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Voxtalisib

Catalog No: tcsc3163

Available Sizes

Size: 5mg

Size: 10mg

Size: 25mg

Size: 50mg

Size: 100mg

Specifications

CAS No:
934493-76-2

Formula:
$C_{13}H_{14}N_6O$

Pathway:
PI3K/Akt/mTOR;PI3K/Akt/mTOR

Target:
PI3K;mTOR

Purity / Grade:
>98%

Solubility:
DMSO : 16 mg/mL (59.20 mM; Need ultrasonic and warming)

Alternative Names:
XL765;SAR245409

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Observed Molecular Weight:
270.29

Product Description

Voxtalisib (XL-765) is a potent **PI3K** inhibitor, which has a similar activity toward class I PI3K (**IC_{50}**s=39, 113, 9 and 43 nM for **p110α**, **p110β**, **p110γ** and **p110δ**, respectively), also inhibits DNA-PK (IC_{50}=150 nM) and mTOR (IC_{50}=157 nM). Voxtalisib (XL-765) inhibits **mTORC1** and **mTORC2** with **IC_{50}**s of 160 and 910 nM, respectively.

IC50 & Target: IC50: 39 nM (p110α), 113 nM (p110β), 9 nM (p110γ), 43 nM (p110δ), 150 nM (DNA-PK), 157 nM (mTOR)[1]

IC50:160 nM (mTORC1), 910 nM (mTORC2)[2]

In Vitro: Voxtalisib (XL-765) displays potent inhibitory activity against class I PI3K isoforms p110α, p110β, p110δ, and p120γ, with IC_{50}s of 39, 110, 43, and 9 nM, respectively. The IC_{50} value for inhibition of PI3Kα by Voxtalisib (XL-765) is determined at various concentrations of ATP, revealing Voxtalisib (XL-765) be an ATP-competitive inhibitor with an equilibrium inhibition constant (K_i) value of 13 nM. Voxtalisib (XL-765) also inhibits mTOR (IC_{50}s of 160 and 910 nM for mTORC1 and mTORC2, respectively) in an immune-complex kinase assay and the PI3K-related kinase DNA-PK (IC_{50} value of 150 nM). In contrast, Voxtalisib (XL-765) has relatively weak inhibitory activity toward the class III PI3K vacuolar sorting protein 34 (VPS34; IC_{50} value of ~9.1 μM). Consistent with its inhibitory activity against purified PI3K proteins, SAR245409 inhibits EGF-induced PIP_3 production in PC-3 and MCF7 cells with IC_{50}s of 290 and 170 nM, respectively. The ability of Voxtalisib (XL-765) 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 by cell-based ELISA. Voxtalisib (XL-765) inhibits these activities with IC_{50}s of 250 and 120 nM, respectively. In MCF7 and PC-3 cells, Voxtalisib (XL-765) inhibits proliferation (monitored by BrdUrd incorporation) with IC_{50}s of 1,070 and 1,840 nM, respectively. To further characterize the effects of Voxtalisib (XL-765) on tumor cell growth, an assay monitoring the anchorage-independent growth of PC-3 and MCF7 cells in soft agar over a 14-day period is used. SAR245409 inhibits colony growth with an IC_{50} value of 270 nM in PC-3 cells and 230 nM in MCF7 cells[2].

In Vivo: Oral administration of Voxtalisib (XL-765) causes a dose-dependent decrease of phosphorylation of AKT, p70S6K, and S6 in the tumors, reaching a maximum of 84% inhibition of S6 phosphorylation at 30 mg/kg at 4 hours. The dose-response relationships derive from the 4 hours time point predict 50% inhibition of AKT, p70S6K, and S6 phosphorylation to occur at doses of 19 mg/kg ($pAKT^{T308}$ and $pAKT^{S473}$), 51 mg/kg (p-p70S6K), and 18 mg/kg (pS6). Inhibition of AKT, p70S6K, and S6 phosphorylation in MCF7 tumors following a 30 mg/kg dose of Voxtalisib (XL-765) is maximal at 4 hours, reaching 61% to 84%; however, the level of inhibition decreases to 0% to 42% by 24 hours, and minimal or no inhibition is evident by 48 hours. Following a 100 mg/kg dose of Voxtalisib (XL-765), inhibition is also maximal at 4 hours (52%-75%)[2].

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