

Product Data Sheet

Product Name: Senexin A

Cat. No.: GC37627

Chemical Properties

Cas. No. 1366002-50-7

SMILES N#CC1=CC=C2C(C(NCCC3=CC=CC=C3)=NC=N2)=C1

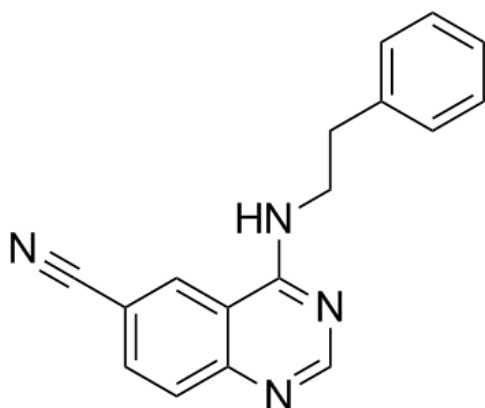
Formula $C_{17}H_{14}N_4$ M.Wt 274.32

Solubility DMSO: ≥ 100 mg/mL (364.54 mM) 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

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

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**Animal
experiment:**

Mice: Senexin A toxicity study is conducted by Taconic in C57BL/6 mice, using five mice per group treated with 20 mg/kg Senexin A or carrier (80% propylene glycol), with five daily i.p. injections. Mice are weighed on days 3 and 6, and killed on day 6. Organ weights are determined for brain, kidney, thymus, spleen, lung, and liver. Terminal blood samples are analyzed to determine the numbers of total white blood cells, neutrophils, lymphocytes, monocytes, eosinophils, and basophils[1].

References:

[1]. Porter DC, et al. Cyclin-dependent kinase 8 mediates chemotherapy-induced tumor-promoting paracrine activities. Proc Natl Acad Sci U S A. 2012 Aug 21;109(34):13799-804.

Background

Senexin A is a CDK8 inhibitor with an IC₅₀ of 280 nM. CDK19|0.31 μM (K_d)|CDK8|0.83 μM (K_d)

Senexin A inhibits CDK8 and CDK19 ATP site binding with K_d50 of 0.83 μM and 0.31 μM, respectively and CDK8 kinase activity with IC₅₀ of 0.28 μM. Senexin A inhibits β-catenin-dependent transcription in HCT116 colon carcinoma cells. The induction of transcription factor EGR1 upon serum starvation, followed by readdition of serum, is strongly inhibited by Senexin A in HT1080 cells. Senexin A inhibits only p21-induced transcription but not other biological effects of p21. Senexin A also decreases the expression of many secreted tumor-promoting factors in doxorubicin-treated wild-type HCT116 cells[1].

Five daily treatment of Senexin A fully reverses tumor-promoting effect of chemotherapy. Senexin A shows no detectable toxicity and no significant effects on body weight, organ weights, or blood cell counts in C57BL/6 mice during the treatment. This effect of doxorubicin treatment is completely abolished, however, when doxorubicin injection is followed by administration of Senexin A. Senexin A treatment strongly improves the response of A549/MEF tumors to doxorubicin[1].

[1]. Porter DC, et al. Cyclin-dependent kinase 8 mediates chemotherapy-induced tumor-promoting paracrine activities. Proc Natl Acad Sci U S A. 2012 Aug 21;109(34):13799-804.

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