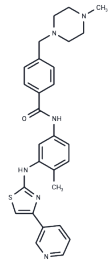
Data Sheet (Cat.No.T2609)

TargetMol

Masitinib

Chemical Properties



CAS No. : 790299-79-5

Formula: C28H30N6OS

Molecular Weight: 498.64

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Masitinib (AB1010) is a tyrosine-kinase inhibitor used in the treatment of mast cell tumors in animals, specifically dogs. Since its introduction in November 2008 it has been distributed under the commercial name Masivet. It has been available in Europe since the second part of 2009. In the USA it is distributed under the name Kinavet and has been available for veterinaries since 2011.
Targets(IC50)	Apoptosis,FAK,c-Fms,FGFR,Bcr-Abl,c-Kit,Hck,PDGFR,Src
In vitro	Compared to a placebo, Masitinib (at a dosage of 12.5 mg/kg/d PO) significantly increased the overall TTP (tumor progression time) in dogs. In the Ba/F3 transplant tumor model expressing Δ27, Masitinib at 30 mg/kg inhibited tumor growth and extended the average survival time, without exhibiting cardiotoxicity or genotoxicity. Additionally, the combination of Masitinib and gemcitabine demonstrated a synergistic inhibitory effect on the proliferation of gemcitabine-resistant cell lines, Mia Paca2 and Panc1.
In vivo	Masitinib inhibits the proliferation of Ba/F3 cells expressing human wild-type KIT induced by stem cell factor, with an IC50 of 150 nM, and the proliferation induced by IL-3 with an IC50 value of >10 μM. In Ba/F3 cells expressing PDGFR-α, masitinib suppresses PDGF-BB-stimulated proliferation and PDGFR-α tyrosine phosphorylation, with an IC50 of 300 nM. At concentrations of ≤500 nM, masitinib acts as an ATP-competitive inhibitor. It also effectively inhibits recombinant PDGFR and the intracellular kinases Lyn and FGFR3. However, masitinib exhibits weak inhibition of ABL and c-Fms. In mammalian cell lines and BMMC, masitinib inhibits SCF-induced human Kit tyrosine phosphorylation. It inhibits KIT gain-of-function mutations in Ba/F3 cells, including the V559D and Δ27 mouse mutations, with IC50 values of 3 and 5 nM, respectively. In two novel ISS cell lines, masitinib inhibits cell growth and PDGFR phosphorylation, indicating its activity against primary and metastatic ISS cell lines and its potential utility in ISS clinical management. Masitinib provides stronger inhibition than imatinib on degranulation, cytokine production, and migration of bone marrow mast cells. It inhibits the proliferation of mastocytoma cell lines, including HMC-1α155 and FMA3, with IC50 values of 10 and 30 nM, respectively.
Kinase Assay	In vitro enzyme-linked immunoassay with recombinant protein kinases: A 96-well microtitre plateis coated overnight with 0.25?mg/ml poly(Glu,Tyr 4:1), rinsed twice with 250?μL of washing buffer (10 mM phosphate-buffered saline [pH?7.4] and 0.05% Tween? 20) and dried for 2 hours at room temperature. Assays are performed at room

Kinase Assay	temperature with a final volume of 50?μL in kinase buffer (10 mM?MgCl2, 1 mM MnCl2, 1 mM sodium orthovanadate, 20 mM HEPES, pH?7.8) containing ATP at a concentration of at least twice the Km for each enzyme and an appropriate amount of recombinant enzyme to ensure a linear reaction rate. Reactions are initiated upon introduction of the enzyme and terminated with the addition of one reaction volume (50 μL) of 100?mM EDTA per 5?M urea mix. Plates are washed three times and incubated with 1:30,000 horseradish peroxidase-conjugated anti-phosphotyrosine monoclonal antibody, then washed three times and incubated with tetramethylbenzidine. The final reaction product is quantified by spectrophotometry at 450?nm.
Cell Research	For the assay of Ba/F3 cell proliferation, microtitre plates are seeded with a total of 104 cells/well in 100 μL of RPMI 1640 medium with 10% foetal bovine serum at 37 °C. These are supplemented, or not, with either 0.1% conditioned medium from X63-IL-3 cells or 250 ng/mL murine SCF. The murine SCF, which activates Kit, is purified from the conditioned medium of SCF-producing CHO cells. Cells are grown for 48 hours at 37 °C with Masitinib and then incubated with 10 μL/well of WST-1 reagent for 3 hours at 37 °C. The amount of formazan dye formed is quantified by its absorbance at 450 nm using a scanning multiwell spectrophotometer. A blank well without cells is used as a background control for the spectrophotometer. (Only for Reference)

Solubility Information

Solubility	DMSO: 250 mg/mL (501.36 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: 4 mg/mL (8.02 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (4.01 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.0055 mL	10.0273 mL	20.0545 mL
5 mM	0.4011 mL	2.0055 mL	4.0109 mL
10 mM	0.2005 mL	1.0027 mL	2.0055 mL
50 mM	0.0401 mL	0.2005 mL	0.4011 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Dubreuil P, et al. PLoS One, 2009, 4(9), e7258.
Lawrence J, et al. Vet Comp Oncol, 2011, doi: 10.1111/j.1476-5829.2011.200291.x.
Hahn KA, et al. J Vet Intern Med, 2008, 22(6), 1301-1309.
Humbert M, et al. PLoS One, 2010, 5(3), e9430.

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