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

Pilaralisib

Catalog No: tcsc1546

Available Sizes

Size: 5mg

Size: 10mg

Size: 50mg

Specifications

CAS No:
934526-89-3

Formula:
$C_{25}H_{25}ClN_6O_4S$

Pathway:
PI3K/Akt/mTOR

Target:
PI3K

Purity / Grade:
>98%

Solubility:
DMSO : 6 mg/mL (11.09 mM; Need ultrasonic and warming)

Alternative Names:
XL-147;SAR245408

Observed Molecular Weight:
541.02

Product Description

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Pilaralisib (XL147; SAR245408) is a potent and highly selective class I **PI3K**s inhibitor with **IC_{50}**s of 39 nM, 383 nM, 23 nM and 36 nM for PI3Kα, PI3Kβ, PI3Kγ, and PI3Kδ.

IC50 & Target: IC50: 39 nM (PI3Kα), 383 nM (PI3Kβ), 36 nM (PI3Kδ), 23 nM (PI3Kγ), 6974 nM (VPS34), 4750 nM (DNA-PK)[1]

In Vitro: Pilaralisib (XL147) displays potent inhibitory activity against Class I PI3K isoforms p110α, p110δ, and p110γ, with IC_{50}s of 39, 36, and 23 nM, respectively. Pilaralisib (XL147) is less potent against the remaining Class I isoform, p110β, with an IC_{50} value of 383 nM. The IC_{50} value for inhibition of PI3Kα by Pilaralisib (XL147) is determined at various concentrations of ATP, revealing XL147 to be an ATP-competitive inhibitor with an equilibrium inhibition constant (K_i) value of 42 nM. Pilaralisib (XL147) has relatively weak inhibitory activity toward the class III PI3K vacuolar sorting protein 34 (VPS34; IC_{50} value of ~7.0 M) and the PI3K-related DNA-dependent protein kinase (DNA-PK; IC_{50} value of 4.75 μM). In an mTOR kinase immunoprecipitation assay using cell lysates, Pilaralisib (XL147) does not inhibit mTOR activity toward the physiologic substrate protein eukaryotic translation initiation factor 4E-binding protein 1 (4EBP1; IC_{50}>15 μM). Consistent with its inhibitory activity against purified PI3K proteins, Pilaralisib (XL147) inhibits EGF-induced PIP_3 production in PC-3 and MCF7 cells in serum-free medium with IC_{50}s of 220 and 347 nM, respectively. The ability of Pilaralisib (XL147) to inhibit phosphorylation of key signaling proteins downstream of PI3K is examined by assessing its effects on EGF-stimulated phosphorylation of AKT and on nonstimulated phosphorylation of S6 in PC-3 cells in serum-free media by cell-based ELISA. Pilaralisib (XL147) inhibits these activities with IC_{50}s of 477 and 776 nM, respectively[1].

In Vivo: The ability of Pilaralisib (XL147) to inhibit this endogenous phosphorylation of AKT, p70S6K, and S6 is examined following a single oral dose of 10, 30, 100, or 300 mg/kg. The tumors are harvested 4, 24, or 48 hours postdose and homogenized in lysis buffer. Tumor lysates from each animal (n=4) are then pooled for each group and analyzed for levels of total and phosphorylated AKT, p70S6K, and S6 by Western immunoblotting. Administration of Pilaralisib (XL147) causes a dose-dependent decrease in phosphorylation of AKT, p70S6K, and S6 in the tumors, reaching a maximum of 81% inhibition of AKT phosphorylation at 300 mg/kg at 4 hours. The dose-response relationships derived from the 4-hour time point predict 50% inhibition of AKT, p70S6K, and S6 phosphorylation at doses of approximately 100 mg/kg ($pAKT^{T308}$), 54 mg/kg ($pAKT^{S473}$), 71 mg/kg (p-p70S6K), and 103 mg/kg (pS6). The inhibition of AKT, p70S6K, and S6 phosphorylation in MCF7 tumors following a 100 mg/kg dose of Pilaralisib (XL147) is maximal at 4 hours, reaching 55% to 75%; however, the level of inhibition decreased to 8% to 45% by 24 hours, and only minimal or no inhibition was evident by 48 hours. Following a 300 mg/kg dose of Pilaralisib (XL147), inhibition is also maximal at 4 hours (65%-81%). However, in contrast with the 100 mg/kg dose, inhibition at 24 hours (51%-78%) is almost comparable with that seen at 4 hours, and partial inhibition (25%-51%) persisted through 48 hours[1].