# Zibotentan

**Cat. No.:** HY-10088

**CAS No.:** 186497-07-4

**Molecular Formula:** $C_{19}H_{16}N_6O_4S$

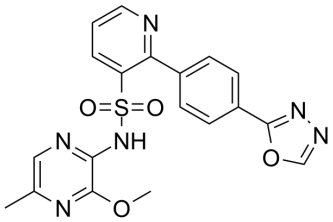
**Molecular Weight:** 424.43

**Target:** Endothelin Receptor; Apoptosis

**Pathway:** GPCR/G Protein; Apoptosis

**Storage:**

| | | |
|---|---|---|
| Powder | -20°C | 3 years |
| | 4°C | 2 years |
| In solvent | -80°C | 2 years |
| | -20°C | 1 year |



## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : 25 mg/mL (58.90 mM; Need ultrasonic)

**Preparing Stock Solutions**

| Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|
| 1 mM | 2.3561 mL | 11.7805 mL | 23.5610 mL |
| 5 mM | 0.4712 mL | 2.3561 mL | 4.7122 mL |
| 10 mM | 0.2356 mL | 1.1781 mL | 2.3561 mL |

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

**In Vivo**

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.89 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

Zibotentan (ZD4054) is a potent, selective and orally active endothelin A ($ET_A$) receptor antagonist with a $K_i$ of 13 nM. Zibotentan has no inhibitory effect on ETB. Zibotentan has anticancer effects and can be used for castration-resistant prostate cancer (CRPC) research[1][2].

**$IC_{50}$ & Target**

$ET_A$
13 nM (Ki)

**In Vitro**

Zibotentan potently inhibits the binding of $^{125}$iodine-ET-1 to cloned human ETA expressed in mouse erythroleukaemic cells, with a $pIC_{50}$ (concentration to inhibit 50% of binding) value of 22 nM[1].
Zibotentan (48 hours) treatment increases the number of early apoptotic cells in serum-starved A2780 WT cells[2].
Zibotentan (ZD4054; 1 μM; 24 hours) treatment shows significant inhibition of cell proliferation in serum-starved HEY, OVCA 433, SKOV-3, and A-2780 cells[3].

Zibotentan (ZD4054; 1 μM; 48 hours) treatment induces an increase in apoptotic cells. Zibotentan inhibits bcl-2 and activates caspase-3 and poly(ADP-ribose) polymerase proteins.[3].
Zibotentan (ZD4054; 1 μM) decreases the endogenous ET-1-induced phosphorylation/activation of both kinases (AKT and p42/44MAPK) in HEY cells[3].
Zibotentan treatment also results in a reduction of ETAR-driven angiogenesis and invasive mediators, such as vascular endothelial growth factor, cyclooxygenase-1/2, and matrix metalloproteinase (MMP)[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[3]

| | |
|---|---|
| Cell Line: | HEY, OVCA 433, SKOV-3, and A-2780 cells |
| Concentration: | 1 μM |
| Incubation Time: | 24 hours |
| Result: | Showed significant inhibition of cell proliferation. |

Apoptosis Analysis[3]

| | |
|---|---|
| Cell Line: | HEY and OVCA 433 cells |
| Concentration: | 1 μM |
| Incubation Time: | 48 hours |
| Result: | Induced an increase in apoptotic cells. |

**In Vivo**

Zibotentan (10 mg/kg; intraperitoneal injection; daily; for 21 days) treatment significantly inhibits tumor growth in mice. And Zibotentan treatment increases E-cadherin expression[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

| | |
|---|---|
| Animal Model: | Female athymic ($nu^+/nu^+$) mice (4-6 week of age) injected with wild-type A2780 cells[2] |
| Dosage: | 10 mg/kg |
| Administration: | Intraperitoneal injection; daily ; for 21 days |
| Result: | Showed significant inhibition in tumor growth in mice. |

## REFERENCES


[1]. C D Morris, et al. Specific inhibition of the endothelin A receptor with ZD4054: clinical and pre-clinical evidence. Br J Cancer. 2005 Jun 20;92(12):2148-52.

[2]. Laura Rosanò, et al. Acquisition of chemoresistance and EMT phenotype is linked with activation of the endothelin A receptor pathway in ovarian carcinoma cells. Clin Cancer Res. 2011 Apr 15;17(8):2350-60.

[3]. Laura Rosanò, et al. ZD4054, a specific antagonist of the endothelin A receptor, inhibits tumor growth and enhances paclitaxel activity in human ovarian carcinoma in vitro and in vivo. Mol Cancer Ther. 2007 Jul;6(7):2003-11.





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