Product Data Sheet

Chemical Properties

**Product Name:** GDC-0068 (RG7440)  
**Cas No.:** 1001264-89-6  
**M.Wt:** 458  
**Formula:** C24H32ClN5O2  
**Synonyms:** GDC0068,RG7440,CS0975  
**Chemical Name:** (2S)-2-(4-chlorophenyl)-1-[4-[(5R,7R)-7-hydroxy-5-methyl-6,7-dihydro-5H-cyclopenta[d]pyrimidin-4-yl]piperazin-1-yl]-3-(propan-2-ylamino)propan-1-one  
**Canonical SMILES:** CC1CC(C2=C1C(=NC=N2)N3CCN(CC3)=O)C(CNC(C(C)C)C4=CC=C(C=C4)Cl)O  
**Solubility:** ≥22.9mg/mL in DMSO  
**Storage:** Desiccate at -20°C  
**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.  
**Shopping Condition:** Evaluation sample solution: ship with blue ice  
All other available size: ship with RT, or blue ice upon request

Biological Activity

**Targets:** PI3K/Akt/mTOR Signaling  
**Pathways:** Akt  
**Description:** GDC-0068 (RG7440) is a highly selective small molecule inhibitor of Akt with IC50s of 5, 18 and 8 nM for Akt1, Akt2 and Akt3. The PI3K-AKT pathway regulates cell growth, survival and tumorigenesis. GDC-0068 binds to and blocks the activation of AKT, which result in cell cycle arrest, inhibition of tumor cell proliferation and induction of tumor cell death. PI3K-AKT is
pathway frequently activated in tumors, thus tumors with PTEN or PI3K mutations, which lead to activation of AKT are with high sensitivity to GDC-0068. GDC-0068 is now used for the treatment of human cancers.

Reference:
1. Discovery and preclinical pharmacology of a selective ATP-competitive Akt inhibitor (GDC-0068) for the treatment of human tumors. JF Blake, R Xu, JR Bencsik, D Xiao... - Journal of medicinal 2012

Protocol

Cell experiment:
- **Cell lines**: PC-3, BT474M1 and IGROV-1 cell lines
- **Preparation method**: The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20° C for several months.
- **Reacting conditions**: 1 h; 25 μmol/L
- **Applications**: The biologic activity of GDC-0068 was evaluated in cell-based assays in vitro. Similar to other ATP-competitive Akt inhibitors, GDC-0068 induced a dose-dependent increase in Akt phosphorylation at both Thr308 (T308) and Ser 473 (S473) residues in all cell lines tested, including lines in which the PI3K/Akt pathway is activated, such as PC-3 (PTEN homozygous deletion mutant, prostate), BT474M1 (PIK3CAK111N mutant and HER2-amplified, breast), IGROV-1 (PTENT319fsX1/Y155C and PIK3CA1069 W, ovarian).

Animal experiment [3]:
- **Animal models**: Nude mice
- **Dosage form**: 100 mg/kg; Oral taken
- **Applications**: The in vitro sensitivity profile of GDC-0068 was recapitulated in vivo in xenograft models representing a spectrum of cancer types including prostate, breast, ovarian, colorectal, non–small cell lung, glioblastoma, and melanoma. GDC-0068 was typically efficacious in xenograft models in which Akt was activated because of genetic alterations including PTEN loss, PIK3CA mutations/amplifications, or
HER2 overexpression. In these models, tumor growth delay, stasis, or regression was achieved at or below 100 mg/kg daily oral dose, which was the maximum dose tested in immunocompromised mice that was well tolerated.

Other notes

Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

Reference:

Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Short-term storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.