Product Data Sheet

Chemical Properties

Product Name: Macitentan

Cas No.: 441798-33-0

M.Wt: 588.27

Formula: C19H20Br2N6O4S

Synonyms: N/A

Chemical Name: 5-(4-bromophenyl)-6-[2-(5-bromopyrimidin-2-yl)oxyethoxy]-N-(propylsulfamoyl)pyrimidin-4-amine

Canonical SMILES: CCCNS(=O)(=O)NC1=C(C(=NC=N1)OCCOC2=NC=C(N=C(N2)Br)C3=CC(=C(C3)Br

Solubility: ≥24.4mg/mL in DMSO

Storage: Store at -20°C

General tips: For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shopping Condition: Evaluation sample solution: ship with blue ice
All other available size: ship with RT, or blue ice upon request

Biological Activity

Targets: GPCR/G protein

Pathways: Endothelin Receptor

Description:

Macitentan is a new dual ETA/ETB endothelin (ET) receptor antagonist, with mean IC50 values of 0.5 ± 0.2 nM (n= 17) to inhibit the binding of 125I-ET-1 to recombinant ETA receptors, and of 391±182 nM (n= 17) for ETB receptors in Chinese hamster ovary cells [1]. ETA and ETB are ET receptors, both of them mediate the detrimental actions of ET-1, and dual blockade of them may be necessary [1].
In microsomal membranes of human-ETA and ETB-overexpressing Chinese hamster ovary cells, macitentan inhibited the binding between 125I-ET-1 and recombinant ETA receptors, with a mean IC50 value of 0.5 ± 0.2 nM (n= 17). The mean IC50 value for ETB receptors was 391±182 nM (n= 17). Macitentan completely inhibited the effect that ET-1 increased intracellular calcium in non-recombinant cells [1]. Intravenous administrated macitentan had a volume of distribution largely exceeding plasma volume and a terminal half-life of 2 h in rats. Macitentan was hence metabolized to its major and the only circulating metabolite, a dual ET receptor antagonist, ACT-132577. ACT-132577 also had a volume of distribution greater than the plasma volume. It showed a longer half-life than macitentan in rats. In rat, multiple oral dosing of macitentan at a dose of 10 mg/kg led to 4 to 5-fold higher exposure levels of ACT-132577 than those of the parent compound [1].

**Reference:**

### Protocol

**Cell experiment:**

| Cell lines | 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 | 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. |

**Animal experiment [3]:**

| 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.

Reference:


**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. Short-term 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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