

Product Data Sheet

Product Name: Pilaralisib

Cat. No.: GC36917

Chemical Properties

Cas. No. 934526-89-3

SMILES CC(C)(N)C(NC1=CC=CC(S(=O)(=O)NC2=NC3=CC=CC=C3N=C2NC4=CC(OC)=CC=C4Cl)=O)=C1)=O

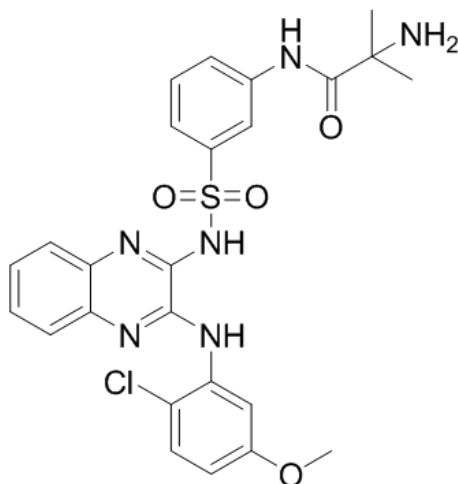
Formula C25H25ClN6O4S M.Wt 541.02

Solubility DMSO: ≥ 100 mg/mL (184.84 mM); Storage Store at -20°C
Water: < 0.1 mg/mL (insoluble)

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Background

Pilaralisib (XL147; SAR245408) is a potent and highly selective class I PI3Ks inhibitor with IC₅₀s of 39 nM, 383 nM, 23 nM and 36 nM for PI3K α , PI3K β , PI3K γ , and PI3K δ . PI3K α |39 nM (IC₅₀)|PI3K β |383 nM (IC₅₀)|PI3K δ |36 nM (IC₅₀)|PI3K γ |23 nM (IC₅₀)|Vps34|6974 nM (IC₅₀)|DNA-PK|4750 nM (IC₅₀)

Caution: Product has not been fully validated for medical applications. For research use only.

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Pilaralisib (XL147) displays potent inhibitory activity against Class I PI3K isoforms p110 α , p110 δ , and p110 γ , with IC₅₀s of 39, 36, and 23 nM, respectively. Pilaralisib (XL147) is less potent against the remaining Class I isoform, p110 β , with an IC₅₀ value of 383 nM. The IC₅₀ value for inhibition of PI3K α 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; IC₅₀ value of ~7.0 M) and the PI3K-related DNA-dependent protein kinase (DNA-PK; IC₅₀ value of 4.75 μ M). 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; IC₅₀>15 μ M). Consistent with its inhibitory activity against purified PI3K proteins, Pilaralisib (XL147) inhibits EGF-induced PIP3 production in PC-3 and MCF7 cells in serum-free medium with IC₅₀s 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 IC₅₀s of 477 and 776 nM, respectively[1].

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 (pAKTT308), 54 mg/kg (pAKTS473), 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].

[1]. Foster P, et al. The Selective PI3K Inhibitor XL147 (SAR245408) Inhibits Tumor Growth and Survival and Potentiates the Activity of Chemotherapeutic Agents in Preclinical Tumor Models. Mol

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