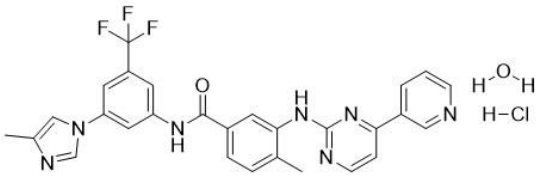
Product data sheet

MedKoo Cat#: 100673 Name: Nilotinib HCl hydrate CAS#: 923288-90-8 (HCl hydrate) Chemical Formula: $C_{28}H_{25}ClF_3N_7O_2$ Exact Mass: 529.1838 Molecular Weight: 584.0	
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:

Nilotinib, also known as AMN-107, is an orally bioavailable aminopyrimidine-derivative Bcr-Abl tyrosine kinase inhibitor with antineoplastic activity. Designed to overcome imatinib resistance, nilotinib binds to and stabilizes the inactive conformation of the kinase domain of the Abl protein of the Bcr-Abl fusion protein, resulting in the inhibition of the Bcr-Abl-mediated proliferation of Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) cells. This agent also inhibits the receptor tyrosine kinases platelet-derived growth factor receptor (PDGF-R) and c-kit, a receptor tyrosine kinase mutated and constitutively activated in most gastrointestinal stromal tumors (GISTs).

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	33.0	56.5

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	1.71	8.56	17.12
5 mM	0.34	1.71	3.42
10 mM	0.17	0.86	1.71
50 mM	0.03	0.17	0.34

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. Hussain T, Zhao D, Shah SZA, Sabir N, Wang J, Liao Y, Song Y, Dong H, Hussain Mangi M, Ni J, Yang L, Zhou X. Nilotinib: A Tyrosine Kinase Inhibitor Mediates Resistance to Intracellular Mycobacterium Via Regulating Autophagy. Cells. 2019 May 26;8(5):506. doi: 10.3390/cells8050506. PMID: 31130711; PMCID: PMC6562972.
2. Cagno V, Magliocco G, Tapparel C, Daali Y. The tyrosine kinase inhibitor nilotinib inhibits SARS-CoV-2 in vitro. Basic Clin Pharmacol Toxicol. 2021 Apr;128(4):621-624. doi: 10.1111/bcpt.13537. Epub 2020 Dec 4. PMID: 33232578; PMCID: PMC7753569.

In vivo study

1. Hussain T, Zhao D, Shah SZA, Sabir N, Wang J, Liao Y, Song Y, Dong H, Hussain Mangi M, Ni J, Yang L, Zhou X. Nilotinib: A Tyrosine Kinase Inhibitor Mediates Resistance to Intracellular Mycobacterium Via Regulating Autophagy. Cells. 2019 May 26;8(5):506. doi: 10.3390/cells8050506. PMID: 31130711; PMCID: PMC6562972.
2. Chahal KK, Li J, Kufareva I, Parle M, Durden DL, Wechsler-Reya RJ, Chen CC, Abagyan R. Nilotinib, an approved leukemia drug, inhibits smoothened signaling in Hedgehog-dependent medulloblastoma. PLoS One. 2019 Sep 20;14(9):e0214901. doi: 10.1371/journal.pone.0214901. PMID: 31539380; PMCID: PMC6754133.

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7. Bioactivity

Biological target:

Nilotinib monohydrochloride monohydrate is a second generation tyrosine kinase inhibitor (TKI), is significantly potent against BCR-ABL, and is active against many BCR-ABL mutants.

In vitro activity

Abl kinase inhibitors were previously reported to exert inhibitory activities against different viruses, including SARS‐CoV and MERS‐CoV by blocking the fusion between viral envelope and endosomal membrane. 4 , 5 , 6 Therefore, at first, we tested three Abl kinase inhibitors, namely nilotinib, imatinib and dasatinib, at non‐toxic concentration in Vero‐E6 cells by treating the cells starting 1h before infection. The only compound showing inhibitory activity is nilotinib with an EC50 of 1.88 μM (Table 1). Subsequently, nilotinib was also tested by only adding the compound 1h after inoculation. Nilotinib showed a comparable inhibitory activity in this condition, with an EC50 of 1.44 μM. In conclusion, although preliminary, the results of this in vitro study demonstrate the promising antiviral activity of nilotinib, a Bcr‐Abl tyrosine kinase inhibitor, not previously investigated to combat SARS‐CoV‐2.

Basic Clin Pharmacol Toxicol. 2020 Dec 4 : 10.1111/bcpt.13537. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7753569/

In vivo activity

Mice were infected with pathogenic M. bovis and after one week of infection, nilotinib was injected at a dose rate of 5 mg/kg and 10 mg/kg on alternate days. The dose of nilotinib used in the current study for in-vivo experiments was under a clinically relevant dose as previously reported. Animals were slaughtered at various time points after infection (Figure 6A). The total body weight of animals and their lung and spleen weights revealed that nilotinib suppressed the degree of pathogenesis of M. bovis (Supplementary Figure S5B–D). Gross analysis showed that nilotinib reduced the development of lesions in the lungs of infected mice as compared to the untreated control group (Figure 6B). At an early stage of infection (35 dpi), there was no significant difference in the spleen size, while in the later stages untreated mice (images labeled with II) showed enlarged spleens compared to those in the treated infected mice (images labeled with III and IV) (Figure 6C). Furthermore, the lung lobe showed a significantly high% area covered by lesions in untreated mice compared to treated M. bovis infected mice at all time points (Figure 6D,E). In addition, the increased number of bacilli was observed in the lung sections of untreated animals in comparison to treated animals after staining with the Ziehl-Neelsen staining method (Supplementary Figure S5E). Next, the harvested lung and spleen tissues were subjected to histopathological analyses. At early stages of infection (35 dpi), treated mice had small foci of inflammation composed of epithelioid macrophages and lymphocytes with no clear evidence of necrosis (Data not shown). However, at a later stage of infection (63 dpi), at high magnification, granulomatous lesions from untreated animals showed necrotic areas (marked with red arrows) in the central region of the lesion, which represent the severity of the disease (Figure 6F). Interestingly, lung sections from nilotinib treated animals showed comparatively less severe lesions with a reduced necrotic core (Figure 6G,H). Notably, no histological changes were observed in the H&E stained sections of the livers and the kidneys of nilotinib treated mice compared to the untreated controls (Supplemental Figure S4A,B). These findings suggested that nilotinib contributed towards minimizing the severity of M. bovis pathogenesis in mice.

Cells. 2019 May; 8(5): 506. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6562972/