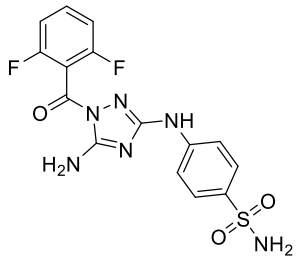
Product data sheet

MedKoo Cat#: 406161 Name: JNJ-7706621 CAS#: 443797-96-4 Chemical Formula: $C_{15}H_{12}F_2N_6O_3S$ Exact Mass: 394.06597 Molecular Weight: 394.36	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
JNJ-7706621 is a novel cell cycle inhibitor that showed potent inhibition of several cyclin-dependent kinases (CDK) and Aurora kinases and selectively blocked proliferation of tumor cells of various origins but was about 10-fold less effective at inhibiting normal human cell growth in vitro. In human cancer cells, treatment with JNJ-7706621 inhibited cell growth independent of p53, retinoblastoma, or P-glycoprotein status; activated apoptosis; and reduced colony formation. At low concentrations, JNJ-7706621 slowed the growth of cells and at higher concentrations induced cytotoxicity.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	79	200.32

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.54 mL	12.68 mL	25.36 mL
5 mM	0.51 mL	2.54 mL	5.07 mL
10 mM	0.25 mL	1.27 mL	2.54 mL
50 mM	0.05 mL	0.25 mL	0.51 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Matsuhashi A, Ohno T, Kimura M, Hara A, Saio M, Nagano A, Kawai G, Saitou M, Takigami I, Yamada K, Okano Y, Shimizu K. Growth suppression and mitotic defect induced by JNJ-7706621, an inhibitor of cyclin-dependent kinases and aurora kinases. Curr Cancer Drug Targets. 2012 Jul;12(6):625-39. doi: 10.2174/156800912801784839. PMID: 22463590.

2. Emanuel S, Rugg CA, Gruninger RH, Lin R, Fuentes-Pesquera A, Connolly PJ, Wetter SK, Hollister B, Kruger WW, Napier C, Jolliffe L, Middleton SA. The in vitro and in vivo effects of JNJ-7706621: a dual inhibitor of cyclin-dependent kinases and aurora kinases. Cancer Res. 2005 Oct 1;65(19):9038-46. doi: 10.1158/0008-5472.CAN-05-0882. PMID: 16204078.

In vivo study

1. Emanuel S, Rugg CA, Gruninger RH, Lin R, Fuentes-Pesquera A, Connolly PJ, Wetter SK, Hollister B, Kruger WW, Napier C, Jolliffe L, Middleton SA. The in vitro and in vivo effects of JNJ-7706621: a dual inhibitor of cyclin-dependent kinases and aurora kinases. Cancer Res. 2005 Oct 1;65(19):9038-46. doi: 10.1158/0008-5472.CAN-05-0882. PMID: 16204078.

7. Bioactivity

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Biological target:

JNJ-7706621 is a potent aurora kinase inhibitor, and also inhibits CDK1 and CDK2, with IC50s of 9 nM, 3 nM, 11 nM, and 15 nM for CDK1, CDK2, aurora-A and aurora-B, respectively.

In vitro activity

The inhibitor arrested various cells at G2 phase at low concentration, and at both G1 and G2 phases at high concentration. JNJ-7706621 did not prevent localization of Aurora A to the spindle poles, but did inhibit other centrosomal proteins such as TOG, Nek2, and TACC3 in early mitotic phase. Similarly, the drug did not prevent localization of Aurora B to the kinetochore, but did inhibit other chromosomal passenger proteins such as Survivin and INCENP. In the cells exposed to JNJ-7706621 after nocodazole release, Aurora B, INCENP, and Survivin became relocated to the peripheral region of chromosomes, but Plk1 and Prc1 were localized on microtubules in later mitotic phase. Treatment of nocodazole-synchronized cells with JNJ-7706621 was able to override mitotic arrest by preventing spindle checkpoint signaling, resulting in failure of chromosome alignment and segregation. Injection of the drug significantly inhibited the growth of TC135 Ewing's sarcoma cells transplanted into athymic mice by cell cycle arrest and apoptosis. JNJ-7706621 is a unique inhibitor regulating cell cycle progression at multiple points, suggesting that it could be useful for cell cycle analysis and therapy of various cancers, including Ewing's sarcoma.

Reference: Curr Cancer Drug Targets. 2012 Jul;12(6):625-39. https://www.eurekaselect.com/98883/article

In vivo activity

The antitumor efficacy of JNJ-7706621 was examined in an A375 melanoma human tumor xenograft model. Two dose levels, 100 and 125 mg/kg, were evaluated and mean tumor size was calculated from six animals per group. Figure 4A shows tumor sizes for the 125 mg/kg dose under various schedules. Daily dosing was the most efficacious and caused tumor regression; however, this schedule could only be tolerated for 22 days before toxicity emerged (Table 2). There were five treatment-related deaths in this dose group; all occurred between days 22 and 39 and were not preceded by detectable weight loss. The 7 on/7 off schedule was nearly as effective as the daily dosing regimen with 93% tumor growth inhibition (TGI) and all animals survived to the end of the study (Fig. 4A; Table 2). The next most effective schedule at 125 mg/kg was 7 on/14 off (88% TGI) followed by Q3D and Q4D, with 69% and 43% TGI, respectively, and all these schedules were well tolerated (Fig. 4A; Table 2). Identical dosing schedules were applied to evaluate the 100 mg/kg dose and the same pattern of efficacy was observed (Table 2). Several schedules and dose combinations resulted in equivalent efficacy. For example, the 125 mg/kg 7 on/7 off schedule and the 100 mg/kg QD schedule produced identical TGI values of 93% (Fig. 4B; Table 2). Figure 4C compares two different dosing schedules at the same dose level. Tumor growth was nearly flat under the QD regimen, whereas under the 7 on/7 off schedule, a pattern of tumor inhibition and regrowth was observed. A reduction in tumor size was apparent during periods of dosing (days 1-7, 14-21, and 29-35), and tumor regrowth was observed during periods of nondosing (days 8-14, 22-28, and 36-41). However, at a slightly higher dose level of 125 mg/kg but under the same schedule of 7 on/7 off, there was a persistent effect evident during dosing holidays with very little tumor regrowth (Fig. 4B). Analysis of the relationship between tumor size and dose indicates that the amount of inhibition of tumor growth was proportional to the total cumulative dose, regardless of the schedule. Figure 4D shows the average tumor size versus the total cumulative dose calculated on day 11 of the study. This relationship held true for analysis done at any time during the study (data not shown). These results identify suitable dosing regimens that could be applied in clinical trials.

Reference: Cancer Res. 2005 Oct 1;65(19):9038-46. http://cancerres.aacrjournals.org/cgi/pmidlookup?view=long&pmid=16204078