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Product Information



CX-4945

Item No. 16779

CAS Registry No.: 1009820-21-6

5-[(3-chlorophenyl)amino]-benzo[c]-Formal Name:

2,6-naphthyridine-8-carboxylic acid

Synonym: Silmitasertib MF: C₁₉H₁₂ClN₃O₂

FW: 349.8 **Purity:** ≥98%

Stability: ≥2 years at -20°C Supplied as: A crystalline solid

λ_{max}: 209, 240, 260, 360 nm UV/Vis.:

Laboratory Procedures

For long term storage, we suggest that CX-4945 be stored as supplied at -20°C. It should be stable for at least two years. CX-4945 is supplied as a crystalline solid. A stock solution may be made by dissolving the CX-4945 in the solvent of choice. CX-4945 is soluble in organic solvents such as DMSO and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of CX-4945 in these solvents is approximately 15 and 20 mg/ml, respectively.

CX-4945 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, CX-4945 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. CX-4945 has a solubility of approximately 0.5 mg/ml in a 1:1 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

CX-4945 is a potent, orally bioavailable inhibitor of casein kinase 2 (CK2; K_i = 0.38 nM) that competes with ATP by filling the small ATP binding site on the catalytic CK2 α subunit, conferring selectivity.¹⁻³ It inhibits proliferation in a panel of cancer cell lines that overexpress CK2 and prevents tumor growth of breast and pancreatic cancer cell xenografts in mice.3 CX-4945 blocks survival and induces apoptosis in cancer stem cells and is effective against glioblastomas and acute myeloid leukemia cells. ^{4,5} CX-4945 also inhibits Cdc2-like kinases (Clk; IC₅₀8 = 82.3, 3.8, and 90 nM for Clk1, Clk2, and Clk3, respectively), interfering with alternative splicing.⁶

References

- 1. Pierre, F., Chua, P.C., O'Brien, S.E., et al. Discovery and SAR of 5-(3-chlorophenylamino)benzo[c][2,6]naphthyridine-8-carboxylic acid (CX-4945), the first clinical stage inhibitor of protein kinase CK2 for the treatment of cancer. J. Med. Chem. 54(2), 635-654 (2011).
- 2. Ferguson, A.D., Sheth, P.R., Basso, A.D., et al. Structural basis of CX-4945 binding to human protein kinase CK2. FEBS Lett. **585(1)**, 104-110 (2011).
- 3. Siddiqui-Jain, A., Drygin, D., Streiner, N., et al. CX-4945, an orally bioavailable selective inhibitor of protein kinase CK2, inhibits prosurvival and angiogenic signaling and exhibits antitumor efficacy. Cancer Res. 70(24), 10288-10298
- 4. Agarwal, M., Nitta, R.T., and Li, G. Casein Kinase 2: A novel player in glioblastoma therapy and cancer stem cells. J. Mol. Genet. Med. 8(1), 1-18 (2013).
- Quotti Tubi, L., Gurrieri, C., Brancalion, A., et al. Inhibition of protein kinase CK2 with the clinical-grade small ATP-competitive compound CX-4945 or by RNA interference unveils its role in acute myeloid leukemia cell survival, p53-dependent apoptosis and daunorubicin-induced cytotoxicity. J. Hematol. Oncol. 6, 1-15 (2013).
- 6. Kim, H., Choi, K., Kang, H., et al. Identification of a novel function of CX-4945 as a splicing regulator. PLoS One 9(4), e94978 (2014).

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