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产品名称: **NS-018**
产品别名: **Ilginatinib**

生物活性:				
Description	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).			
IC ₅₀ & Target	JAK2	Tyk2	JAK1	JAK3
	0.72 nM (IC ₅₀)	22 nM (IC ₅₀)	33 nM (IC ₅₀)	39 nM (IC ₅₀)
In Vitro	Ilginatinib (NS-018) is a highly active JAK2 inhibitor, with an IC₅₀ of 0.72 nM, 46-, 54-, and 31-fold selectivity for JAK2 over JAK1 (IC₅₀, 33 nM), JAK3 (IC₅₀, 39 nM), and Tyk2 (IC₅₀, 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 IC₅₀ 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 unit/granulocyte/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			
Solvent&Solubility	In Vitro: DMSO : ≥ 34 mg/mL (87.31 mM) * "≥" means soluble, but saturation unknown.			
	Preparing Stock Solutions	Solvent	Mass	
		Concentration	1 mg	5 mg
				10 mg
		1 mM	2.5679 mL	12.8393 mL
		5 mM	0.5136 mL	2.5679 mL
		10 mM	0.2568 mL	1.2839 mL
	*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液。一旦配成溶液, 请分装保存, 避免反复冻融造成的产品失效。 储备液的保存方式和期限: -80°C, 6 months; -20°C, 1 month。 -80°C 储存时, 请在 6 个月内使用, -20°C 储存时, 请在 1 个月内使用。			
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			



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	bone marrow mononuclear cells from high-risk myelodysplastic syndrome patients. Leuk Res. 2014 May;38(5):619-24.
实验参考:	
Cell Assay	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	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.

源叶生物