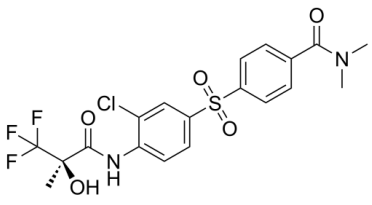
Data Sheet

Product Name:	AZD7545
Cat. No.:	CS-1740
CAS No.:	252017-04-2
Molecular Formula:	$C_{19}H_{18}ClF_3N_2O_5S$
Molecular Weight:	478.87
Target:	PDHK
Pathway:	Metabolic Enzyme/Protease
Solubility:	DMSO : ≥ 46 mg/mL



BIOLOGICAL ACTIVITY:

AZD7545 is a potent, competitive, selective **PDHK2** (pyruvate dehydrogenase kinase 2) inhibitor with **IC_{50}**s of 36.8 nM, 6.4 nM for **PDHK1** and **PDHK2**, respectively[1]. IC50 & Target: IC50: 6.4 nM (PDHK2), 36.8 nM (PDHK1)[1] ***In Vitro:*** AZD7545 (10 μM; 90 hours for $BRAF^{V600E}$ human melanoma cells and 120 hours for $NRAS^{mut}$ human melanoma cells) specifically suppresses growth of cells harboring BRAF and NRAS mutations as well as in inhibitor-resistant human melanoma[2].
In Vivo: A single dose of AZD7545 (Oral administration; 10 mg/kg once a day (08:00 h) or Twice a day (08:00 and 18:00 h); for 7 days) to Wistar rats increases the proportion of liver PDH in its active, dephosphorylated form in a dose-related manner. A single dose of 10 mg/kg also significantly elevates muscle PDH activity in obese Zucker (fa/fa) rats[3].

PROTOCOL (Extracted from published papers and Only for reference)

nimal administration [1] AZD7545 is given orally to Wistar rats and 3 h later tissues are removed to assay for PDH activity. Total PDH activity is measured following incubation of extracts with PDH phosphatase and bivalent cations and PDH activity is expressed as a percentage of the total activity. Fasted rats are deprived of food for 14 h prior to administration of the compound. Results are means±S.E.M. from six animals. *, ** and *** indicate significant differences (P<0.05, P<0.01, P<0.001 respectively) from the corresponding values for control animals.

References:

[1]. Morrell JA, et al. AZD7545 is a selective inhibitor of pyruvate dehydrogenase kinase 2. Biochem Soc Trans. 2003 Dec;31(Pt 6):1168-70.

[2]. Cesi G et al. ROS production induced by BRAF inhibitor treatment rewires metabolic processes affecting cell growth of melanoma cells. Mol Cancer. 2017 Jun 8;16(1):102.

[3]. Mayers RM, et al. AZD7545, a novel inhibitor of pyruvate dehydrogenase kinase 2 (PDHK2), activates pyruvate dehydrogenase in vivo and improves blood glucose control in obese (fa/fa) Zucker rats. Biochem Soc Trans. 2003 Dec;31(Pt 6):1165-7.

CAIndexNames:

Benzamide, 4-[[3-chloro-4-[[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]amino]phenyl]sulfonyl]-N,N-dimethyl-

SMILES:

O=C(N(C)C)C1=CC=C(S(=O)(C2=CC=C(NC([C@@](C)(O)C(F)(F)F)=O)C(Cl)=C2)=O)C=C1

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

Tel: 610-426-3128 Fax: 888-484-5008 E-mail: sales@ChemScene.com
Address: 1 Deer Park Dr, Suite F, Monmouth Junction, NJ 08852, USA