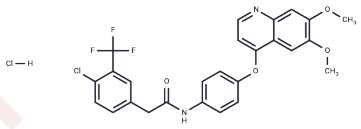
Data Sheet (Cat.No.T19220)

TargetMol

c-Kit-IN-3 hydrochloride

Chemical Properties



CAS No. :

Formula: C26H21Cl2F3N2O4

Molecular Weight: 553.36

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	c-Kit-IN-3 hydrochloride is a potent and selective c-KIT kinase inhibitor (IC50s: 4 nM, 8 nM for c-KIT wt, and c-KIT T670I).
Targets(IC50)	Others
In vitro	c-Kit-IN-3 hydrochloride (Compound 18; 0.1-10 μM; 6 days; primary GIST patient cells) exhibits dose-dependent antiproliferative effects. c-Kit-IN-3 (0.01-1 μM; 24 hours; GIST-T1, GIST-T1-T670I, and GIST-5R cells) treatment induces dose-dependent cell apoptotic death. c-Kit-IN-3 (0.01-1 μM; 24 hours; GIST-T1, GIST-T1-T670I, and GIST-5R cells) treatment arrests the cell cycle into the G0/G1 phase in all of these three cell lines. c-Kit-IN-3 (0-1 μM; 24 hours) blocks the autophosphorylation of c-KIT pY703, pY719, and pY823 in GIST-T1, GIST-T1-T670I, and GIST-5R, respectively, cells at a concentration of 30 nM and inhibits the downstream signaling mediators pAKT (T308/S473), pS6 (S235/236), and pERK (T202/204). c-Kit-IN-3 potently inhibits the activity of CSF1R (IC50: 18 nM), PDGFRα (IC50: 25 nM), RET (IC50: 34 nM), and it relatively less potently inhibits DDR1 (IC50: 135 nM), FLT4 (IC50: 121 nM), and PDGFRβ (IC50: 97 nM). c-Kit-IN-3 (0.006 μM-1.37 μM) potently inhibits the growth of c-KIT-dependent GIST cancer cells, such as GIST-T1 (IC50: 0.006 μM); GIST-882 (IC50: 0.013 μM); GIST-T1-T670I (IC50 : 0.011 μM); GIST-5R (IC50: 0.073 μM); GIST-48B (IC50: 1.37 μM), respectively.
In vivo	c-Kit-IN-3 hydrochloride (oral gavage; 20-100 mg/kg/day; for 11 days; female BALB/C-nu mice) treatment dose-dependently inhibits the tumor progression. c-Kit-IN-3 (1 mg/kg iv for mice, rats, dog; 10 mg/kg p.o. for mice, rats; and 5 mg/kg p.o. for dog) has T1/2 of 4.5 h, 6.4 h, 19.4 h for mice, rats and dogs, respectively. And it possesses acceptable bioavailability in mice (F = 43%), rats (F = 50%), and dogs (F = 81%).

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.8071 mL	9.0357 mL	18.0714 mL
5 mM	0.3614 mL	1.8071 mL	3.6143 mL
10 mM	0.1807 mL	0.9036 mL	1.8071 mL
50 mM	0.0361 mL	0.1807 mL	0.3614 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Wu Y, et al. Discovery of 2-(4-Chloro-3-(trifluoromethyl)phenyl)-N-(4-((6,7-dimethoxyquinolin-4-yl)oxy)phenyl) acetamide (CHMFL-KIT-64) as a Novel Orally Available Potent Inhibitor against Broad-Spectrum Mutants of c-KIT Kinase for Gastrointestinal Stromal Tumors. J Med Chem. 2019 Jul 11;62(13):6083-6101.