



上海源叶生物科技有限公司
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产品名称: **NS-018 (maleate)**
产品别名: **Ilginatinib maleate**

生物活性:																										
Description	Ilginatinib maleate (NS-018 maleate) 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).																									
	JAK2	Tyk2	JAK1	JAK3																						
IC ₅₀ & Target	0.72 nM (IC ₅₀)	22 nM (IC ₅₀)	33 nM (IC ₅₀)	39 nM (IC ₅₀)																						
	Ilginatinib maleate (NS-018 maleate) 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 maleate also inhibits Src-family kinases, especially SRC and FYN, and weakly inhibits ABL and FLT3 with 45- and 90-fold selectivity for JAK2, respectively. Ilginatinib maleate 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 maleate (0.5 μM) preferentially suppresses colony-forming unitgranulocyte/macrophage (CFU-GM) formation from myelodysplastic syndrome (MDS)-derived bone marrow mononuclear cells (BMMNCs). Ilginatinib maleate (1 μM) suppresses the phosphorylation of STAT3 (the downstream kinase of JAK2) in CFU-GM-forming cells from MDS patients ^[2] .																									
In Vivo	Ilginatinib maleate (NS-018 maleate) (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 maleate (25, 50 mg/kg, p.o.) significantly reduces leukocytosis, hepatosplenomegaly and extramedullary hematopoiesis, improves nutritional status, and prolongs survival in JAK2V617F transgenic mice ^[1] .																									
	In Vitro: DMSO : ≥ 30 mg/mL (59.35 mM) H₂O : < 0.1 mg/mL (insoluble) * "≥" means soluble, but saturation unknown. <table><tr><td rowspan="4">Preparing Stock Solutions</td><td>Solvent</td><td>Mass</td><td rowspan="2">1 mg</td><td rowspan="2">5 mg</td><td rowspan="2">10 mg</td></tr><tr><td>Concentration</td><td></td></tr><tr><td>1 mM</td><td></td><td>1.9782 mL</td><td>9.8912 mL</td><td>19.7824 mL</td></tr><tr><td>5 mM</td><td></td><td>0.3956 mL</td><td>1.9782 mL</td><td>3.9565 mL</td></tr><tr><td>10 mM</td><td></td><td>0.1978 mL</td><td>0.9891 mL</td><td>1.9782 mL</td></tr></table> *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℃, 6 months; -20℃, 1 month。 -80℃ 储存时，请在 6 个月内使用， -20℃ 储存时，请在 1 个月内使用。 In Vivo: 请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：				Preparing Stock Solutions	Solvent	Mass	1 mg	5 mg	10 mg	Concentration		1 mM		1.9782 mL	9.8912 mL	19.7824 mL	5 mM		0.3956 mL	1.9782 mL	3.9565 mL	10 mM		0.1978 mL	0.9891 mL
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Solvent&Solubility																										



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	——为保证实验结果的可靠性,澄清的储备液可以根据储存条件,适当保存;体内实验的工作液,建议您现用现配,当天使用;以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比;如在配制过程中出现沉淀、析出现象,可以通过加热和/或超声的方式助溶 1.请依序添加每种溶剂: 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.5 mg/mL (4.95 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.95 mM, 饱和度未知) 的澄清溶液。 以 1 mL 工作液为例,取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中,混合均匀向上述体系中加入 50 μL Tween-80,混合均匀;然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂: 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (4.95 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.95 mM, 饱和度未知) 的澄清溶液。 以 1 mL 工作液为例,取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中,混合均匀。
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.
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 NS-018 at 37°C in a humidified atmosphere of 5% CO₂. 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 Ilgatinib (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.