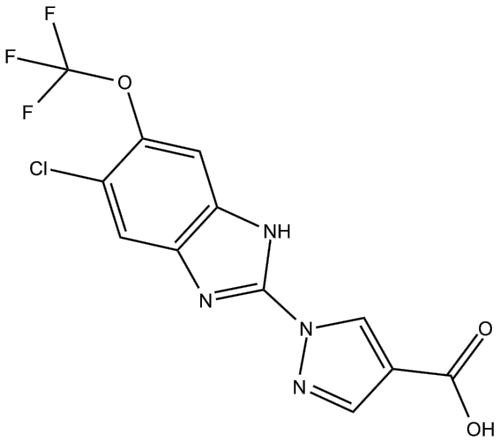
Product Data Sheet

Product Name: JNJ-42041935
Cat. No.: GC15379

Chemical Properties

Cas. No.	1193383-09-3		
Chemical Name	1-[6-chloro-5-(trifluoromethoxy)-1H-benzimidazol-2-yl]-1H-pyrazole-4-carboxylic acid		
SMILES	ClC1=CC2=C(NC(N3C=C(C(O)=O)C=N3)=N2)C=C1OC(F)(F)F		
Formula	$C_{12}H_6ClF_3N_4O_3$	M.Wt	346.7
Solubility	≤10mg/ml in ethanol;30mg/ml in DMSO;25mg/ml in dimethyl formamide	Storage	Store 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.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure			

Protocol

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Kinase experiment: The potency of JNJ-42041935 for inhibition of the structurally related enzyme FIH is assessed by methods similar to those described for PHD2. In brief, activity of FIH is determined using purified glutathione transferase-tagged full-length FIH amino acids 1 to 350 and a synthetic HIF-1α peptide corresponding to residues Asp788 to Leu822. Compounds are preincubated with 17.1 nM FIH for 30 min, followed by a 10-min incubation with 1 μM [2-14C]2-oxoglutarate, in the presence of 10 μM FeNH4SO4 in reaction buffer. The selectivity of JNJ-42041935 for inhibition of a range of other targets available for testing in commercial assays is also assessed at concentrations of 1 and 10 μM[1].

Animal experiment: Mice: JNJ-42041935 is administered at doses of 30, 100, and 300 μmol/kg to Balb/C mice . Plasma is collected 6 h after the dose. Plasma erythropoietin concentration is measured. The hematological effects of JNJ-42041935 are assessed by administering the 100 μmol/kg dose on 5 consecutive days and collecting blood anticoagulated with EDTA on day 8 (3 days after the last dose) [1].

References:

[1]. Barrett TD, et al. Pharmacological characterization of 1-(5-chloro-6-(trifluoromethoxy)-1H-benzoimidazol-2-yl)-1H-pyrazole-4-carboxylic acid (JNJ-42041935), a potent and selective hypoxia-inducible factor prolyl hydroxylase inhibitor. Mol Pharmacol. 2011

Background

JNJ-42041935 is a potent, competitive and selective inhibitor of prolyl hydroxylase PHD; inhibits PHD1, PHD2, and PHD3 with pKi values of 7.91±0.04, 7.29 ±0.05, and 7.65±0.09, respectively.

JNJ-42041935 is the most potent inhibitor of PHD2181–417 with a pIC50 value of 7.0±0.03. JNJ-42041935 also inhibits full-length PHD1, PHD2, andPHD3 enzymes (pKi values 7.91±0.04, 7.29 ±0.05, and 7.65±0.09, respectively) [1].

JNJ-42041935 is used to compare the effect of selective inhibition of PHD to intermittent, high doses

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(50 µg/kg i.p.) of an exogenous erythropoietin receptor agonist in an inflammation induced anemia model in rats. JNJ-42041935 (100 µmol/kg, once a day for 14 days) is effective in reversing inflammation induced anemia, whereas erythropoietin has no effect. Administration of JNJ-42041935 (100 µmol/kg p.o.) for 5 consecutive days resulted in a 2-fold increase in reticulocytes, an increase in hemoglobin by 2.3 g/dl, and an increase in the hematocrit of 9%. Two hours after oral administration of 300 µmol/kg JNJ-42041935, the bioluminescence over the peritoneal area is increased by 2.2 ± 0.3-fold relative to luciferase-treated vehicle controls in the mouse [1].

References:

[1]. Barrett TD, et al. Pharmacological characterization of 1-(5-chloro-6-(trifluoromethoxy)-1H-benzoimidazol-2-yl)-1H-pyrazole-4-carboxylic acid (JNJ-42041935), a potent and selective hypoxia-inducible factor prolyl hydroxylase inhibitor. Mol Pharmacol. 2011

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA