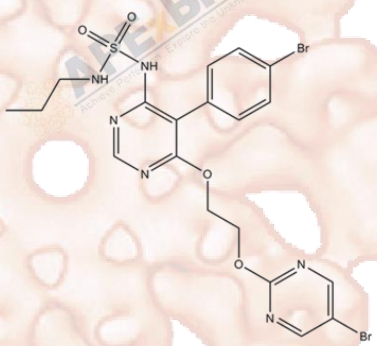
Product Data Sheet

Macitentan



Cat. No.:	A1929
CAS No.:	441798-33-0
Formula:	C19H20Br2N6O4S
M.Wt:	588.27
Synonyms:	
Target:	GPCR/G protein
Pathway:	Endothelin Receptor
Storage:	Store at -20°C

Solvent & Solubility

In Vitro

≥24.4 mg/mL in DMSO; insoluble in H2O; insoluble in EtOH

Preparing Stock Solutions

Mass / Solvent / Concentration	1mg	5mg	10mg
1 mM	1.6999 mL	8.4995 mL	16.9990 mL
5 mM	0.3400 mL	1.6999 mL	3.3998 mL
10 mM	0.1700 mL	0.8499 mL	1.6999 mL

Please refer to the solubility information to select the appropriate solvent.

Biological Activity

Shortsummary	Endothelin (ET)(A) and ET(B) receptor antagonist
IC_{50} & Target	

In Vitro

Cell Viability Assay

Cell Line:	Primary human pulmonary smooth muscle cells, microvascular endothelial cells
Preparation method：	The solubility of this compound in DMSO is >21.2 mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

	Reacting conditions:	IC50: 1 nM
	Applications:	Macitentan completely inhibited intracellular calcium increase induced by ET-1 on primary human pulmonary smooth muscle cells with approximate IC50 of 1 nM. Macitentan inhibited ET-1-induced contractions on isolated rat aortic rings or S6c-induced contractions on isolated rat tracheal rings with pA2 of 7.6 and 5.9, respectively. In microvascular endothelial cells, pretreatment with macitentan restored tube formation ability and reduced the expression of mesenchymal markers and restored CD31 expression and the imbalance between VEGF-A and VEGF-A165b.
In Vivo	**Animal experiment**	
	Animal models:	Hypertensive DOCA-salt rats, monocrotaline rat model of pulmonary hypertension, SKOV3ip1 ovarian cancer model
	Dosage form:	Oral administration, 25 mg/kg/day
	Applications:	In normotensive rats, macitentan increased plasma ET-1 concentration. Macitentan dose-dependently decreased mean arterial blood pressure in hypertensive DOCA-salt rats with a maximal effect of -26 mm Hg at a dose of 10 mg/kg. Oral administration of macitentan dose-dependently prevented the development of pulmonary hypertension and the development of right ventricle hypertrophy with a maximal efficacy of 30 mg/kg/day in monocrotaline rat model of pulmonary hypertension. Chronic oral administration of macitentan at 30 mg/kg/day significantly improved the 42-day survival in monocrotaline rats. Macitentan (25 mg/kg/day, p.o.) prevented increased production of vasoactive and fibrogenic factors, NF-κB activation, structural and functional changes, and increased extracellular matrix protein production in type 2 diabetes. Macitentan (10 mg/kg, p.o.) in combination with once-per-week 5 mg/kg taxol significantly reduced the weight (size) of HeyA8-MDR tumors in mice. Combination therapy with macitentan (10 or 50 mg/kg) and taxol or macitentan (10 mg/kg) and cisplatinum significantly reduced the number of proliferating Ki-67-positive cells. Macitentan (100 mg/kg) treatment combined with paclitaxel (5 mg/kg) reduced tumor incidence and further reduced tumor weight and incidences of ascites in SKOV3ip1 ovarian cancer model. Macitentan plus paclitaxel inhibited the phosphorylation of ETRs and suppressed the survival pathways of tumor cells by decreasing the levels of pVEGFR2, pAkt, and pMAPK. Macitentan enhanced effects of paclitaxel on tumor cells dividing and apoptosis.
	Other notes:	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

Product Citations

See more customer validations on www.apexbt.com.

References

[1]. Marc Iglarz, Christoph Binkert, Keith Morrison, et al. Pharmacology of Macitentan, an Orally Active Tissue-Targeting Dual Endothelin Receptor Antagonist. Journal of Pharmacology and Experimental Therapeutics, 2008, 327:736-745.

[2]. Corallo C, et al. Bosentan and macitentan prevent the endothelial-to-mesenchymal transition (EndoMT) in systemic sclerosis: in vitro study. Arthritis Res Ther. 2016 Oct 6;18(1):228.

[3]. Sen S, et al. Renal, retinal and cardiac changes in type 2 diabetes are attenuated by macitentan, a dual endothelin receptor antagonist. Life Sci. 2012 Apr 13.

[4]. Kim SJ, et al. Antivascular therapy for multidrug-resistant ovarian tumors by macitentan, a dual endothelin receptor antagonist. Transl Oncol. 2012 Feb;5(1):39-47.

[5].Kim S J, Kim J S, Kim S W, et al. Macitentan (ACT-064992), a tissue-targeting endothelin receptor antagonist, enhances therapeutic efficacy of paclitaxel by modulating survival pathways in orthotopic models of metastatic human ovarian cancer[J]. Neoplasia, 2011, 13(2): 167-IN12.

Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most APExBIO products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.

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