

Ipatasertib dihydrochloride

Catalog No: tcsc4037



Available Sizes

Size: 5mg

Size: 10mg

Size: 50mg

Size: 100mg



Specifications

CAS No:

1396257-94-5

Formula:

$C_{24}H_{34}Cl_3N_5O_2$

Pathway:

PI3K/Akt/mTOR

Target:

Akt

Purity / Grade:

>98%

Solubility:

H₂O : ≥ 41 mg/mL (77.22 mM)

Alternative Names:

GDC-0068 (dihydrochloride);RG-7440 dihydrochloride

Observed Molecular Weight:

530.92

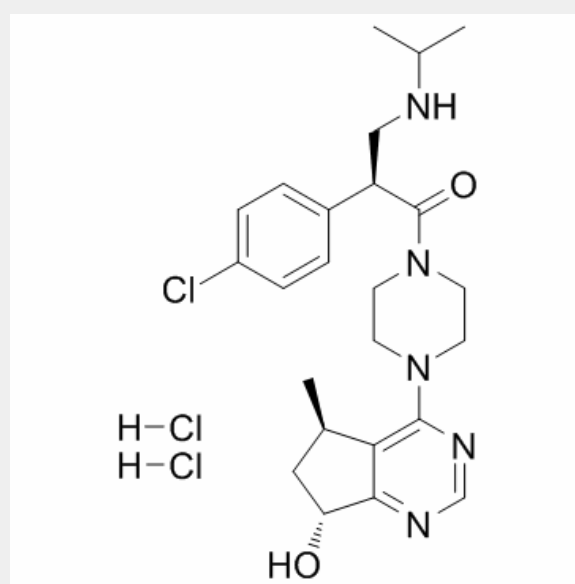
Product Description

Ipatasertib dihydrochloride (GDC-0068 dihydrochloride) is a highly selective pan-**Akt** inhibitor targeting **Akt1/2/3** with **IC₅₀** of 5/18/8 nM, 620-fold selectivity over PKA.

IC₅₀ & Target: IC₅₀: 5±7 nM (Akt1), 18±10 nM (Akt2), 8±9 nM (Akt3) 3100±705 nM (PKA)^[1]

In Vitro: Ipatasertib shows more than 600 and more than 100-fold selectivity for Akt1 in IC₅₀ against the closely related kinases PKA and p70S6K, respectively. When tested at 1 μM in a panel of 230 protein kinases, which includes 36 human AGC family members, Ipatasertib inhibits only 3 other kinases by more than 70% at 1 μM concentration (PRKG1α, PRKG1β, and p70S6K). IC₅₀s measured for these 3 kinases are 98, 69, and 860 nM, respectively. Thus, with the exception of PKG1 (relative to which Ipatasertib is >10-fold more selective for Akt1), Ipatasertib displays a more than 100-fold selectivity for Akt1 over the next most potently inhibited non-Akt kinase, p70S6K, in the screening kinase panel. The relationship between pharmacokinetics (PK) and pharmacodynamics (PD) of Ipatasertib is investigated in 3 xenograft models that showed dose-dependent response to drug treatment: MCF7-neo/HER2, TOV-21G.x1, and LNCaP. The mean cell viability IC₅₀ of Ipatasertib in these 3 cell lines is 2.56, 0.44, and 0.11 μM, respectively^[2].

In Vivo: Ipatasertib is typically efficacious in xenograft models in which Akt is activated because of genetic alterations including PTEN loss, PIK3CA mutations/amplifications, or HER2 overexpression. In these models, tumor growth delay, stasis, or regression is achieved at or below 100 mg/kg daily oral dose, which is the maximum dose tested in immunocompromised mice that is well tolerated. When tested in vivo, daily dosing of Ipatasertib in combination with Docetaxel induces tumor regression and stasis in the PC-3 and MCF7-neo/HER2 xenograft models, at doses where each single agent is ineffective or only causes modest tumor growth delay. Similarly, increased TGI is observed in the OVCAR3 ovarian cancer xenograft model when Ipatasertib is combined with Carboplatin. The combination of Ipatasertib with Docetaxel or Carboplatin is tolerated with less than 5% body weight loss when compared with treatment with each chemotherapeutic agent alone^[2].



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