

# A-443654

Catalog No: tcsc0405



## Available Sizes

**Size:** 1mg

**Size:** 5mg

**Size:** 10mg



## Specifications

**CAS No:**

552325-16-3

**Formula:**

$C_{24}H_{23}N_5O$

**Pathway:**

PI3K/Akt/mTOR

**Target:**

Akt

**Purity / Grade:**

>98%

**Solubility:**

10 mM in DMSO

**Observed Molecular Weight:**

397.47

## Product Description

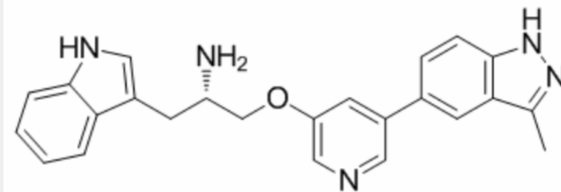
A-443654 is a potent small-molecule inhibitor of all three **Akt serine/threonine kinases**, with **K<sub>i</sub>** of 160 pM for Akt1.

IC50 & Target: Ki: 160 pM (Akt1)

***In Vitro:***

A-443654 exhibits a  $K_i$  of 160 pM, a 30,000-fold improvement in potency versus the initial lead molecule. A-443654 is 40-fold selective for Akt over PKA. A-443654 inhibits Akt1, Akt2, or Akt3 equally within cells. A-443654 reduces the P-GSK3 in a dose-responsive manner in all three cell lines. A-443654 inhibits the proliferation of tumor cells with  $EC_{50}$  of 0.1  $\mu$ M<sup>[1]</sup>. A-443654-induced morphological changes occur very rapidly (within 2 to 4 h) in both 10A and 10CA1a cells, with 10CA1a cells more sensitive to A-443654 than the 10A cells. A-443654 alone at 2  $\mu$ M causes the 10CA1a cells, but not the 10A cells, to detach from the plate after 12 h, whereas 1  $\mu$ M of A-443654 causes 10CA1a cells to detach from the plate after 12 h. FACSscan Analysis of rapamycin and A-443654 effects on DNA content in 10A and 10CA1a cells. In contrast, A-443654 at 2 and 5  $\mu$ M decreases Bcl-2 levels by 30 to 40% in the 10CA1a cells at 8h. The combination of rapamycin with 2 or 5  $\mu$ M A-443654, however, markedly decreases Bcl-2 protein levels by appr 40 to 50% in the 10A cells and by appr 70% in the 10CA1a cells, respectively<sup>[2]</sup>. A-443654 demonstrates the greatest selective effect on the mutant cells compared to the WT cells with greater than 3.5 fold relative growth inhibition of the mutant cells<sup>[3]</sup>.

**In Vivo:** A-443654 (7.5 mg/kg/d, s.c.) inhibits tumor growth in the 3T3-Akt1 flank tumor model. A-443654 (50 mg/kg, s.c.) induces apoptosis in 3T3-Akt1 flank tumors. A-443654 (30 mg/kg, s.c.) leads to increased levels of phosphorylated Akt1 in MiaPaCa-2 tumors [1].



All products are for RESEARCH USE ONLY. Not for diagnostic & therapeutic purposes!