

# Nilotinib



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## Background

Nilotinib (AMN-107) is a novel tyrosine kinase inhibitor that potently inhibits Bcr-Abl. Nilotinib is more effective than imatinib at decreasing the proliferation and viability in cells expressing wild-type Bcr-Abl and is active against many imatinib-resistant Bcr-Abl mutants, with the exception of T315I (1-4). Nilotinib has been shown to inhibit Abl activity in cells expressing wild-type Abl and imatinib-resistant mutant Abl, with ~20-fold greater potency than imatinib. Nilotinib is similarly effective at inhibiting Abl autophosphorylation (3). Research studies have demonstrated that nilotinib treatment of Bcr-Abl-expressing K-562 cells attenuates Stat5 and CrkL phosphorylation, decreases Bcl-xL and c-Myc expression, induces p27 and Bim expression, and induces PARP cleavage. Many of these effects are enhanced by cotreatment with the histone deacetylase inhibitor LBH589 (5).

## Molecular Formula

C<sub>28</sub>H<sub>22</sub>F<sub>3</sub>N<sub>7</sub>O

## Molecular Weight

529.52 g/mol

## Purity

>99%

## CAS

641571-10-0

## Solubility

Soluble in DMSO at 50mg/ml.

## Storage

Store lyophilized or in solution at -20°C, desiccated. Protect from light. In lyophilized form, the chemical is stable for 24 months. Once in solution, use within 3 months to prevent loss of potency. Aliquot to avoid multiple freeze/thaw cycles.

## Directions for Use

Nilotinib is supplied as a lyophilized powder. For a 5 mM stock, reconstitute the 5 mg in 1.89 ml DMSO. Working concentrations and length of treatment can vary depending on the desired effect, but it is typically used at 10-1000 nM for 2-72 hr. Nilotinib is soluble in DMSO at 50 mg/ml; very poorly soluble in ethanol and water with maximum solubility in water at ~10-20 µM.

## Background References

1. Weisberg, E. et al. (2006) *Br J Cancer* 94, 1765-9.
2. Golemovic, M. et al. (2005) *Clin Cancer Res* 11, 4941-7.
3. O'Hare, T. et al. (2005) *Cancer Res* 65, 4500-5.
4. Weisberg, E. et al. (2005) *Cancer Cell* 7, 129-41.
5. Fiskus, W. et al. (2006) *Blood* 108, 645-52.

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