Web: www.taiclone.com
Tel: +886-2-2735-9682
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Tivantinib

Catalog No: tcsc0030

Available Sizes

Size: 5mg

Size: 10mg

Size: 50mg

Size: 100mg

Size: 200mg

Size: 500mg

Specifications

CAS No:
905854-02-6

Formula:
$C_{23}H_{19}N_3O_2$

Pathway:
Protein Tyrosine Kinase/RTK

Target:
c-Met/HGFR

Purity / Grade:
>98%

Solubility:
DMSO : ≥ 100 mg/mL (270.69 mM)

Alternative Names:
ARQ 197

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Observed Molecular Weight:
369.42

Product Description

Tivantinib is a novel and highly selective **c-Met** tyrosine kinase inhibitor with $\mathbf{K_i}$ of 355 nM.

IC50 & Target: Ki: 355 nM (c-Met)[1]

In Vitro: Tivantinib (ARQ 197) selectively inhibits c-Met activity in cell-free and cell-based assays. c-Met-expressing cancer cell lines treated with Tivantinib display either a dose-dependent loss of proliferative capacity or caspase-dependent apoptosis that positively correlates with either ligand-dependent c-Met activity or constitutively active c-Met. To examine the biochemical mode of inhibition of Tivantinib, kinetic analyses are done using recombinant human c-Met in a filtermat-based assay. The K_m of ATP is 50.5±2.2 μM, which is similar to the K_m value of ATP. In these kinetic studies, Tivantinib inhibits human recombinant c-Met with a calculated inhibitory constant (K_i) of ~355 nM. In vitro exposure to Tivantinib inhibits constitutive c-Met phosphorylation in HT29 and MKN-45 cells, and HGF-induced c-Met phosphorylation in MDA-MB-231 and NCI-H441 cells with an IC_{50} of 100 to 300 nM[1]. Tivantinib is a low-molecular-weight compound, and is the first in class orally available selective inhibitor of c-Met[2].

In Vivo: Pharmacodynamically, the phosphorylation of c-Met in human colon xenograft tumors (HT29) is strongly inhibited by Tivantinib (ARQ 197), as assessed by a dramatic reduction of c-Met autophosphorylation 24 hours after a single oral dose of 200 mg/kg of Tivantinib. This same dosage in mice shows that tumor xenografts are exposed to sustained plasma levels of Tivantinib, consistent with the observed pharmacodynamic inhibition of c-Met phosphorylation and inhibition of proliferation of c-Met harboring cancer cell lines. A C_{max} of 5.73 μg/mL (13 μM), an area under the concentration-time curve of 12.1 μg/mL h, and a $t_{1/2}$ of 2.4 hours are measured. Plasma levels of Tivantinib 10 hours after dosing are determined to be 1.3 μM, >3-fold above the biochemical inhibitory constant of Tivantinib for c-Met[1].

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