

Product Data Sheet

Product Name: NVP-BEP800

Cat. No.: GC11179

Chemical Properties

Cas. No. 847559-80-2

Chemical Name 2-amino-4-[2,4-dichloro-5-(2-pyrrolidin-1-ylethoxy)phenyl]-N-ethylthieno[2,3-d]pyrimidine-6-carboxamide

SMILES CCNC(=O)C1=CC2=C(N=C(N=C2S1)N)C3=CC(=C(C=C3Cl)Cl)OCCN4CCCC4

Formula $C_{21}H_{23}Cl_2N_5O_2S$ M.Wt 480.4

Solubility ≥ 24.7 mg/mL in DMSO with ultrasonic and warming, ≥ 16 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.

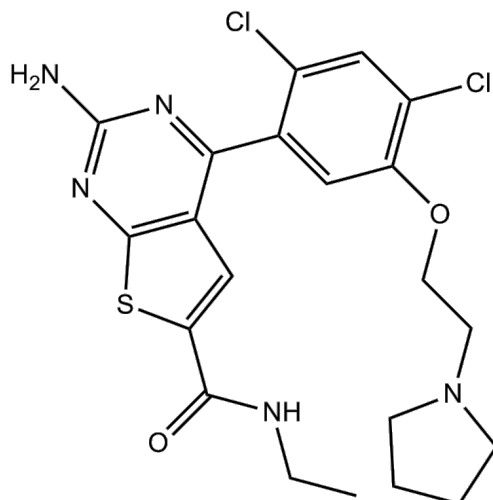
Caution: Product has not been fully validated for medical applications. For research use only.

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Structure



Protocol

Kinase experiment [1]:

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Competitive binding fluorescent polarization assay

Recombinant Hsp90 β , TAMRA-radicicol, or various concentrations of NVP-BEP800 was added in assay buffer (50 mM TRIS pH 7.4, 5 mM MgCl₂, 150 mM KCl and 0.1% CHAPS), mixed and incubated at room temperature for 30 ~ 45 mins prior to reading. The 2D-FIDA-based HTS assay based on confocal technologies monitored the decreased fluorescence polarization on displacement of the high affinity ligand TAMRA-radicicol from Hsp90 β by NVP-BEP800. The concentration of NVP-BEP800 which inhibited Hsp90 β by 50% was determined from the competition curve.

Cell experiment [1]:

Cell lines BT-474 cells

Preparation method

The solubility of this compound in DMSO is limited. 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 50 ~ 500 nM; 24 hrs

Applications

In BT-474 cells, NVP-BEP800 concentration-dependently decreased phospho-Akt (Ser473) and ErbB2 levels. At the dose of 500 nM, phosphorylation of Akt at Ser473 was not detectable, and lower levels of Akt and ErbB2 were also detected.

Animal experiment [1]:

Animal models Mice bearing breast cancer BT-474 cell xenografts

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Dosage form 15 or 30 mg/kg/day; p.o.

Applications In mice bearing breast cancer BT-474 cell xenografts, NVP-BEP800 dose-dependently increased Hsp90-p23 complex dissociation and lowered the levels of steady-state ErbB2, phospho-Akt as well as phospho-S6. NVP-BEP800 induced 38% tumor regression at dose of 30 mg/kg/day and a T/C value of 36% at dose of 15 mg/kg/day.

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]. Massey AJ, Schoepfer J, Brough PA, Brueggen J, Chène P, Drysdale MJ, Pfaar U, Radimerski T, Ruetz S, Schweitzer A, Wood M, Garcia-Echeverria C, Jensen MR. Preclinical antitumor activity of the orally available heat shock protein 90 inhibitor NVP-BEP800. Mol Cancer Ther. 2010 Apr;9(4):906-19.

Background

NVP-BEP800 is a fully synthetic, orally bioavailable inhibitor of Hsp90 with IC₅₀ value of 58nM [1].

NVP-BEP800 binds to the N-terminal ATP-binding pocket of Hsp90. In a competitive binding fluorescence polarization assay, NVP-BEP800 inhibits Hsp90 β with IC₅₀ value of 58nM. And to other 20 protein kinases, NVP-BEP800 shows a IC₅₀ of >10 μ M. In BT-474 cells and A375 cells, NVP-BEP800 causes the Hsp90-p23 dissociation and client protein degradation (ErbB2) as well as the reduction of client protein phosphorylation (phospho-Akt). Degradation of these oncogenic client proteins results in tumor cell growth arrest and death. NVP-BEP800 inhibits proliferation of tumor cells with an average GI₅₀ of 245nM. And in 46 primary human tumors including small cell lung, mammary cancer and melanoma, the mean IC₅₀ is 750nM. Additionally, treatment of NVP-BEP800 induces apoptosis in human breast cancer cell lines. The antitumor efficacy of NVP-BEP800 is also

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observed with a dose of 15 or 30 mg/kg/d in A375 xenograft-bearing mice as well as in BT-474 breast cancer xenografts [1].

References:

[1] Massey AJ, Schoepfer J, Brough PA, Brueggen J, Chène P, Drysdale MJ, Pfaar U, Radimerski T, Ruetz S, Schweitzer A, Wood M, Garcia-Echeverria C, Jensen MR. Preclinical antitumor activity of the orally available heat shock protein 90 inhibitor NVP-BEP800. *Mol Cancer Ther.* 2010 Apr;9(4):906-19.

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