

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

Observed Molecular Weight:

270.29

Product Description

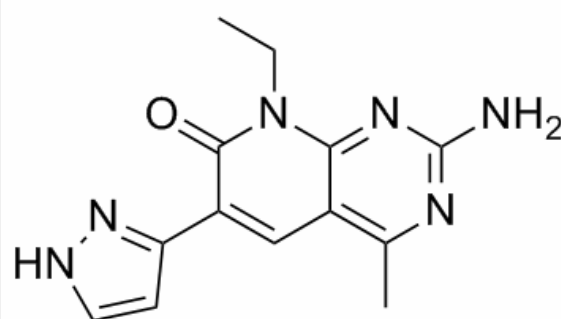
Voxtalib (XL-765) is a potent **PI3K** inhibitor, which has a similar activity toward class I PI3K (**IC₅₀**s=39, 113, 9 and 43 nM for **p110α**, **p110β**, **p110γ** and **p110δ**, respectively), also inhibits DNA-PK (**IC₅₀**=150 nM) and mTOR (**IC₅₀**=157 nM). Voxtalib (XL-765) inhibits **mTORC1** and **mTORC2** with **IC₅₀**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: Voxtalib (XL-765) displays potent inhibitory activity against class I PI3K isoforms p110α, p110β, p110δ, and p120γ, with **IC₅₀**s of 39, 110, 43, and 9 nM, respectively. The **IC₅₀** value for inhibition of PI3Kα by Voxtalib (XL-765) is determined at various concentrations of ATP, revealing Voxtalib (XL-765) be an ATP-competitive inhibitor with an equilibrium inhibition constant (**K_i**) value of 13 nM. Voxtalib (XL-765) also inhibits mTOR (**IC₅₀**s of 160 and 910 nM for mTORC1 and mTORC2, respectively) in an immune-complex kinase assay and the PI3K-related kinase DNA-PK (**IC₅₀** value of 150 nM). In contrast, Voxtalib (XL-765) has relatively weak inhibitory activity toward the class III PI3K vacuolar sorting protein 34 (VPS34; **IC₅₀** value of ~9.1 μM). Consistent with its inhibitory activity against purified PI3K proteins, SAR245409 inhibits EGF-induced PIP₃ production in PC-3 and MCF7 cells with **IC₅₀**s of 290 and 170 nM, respectively. The ability of Voxtalib (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. Voxtalib (XL-765) inhibits these activities with **IC₅₀**s of 250 and 120 nM, respectively. In MCF7 and PC-3 cells, Voxtalib (XL-765) inhibits proliferation (monitored by BrdUrd incorporation) with **IC₅₀**s of 1,070 and 1,840 nM, respectively. To further characterize the effects of Voxtalib (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 **IC₅₀** value of 270 nM in PC-3 cells and 230 nM in MCF7 cells^[2].

In Vivo: Oral administration of Voxtalib (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 Voxtalib (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 Voxtalib (XL-765), inhibition is also maximal at 4 hours (52%-75%)^[2].



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