 Dec;302(12):2193-2200. https://pubmed.ncbi.nlm.nih.gov/31569304/

In vivo activity

Bosutinib as adjunctive therapy to a balanced transfusion strategy was associated with reduced transfusion requirement, improved shock reversal, and reduced endothelial leakage with concomitant reduction in pulmonary oedema and lung injury when compared with a vehicle-treated control group. Bosutinib-treated rats also had less evidence of endothelial damage. Collectively, these data suggest that bosutinib can protect endothelial barrier integrity in traumatic bleeding, and can reduce transfusion requirements to restore circulation in a trauma model. IL-6 levels were lower in bosutinib-compared with vehicle-treated rats with traumatic injury. The immunomodulatory effects of bosutinib have been shown in mouse-derived macrophages, in which bosutinib reduced IL-6 production. Less endothelial damage might lead to a reduced inflammatory response as well. The bosutinib-treated group required less transfusion products (and hence less plasma and platelets) than the vehicle group, whereas coagulation parameters in the ROTEM assays did not differ. In addition to an effect on endothelial barrier function, bosutinib may also reduce endothelial-driven coagulopathy in this model. Further evaluation is necessary to pinpoint the effects of bosutinib on trauma-induced coagulopathy, including platelet function and coagulation factors.

Reference: Br J Anaesth. 2021 May;126(5):958-966. https://bjanaesthesia.org/article/S0007-0912(21)00090-8/fulltext