Small Molecules

Nilotinib

Tyrosine kinase inhibitor; Inhibits BCR/ABL and ABL

Catalog #	73302	10 mg
	73304	50 mg

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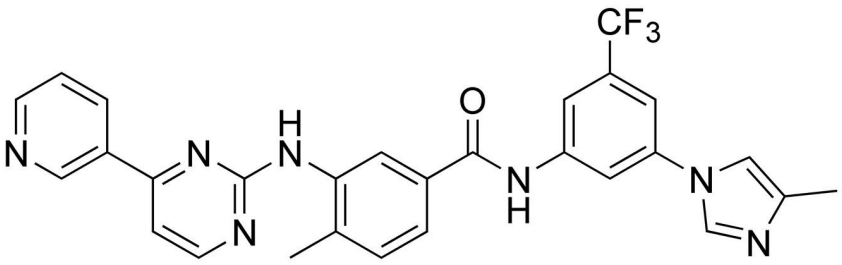
Product Description

Nilotinib is a second-generation inhibitor of the oncogenic tyrosine kinase BCR-ABL with IC_{50} values of 19, 140, and 9,200 nM for wild-type, E255K, and T315I mutant forms of BCR-ABL, respectively (Kitagawa et al.; O'Hare; Verstovsek et al.). It binds to the ATP binding pocket of ABL, with higher affinity than Imatinib (Catalog #72532) (Manley et al. 2006; Verstovsek et al.). It also has activity below 1 µM against discoidin domain receptors (DDR) -1 and -2, platelet-derived growth factor receptors (PDGFR) –α and -β, stem cell factor receptor (c-KIT), and colony-stimulating factor 1 receptor (CSF-1R; Manley et al. 2010).

Molecular Name:	Nilotinib
Alternative Names:	AMN107; Tasigna
CAS Number:	641571-10-0
Chemical Formula:	$C_{28}H_{22}F_3N_7O$
Molecular Weight:	529.5 g/mol
Purity:	≥ 95%
Chemical Name:	4-methyl-N-[3-(4-methylimidazol-1-yl)-5-(trifluoromethyl)phenyl]-3-[(4-pyridin-3-ylpyrimidin-2-yl)amino]benzamide
Structure:	

Properties

Physical Appearance:	A crystalline solid
Storage:	Product stable at -20°C as supplied. Protect from prolonged exposure to light. Stable as supplied for 12 months from date of receipt.
Solubility:	· DMSO ≤ 3.8 mM For example, to prepare a 2 mM stock solution in DMSO, resuspend 10 mg in 9.4 mL of DMSO. Prepare stock solution fresh before use. Information regarding stability of small molecules in solution has rarely been reported, however, as a general guide we recommend storage in DMSO at -20°C. Aliquot into working volumes to avoid repeated freeze-thaw cycles. The effect of storage of stock solution on compound performance should be tested for each application. Compound has low solubility in aqueous media. For use as a cell culture supplement, stock solution should be diluted into culture medium immediately before use. Avoid final DMSO concentration above 0.1% due to potential cell toxicity.

Published Applications

MAINTENANCE AND SELF-RENEWAL
· Reduces fibrosis by promoting TNF-mediated apoptosis of mesenchymal stem cells (Lemos et al.).
CANCER RESEARCH
· Inhibits cellular proliferation in many wild-type and mutant forms of Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) and chronic myeloid leukemia (CML) cells (O'Hare; Verstovsek et al.).
· Inhibits cell proliferation and progression through S phase in human lung cell line A549 through transcriptional changes in DNA helicase complex, cyclins, and cyclin-dependent kinases (Ji et al.).

References

Ji RR et al. (2009) Transcriptional profiling of the dose response: A more powerful approach for characterizing drug activities. PLoS Comput Biol 5(9): e1000512.
Kitagawa D et al. (2013) Activity-based kinase profiling of approved tyrosine kinase inhibitors. Genes Cells 18(2): 110–22.
Lemos DR et al. (2015) Nilotinib reduces muscle fibrosis in chronic muscle injury by promoting TNF-mediated apoptosis of fibro/adipogenic progenitors. Nat Med 21(7): 786–94.
Manley PW et al. (2006) Bcr-Abl binding modes of dasatinib, imatinib and nilotinib: An NMR study. ASH Annu Meet Abstr 108(11): 747.
Manley PW et al. (2010) Extended kinase profile and properties of the protein kinase inhibitor nilotinib. Biochim Biophys Acta 1804(3): 445–53.
O'Hare T. (2005) In vitro activity of Bcr-Abl inhibitors AMN107 and BMS-354825 against clinically relevant imatinib-resistant Abl kinase domain mutants. Cancer Res 65(11): 4500–5.
Verstovsek S et al. (2005) AMN107, a novel aminopyrimidine inhibitor of p190 Bcr-Abl activation and of in vitro proliferation of Philadelphia-positive acute lymphoblastic leukemia cells. Cancer 104(6): 1230–6.

Related Small Molecules

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