# Product data sheet

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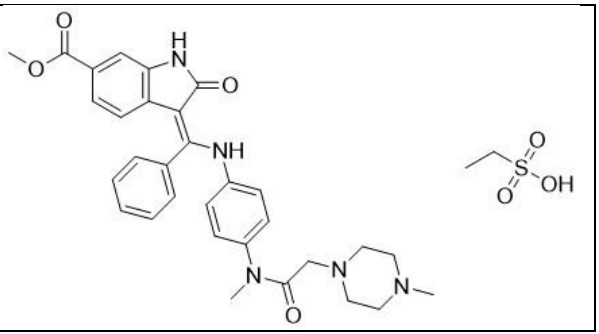
|---|---|
| MedKoo Cat#: 100944<br>Name: Nintedanib esylate<br>CAS#: 656247-18-6 (esylate)<br>Chemical Formula: $C_{33}H_{39}N_5O_7S$<br>Molecular Weight: 649.76 |  |
| Product supplied as: | Powder |
| Purity (by HPLC): | ≥ 98% |
| Shipping conditions | Ambient temperature |
| Storage conditions: | Powder: -20°C 3 years; 4°C 2 years. |
| | In solvent: -80°C 3 months; -20°C 2 weeks. |

**1. Product description:**

Nintedanib, also known as BIBF1120, is a potent inhibitor of multiple receptor tyrosine kinases (RTKs) and non-receptor tyrosine kinases (nRTKs). Nintedanib inhibits the following RTKs: platelet-derived growth factor receptor (PDGFR) α and β, fibroblast growth factor receptor (FGFR) 1-3, vascular endothelial growth factor receptor (VEGFR) 1-3, and Fms-like tyrosine kinase-3 (FLT3). Nintedanib binds competitively to the adenosine triphosphate (ATP) binding pocket of these receptors and blocks the intracellular signaling which is crucial for the proliferation, migration, and transformation of fibroblasts representing essential mechanisms of the IPF pathology. Nintedanib esylate was approved in 2014 for the treatment of idiopathic pulmonary fibrosis (IPF).

**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 | 66.0 | 101.6 |

**4. Stock solution preparation table:**

| Concentration / Solvent Volume / Mass | 1 mg | 5 mg | 10 mg |
|---|---|---|---|
| 1 mM | 1.54 | 7.70 | 15.39 |
| 5 mM | 0.31 | 1.54 | 3.08 |
| 10 mM | 0.15 | 0.77 | 1.54 |
| 50 mM | 0.03 | 0.15 | 0.31 |

**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. Patel P, Patel M. Enhanced oral bioavailability of nintedanib esylate with nanostructured lipid carriers by lymphatic targeting: In vitro, cell line and in vivo evaluation. Eur J Pharm Sci. 2021 Apr 1;159:105715. doi: 10.1016/j.ejps.2021.105715. Epub 2021 Jan 13. PMID: 33453388.

2.Tai WT, Shiau CW, Li YS, Chang CW, Huang JW, Hsueh TT, Yu HC, Chen KF. Nintedanib (BIBF-1120) inhibits hepatocellular carcinoma growth independent of angiokinase activity. J Hepatol. 2014 Jul;61(1):89-97. doi: 10.1016/j.jhep.2014.03.017. Epub 2014 Mar 18. PMID: 24657398.

In vivo study

1. Patel P, Patel M. Enhanced oral bioavailability of nintedanib esylate with nanostructured lipid carriers by lymphatic targeting: In vitro, cell line and in vivo evaluation. Eur J Pharm Sci. 2021 Apr 1;159:105715. doi: 10.1016/j.ejps.2021.105715. Epub 2021 Jan 13. PMID: 33453388.

2. . Xue C, Tian Y, Zhang J, Zhao Y, Zhan J, Fang W, Zhang L. Efficacy of BIBF 1120 or BIBF 1120 plus chemotherapy on nasopharyngeal carcinoma in vitro and in vivo. Drug Des Devel Ther. 2016 Mar 15;10:1173-80. doi: 10.2147/DDDT.S96634. PMID: 27042009; PMCID: PMC4801128.

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**7. Bioactivity**

Biological target:

Nintedanib esylate (BIBF 1120 esylate) is a potent triple angiokinase inhibitor for VEGFR1/2/3, FGFR1/2/3 and PDGFRα/β with IC50s of 34 nM/13 nM/13 nM, 69 nM/37 nM/108 nM and 59 nM/65 nM, respectively.

In vitro activity

To further elucidate whether the effect of nintedanib on SHP-1 is dependent on its angiokinase inhibition activity, a novel kinaseindependent derivative of nintedanib, ΔN was developed. HCC cell lines were treated with nintedanib or its derivative (ΔN) and apoptosis, signal transduction, and phosphatase activity were analyzed. Purified SHP-1 proteins or HCC cells expressing deletion NSH2 domain or D61A point mutants were used to investigate the potential effect of nintedanib on SHP-1. Nintedanib induced antiproliferation in HCC cell lines by targeting STAT3. Ectopic STAT3 abolished nintedanib-mediated apoptosis in HCC cells. Nintedanib further activated SHP-1 in purified SHP-1 proteins suggesting that nintedanib directly affects SHP-1 for STAT3 inhibition. HCC cells or recombinant SHP-1 proteins expressing deletion of N-SH2 domain or D61A mutants restored the activity of nintedanib suggesting that the auto-inhibition structure of SHP-1 was relieved by nintedanib.

Reference: J Hepatol. 2014 Jul;61(1):89-97. https://pubmed.ncbi.nlm.nih.gov/24657398/

In vivo activity

Since the IC50 value of BIBF 1120 was found to be the lowest for HNE-1 cells, we further evaluated the efficacy of BIBF 1120 in the HNE-1 xenograft model in nude mice, both as a single agent or in combination with cisplatin. The tumor sizes and weights were evaluated. As shown in Figure 2, BIBF 1120 demonstrated significant growth inhibition of NPC tumors in the HNE-1 xenograft model in nude mice as a single agent; the growth was significantly lower than that in the control group. At the same time, BIBF 1120 showed a greater inhibition of tumor growth in the human NPC cell line xenograft model in nude mice when combined with DDP than in the DDP single-agent group or the control group. Body weight reduction was observed in the DDP single-agent group and combination group, and temporary body weight reduction was observed in the BIBF 1120 single-agent group (Figure 3).

Reference: Drug Des Devel Ther. 2016; 10: 1173–1180. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4801128/

*Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.*