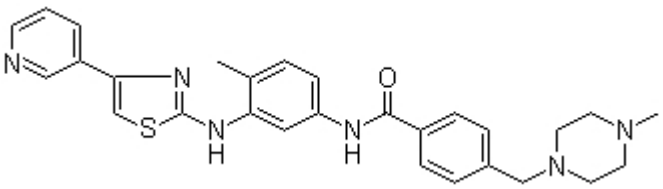
Product Introduction

Masitinib (AB1010)

Masitinib is a novel inhibitor for **Kit** and **PDGFRα/β** with **IC50** of 200 nM and 540 nM/800 nM, weak inhibition to ABL and c-Fms. Phase 2/3.

Technical Data:

Molecular Weight (MW):	498.64	
Formula:	$C_{28}H_{30}N_6OS$	
Solubility (25°C) *** <1 mg/ml means slightly soluble or insoluble:**	DMSO 100 mg/mL	
	Water <1 mg/mL	
	Ethanol 4 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	790299-79-5	

Biological Activity

Masitinib is a competitive inhibitor against ATP at concentrations ≤500 nM. Masitinib also potently inhibits recombinant PDGFR and the intracellular kinase Lyn, and to a lesser extent, fibroblast growth factor receptor 3. In contrast, Masitinib demonstrates weak inhibition of Abl and c-Fms. Masitinib more strongly inhibits degranulation, cytokine production, and bone marrow mast cell migration than imatinib. In Ba/F3 cells expressing human wild-type Kit, Masitinib inhibits SCF (stem cell factor)-induced cell proliferation with an IC50 of 150 nM, while the IC50 for inhibition of IL-3-stimulated proliferation is at approximately

>10 μM. In Ba/F3 cells expressing PDGFRα, Masitinib inhibits PDGF-BB-stimulated proliferation and PDGFRα tyrosine phosphorylation with IC50 of 300 nM. Masitinib also causes inhibition of SCF-stimulated tyrosine phosphorylation of human Kit in mastocytoma cell-lines and BMMC. Masitinib inhibits Kit gain-of-function mutants, including V559D mutant and Δ27 mouse mutant with IC50 of 3 and 5 nM in Ba/F3 cells. Masitinib inhibits the cell proliferation of mastocytoma cell lines including HMC-1α155 and FMA3 with IC50 of 10 and 30 nM, respectively. [1] Masitinib inhibits cell growth and PDGFR phosphorylation in two novel ISS cell lines, which suggest that Masitinib displays activity against both primary and metastatic ISS cell line and may aid in the clinical management of ISS. [2]

Masitinib inhibits tumour growth and increases the median survival time in Δ27-expressing Ba/F3 tumor models at 30 mg/kg, without cardiotoxicity or genotoxicity. [1] Masitinib (12.5 mg/kg/d PO) increases overall TTP (time-to-tumor progression) compared with placebo in dogs. [3] The combination of masitinib/gemcitabine shows synergy in vitro on proliferation of gemcitabine-refractory cell lines Mia Paca2 and Panc1, and to a lesser extent on Mia Paca-2 pancreatic tumours in Nog 璞 CID mice. [4]

Potential low side-effect profile.

References

[1] Dubreuil P, et al. PLoS One, 2009, 4(9), e7258.

[2] Lawrence J, et al. Vet Comp Oncol, 2011, doi: 10.1111/j.1476-5829.2011.00291.x.

[3] Hahn KA, et al. J Vet Intern Med, 2008, 22(6), 1301-1309.

[4] Humbert M, et al. PLoS One, 2010, 5(3), e9430.

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