

Product Data Sheet

Product Name: CVT-313

Cat. No.: GC18028

Chemical Properties

Cas. No. 199986-75-9

Chemical Name 2-[2-hydroxyethyl-[6-[(4-methoxyphenyl)methylamino]-9-propan-2-ylpurin-2-yl]amino]ethanol

SMILES CC(C)N1C=NC2=C1N=C(N=C2NCC3=CC=C(C=C3)OC)N(CCO)CCO

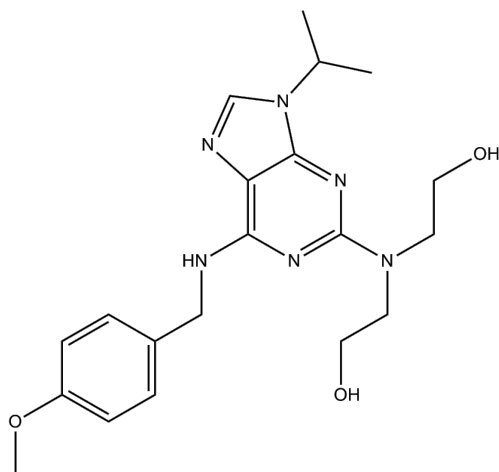
Formula $C_{20}H_{28}N_6O_3$ M.Wt 400.47

Solubility ≥ 20 mg/mL in DMSO, ≥ 51.1 mg/mL in EtOH with gentle warming 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

Cell experiment [1,2]:

Cell lines Human DLBCL cells

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

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Preparation method	The solubility of this compound in DMSO is >20 mg/mL. 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 condition	25 µM, 24 hr
Applications	CVT-313 inhibited cdk2 in several human DLBCL cells. Incubation of DLBCL cells with 25 µM CVT-313 reduced phosphorylation of endogenous Rb on Thr821. CVT-313 (48 and 72 hr) induced cell apoptosis in human DLBCL cells in a time-dependent manner. CVT-313 treatment did not result in cell cycle arrest at 20 hr or at 48 hr. Treatment of LY3, LY8 cells and LY18 cells with CVT-313 led to parallel changes in XIAP and Mcl-1 mRNA levels. In normal and tumor human/murine cell lines, CVT-313 inhibited cell proliferation with the IC ₅₀ ranged from 1.25 to 20 µM. CVT-313 (12.5 µM, 18 h) induced cell arrest at the G1/S and G2/M boundary. In nonsynchronized MRC-5 cells, treatment with CVT-313 (6.25 µM) for 36 h induced a 2 N DNA content. Treatment with CVT-313 (6.25 µM) for 4 or 8 h after serum stimulation inhibited Rb hyperphosphorylation.
Animal experiment [2]:	
Animal models	Injured rat carotid artery model of restenosis
Dosage form	0.75 and 0.25 mg/kg

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Application In the injured rat carotid artery model of restenosis, lower doses of CVT-313 (0.75 and 0.25 mg/kg) were less efficacious, reducing mean neointimal area by about 30%, whereas the lowest dose tested (0.025 mg/kg) did not achieve any significant reduction in neointimal area. Treatment with CVT-313 for 14 days blocked restenosis in the rat carotid model.

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.

References:

- [1]. Faber A C, Chiles T C. Inhibition of cyclin-dependent kinase-2 induces apoptosis in human diffuse large B-cell lymphomas[J]. Cell Cycle, 2007, 6(23): 2982-2989.
- [2]. Brooks E E, Gray N S, Joly A, et al. CVT-313, a specific and potent inhibitor of CDK2 that prevents neointimal proliferation[J]. Journal of Biological Chemistry, 1997, 272(46): 29207-29211.

Background

CVT-313 is a potent inhibitor of cyclin-dependent kinase 2 (CDK2) with IC₅₀ value of 0.5 μ M [1]. CDK2 is a serine/threonine kinase that is essential for the G1-S phase during cell division. CDK2 is an important target for prevention of aberrant cell proliferation [1]. In MRC-5 cells, CVT-313 inhibited Rb hyperphosphorylation in a time-dependant way and the cell cycle was arrested at the G1/S phase. Also, CVT-313 inhibited the growth of mouse, rat and human cells with IC₅₀ values from 1.25 to 20 mM [1]. In human diffuse large B-cell lymphoma (DLBCL) cells, CVT-313 reduced CDK2-mediated phosphorylation of the retinoblastoma gene product (Rb) on T821. Also, CVT-313 reduced the anti-apoptotic factor Myeloid cell leukemia-1 (Mcl-1) and induced apoptosis [2].

In the injured rat carotid artery model of restenosis, CVT-313 (1.25 mg/kg) reduced neointima formation by 80%. Moreover, Treatment animals with CVT-313, the neointimal areas were inhibited by at least 70%. These suggested that CDK2 was an antiproliferative target and CVT-313 is an ideal

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candidate for the treatment of proliferative diseases [1].

References:

[1]. Brooks EE, Gray NS, Joly A, et al. CVT-313, a specific and potent inhibitor of CDK2 that prevents neointimal proliferation. *J Biol Chem*, 1997, 272(46): 29207-29211.

[2]. Faber AC, Chiles TC. Inhibition of cyclin-dependent kinase-2 induces apoptosis in human diffuse large B-cell lymphomas. *Cell Cycle*, 2007, 6(23): 2982-2989.

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