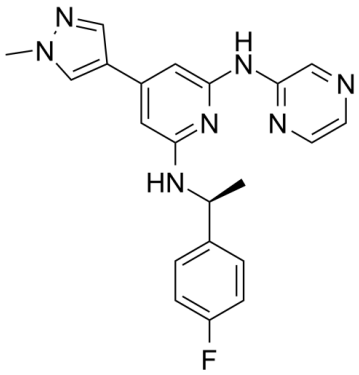
Data Sheet

Product Name:	Ilginatinib
Cat. No.:	CS-5358
CAS No.:	1239358-86-1
Molecular Formula:	C21H20FN7
Molecular Weight:	389.43
Target:	JAK
Pathway:	Epigenetics; JAK/STAT Signaling; Stem Cell/Wnt
Solubility:	DMSO : ≥ 34 mg/mL (87.31 mM)



BIOLOGICAL ACTIVITY:

Ilginatinib (NS-018) is a highly active and orally bioavailable **JAK2** inhibitor, with an **IC_{50}** of 0.72 nM, 46-, 54-, and 31-fold selectivity for JAK2 over JAK1 (**IC_{50}**, 33 nM), JAK3 (**IC_{50}**, 39 nM), and Tyk2 (**IC_{50}**, 22 nM). IC50 & Target: IC50: 0.72 nM (JAK2), 33 nM (JAK1), 39 nM (JAK3), 22 nM (Tyk2)[1] **In Vitro:** Ilginatinib (NS-018) is a highly active JAK2 inhibitor, with an IC_{50} of 0.72 nM, 46-, 54-, and 31-fold selectivity for JAK2 over JAK1 (IC_{50}, 33 nM), JAK3 (IC_{50}, 39 nM), and Tyk2 (IC_{50}, 22 nM). Ilginatinib (NS-018) also inhibits Src-family kinases, especially SRC and FYN, and weakly inhibits ABL and FLT3 with 45- and 90-fold selectivity for JAK2, respectively. NS-018 shows potent inhibitory activity against cell lines JAK2V617F or MPLW515L mutations or the TEL-JAK2 fusion gene (expressing a constitutively activated JAK2) with IC_{50} of 11-120 nM, but has only minimal cytotoxicity against most other hematopoietic cell lines that have no constitutively activated JAK2[1].

Ilginatinib (NS-018) (0.5 μM) preferentially suppresses colony-forming unitgranulocyte/macrophage (CFU-GM) formation from myelodysplastic syndrome (MDS)-derived bone marrow mononuclear cells (BMMNCs). Ilginatinib (NS-018) (1 μM) suppresses the phosphorylation of STAT3 (the downstream kinase of JAK2) in CFU-GM-forming cells from MDS patients[2]. **In Vivo:** Ilginatinib (NS-018) (12.5, 25, 50, 100 mg/kg, p.o.) potently prolongs the survival of mice and reduces splenomegaly in a mouse Ba/F3-JAK2V617F disease model[1].

Ilginatinib (NS-018) (25, 50 mg/kg, p.o.) significantly reduces leukocytosis, hepatosplenomegaly and extramedullary hematopoiesis, improves nutritional status, and prolongs survival in JAK2V617F transgenic mice

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [2]**Bone marrow mononuclear cells** (BMMNCs) from healthy volunteers and myelodysplastic syndrome (MDS) patients are incubated in MethoCult GF H4434 methylcellulose medium containing various hematopoietic cytokines at **1.0 × 10^5 cells/mL** with or without **Ilginatinib (NS-018)** at 37°C in a humidified atmosphere of 5% CO_2. Commercially available purified normal human CD34-positive ($CD34^+$) BM cells are used as a control. Burst-forming unit-erythroid (BFU-E) and colonyforming unit-granulocyte/macrophage (CFU-GM) colonies are counted under an inverted microscope on day 14 of culture[2].

Animal Administration: NS-018 is formulated in 0.5% methylcellulose[1].[1]Mice[1]

Female BALB/c nude mice are placed in blanket cages in an environment maintained at 21-25°C and 45-65% relative humidity, with artificial illumination for 12 h and a ventilation frequency of at least 15 times/h. They are allowed free access to food pellets and tap water. **Ba/F3-JAK2V617F cells (10^6 per mouse)** are inoculated intravenously into 7-week-old mice. Administration of vehicle (**0.5% methylcellulose**) or **Ilginatinib (NS-018)** twice daily by **oral gavage** begins the day after cell inoculation. Survival is monitored daily, and moribund mice are humanely killed and their time of death is recorded for purposes of survival analysis. In a parallel study, all mice are humanely killed after 8 days of administration, and their spleens are removed and weighed[1].

References:

[1]. Nakaya Y, et al. Efficacy of NS-018, a potent and selective JAK2/Src inhibitor, in primary cells and mouse models of myeloproliferative neoplasms. Blood Cancer J. 2011 Jul;1(7):e29.

[2]. Kuroda J, et al. NS-018, a selective JAK2 inhibitor, preferentially inhibits CFU-GM colony formation by bone marrow mononuclear cells from high-risk myelodysplastic syndrome patients. Leuk Res. 2014 May;38(5):619-24.

CAIndexNames:

2,6-Pyridinediamine, N2-[(1S)-1-(4-fluorophenyl)ethyl]-4-(1-methyl-1H-pyrazol-4-yl)-N6-2-pyrazinyl-

SMILES:

CN1N=CC(C2=CC(N[C@H](C3=CC=C(F)C=C3)C)=NC(NC4=NC=CN=C4)=C2)=C1

Caution: Product has not been fully validated for medical applications. For research use only.

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