Web: www.taiclone.com
Tel: +886-2-2735-9682
Email: order@taiclone.com

TAK-733

Catalog No: tcsc1283

Available Sizes

Size: 5mg

Size: 10mg

Size: 50mg

Specifications

CAS No:
1035555-63-5

Formula:
$C_{17}H_{15}F_2IN_4O_4$

Pathway:
MAPK/ERK Pathway

Target:
MEK

Purity / Grade:
>98%

Solubility:
DMSO : ≥ 33 mg/mL (65.45 mM)

Observed Molecular Weight:
504.23

Product Description

TAK-733 is a potent and selective **MEK** allosteric site inhibitor with an **IC_{50}** of 3.2 nM.

IC50 & Target: IC50: 3.2 nM (MEK)[1]

In Vitro:

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TAK-733 exhibits potent enzymatic and cell activity with an IC_{50} of 3.2 nM against constitutively active MEK enzyme and an EC_{50} of 1.9 nM against ERK phosphorylation in cells. TAK-733 does not inhibit any other kinases, receptors or ion channels that are tested with inhibitor concentrations up to 10 μM. TAK-733 is found to bind plasma protein moderately (ca. 97% for human and 96% for mouse), and exhibits high permeability and high microsomal stability across species. It does not inhibit P450s up to 30 μM[1]. TAK-733 demonstrates broad activity in most melanoma cell lines with relative resistance observed at IC_{50} >0.1 μM in vitro. Thirty-four melanoma cell lines are exposed in vitro to increasing concentrations of TAK-733 for 72 hours. Of the 34 cell lines, 27 are $BRAF^{V600E}$ mutant and 7 are wild-type. SRB proliferation assays are performed and the resulting IC_{50} concentrations allowed stratification of cell lines into three categories: relatively resistant, intermediate, and highly sensitive. Relatively resistant and highly sensitive lines are assigned based on an IC_{50} that differ by at least 10 fold[2].

In Vivo: The pharmacokinetics of TAK-733 is evaluated in nude mouse, rat, dog and monkey. Low clearance and high oral bioavailability are observed in all species. TAK-733 demonstrates broad antitumor activity in mouse xenograft models of human cancer including models of melanoma, colorectal, NSCLC, pancreatic and breast cancer[1]. Daily oral administration of 1, 3, 10, and 30 mg/kg of TAK-733 for 14 days (Days 10 to 23) results in tumor growth delay in the A375 cell-implanted mice (5/group). TAK-733 (35, 70, 100, and 160 mg/kg) also significantly inhibits tumor growth on an intermittent dosing schedule of 3 days per week for 2 weeks (Days 10, 13, 15, 17, 20, and 22). Three partial regressions (PR), a 60% response rate, are observed in mice administered with 30 mg/kg of TAK-733 daily and in mice administered with 160 mg/kg of TAK-733 intermittently. Responses, CR (complete regression) and partial regressions (PR) are also observed in mice administered with 70, 100, and 160 mg/kg of TAK-733 intermittently. The tumor regression rate is more pronounced with the intermittent administration regimen; the greatest reduction in tumor volume is observed at 160 mg/kg (57.29%), versus a maximum reduction of 46.97% at 30 mg/kg once daily. By the last day of administration, tumor growth is significantly (p[2].