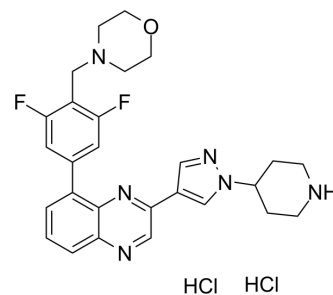


NVP-BSK805 dihydrochloride

| | |
|---------------------------|--|
| Cat. No.: | HY-14722A |
| CAS No.: | 1942919-79-0 |
| Molecular Formula: | C ₂₇ H ₃₀ Cl ₂ F ₂ N ₆ O |
| Molecular Weight: | 563.47 |
| Target: | JAK |
| Pathway: | Epigenetics; JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Stem Cell/Wnt |
| Storage: | 4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture) |



SOLVENT & SOLUBILITY

| | | | | | | |
|---|--|----------------------|-------------|-------------|-------------|--------------|
| In Vitro | DMSO : 50 mg/mL (88.74 mM; Need ultrasonic) | | | | | |
| | H ₂ O : < 0.1 mg/mL (insoluble) | | | | | |
| | Preparing Stock Solutions | Solvent | Mass | 1 mg | 5 mg | 10 mg |
| | | Concentration | | | | |
| | | 1 mM | | 1.7747 mL | 8.8736 mL | 17.7472 mL |
| 5 mM | | | 0.3549 mL | 1.7747 mL | 3.5494 mL | |
| | 10 mM | | 0.1775 mL | 0.8874 mL | 1.7747 mL | |
| Please refer to the solubility information to select the appropriate solvent. | | | | | | |
| In Vivo | 1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 2.5 mg/mL (4.44 mM); Clear solution | | | | | |
| | 2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (4.44 mM); Clear solution | | | | | |
| | 3. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (4.44 mM); Clear solution | | | | | |

BIOLOGICAL ACTIVITY

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|-------------------------------------|--|--|---|--|
| Description | NVP-BSK805 dihydrochloride is an ATP-competitive JAK2 inhibitor, with IC ₅₀ s of 0.48 nM, 31.63 nM, 18.68 nM, and 10.76 nM for JAK2 JH1 (JAK homology 1), JAK1 JH1, JAK3 JH1, and TYK2 JH1, respectively ^[1] . | | | |
| IC₅₀ & Target | JAK2 JH1 0.48 nM (IC ₅₀) | FL JAK2 V617F 0.56 nM (IC ₅₀) | FL JAK2 wt 0.58 nM (IC ₅₀) | TYK2 JH1 10.76 nM (IC ₅₀) |
| | JAK3 JH1 18.68 nM (IC ₅₀) | JAK1 JH1 31.63 nM (IC ₅₀) | | |

| | |
|-----------------|---|
| In Vitro | <p>NVP-BSK805 dihydrochloride (BSK805 dihydrochloride) is a JAK2 inhibitor, with IC₅₀s of 0.48 nM, 31.63 nM, 18.68 nM, and 10.76 nM for JAK2 JH1 (JAK homology 1), JAK1 JH1, JAK3 JH1, and TYK2 JH1, respectively. NVP-BSK805 inhibits the full-length wild-type JAK2 (FL JAK2 wt) and FL JAK2 V617F activity, with IC₅₀s of 0.58 ± 0.03 and 0.56 ± 0.04 nM. NVP-BSK805 is ATP-competitive, with calculated K_i of 0.43 ± 0.02 nM. NVP-BSK805 suppresses the growth of JAK2^{V617F}-bearing acute myeloid leukemia cell lines with GI₅₀ of <100 nM. NVP-BSK805 blocks the STAT5 phosphorylation at ≥100 nM concentrations, and shows a bias for JAK2 over JAK1 and JAK3 inhibition in the JAK2^{V617F}-mutant cell lines^[1].</p> <p>NVP-BSK805 dihydrochloride (5 μM) improves P-gp inhibitory activity. NVP-BSK805 increases sensitization of drug-resistant KBV20C cancer cells to VIC treatment at 10 μM, and such an effect is more effective than a 5 μM dose^[2].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> |
| In Vivo | <p>NVP-BSK805 (BSK805 dihydrochloride; 150 mg/kg, p.o.) blocks STAT5 phosphorylation, splenomegaly, and leukemic cell spreading in a Ba/F3 JAK2^{V617F} cell-driven mouse model^[1].</p> <p>NVP-BSK805 (50, 75, and 100 mg/kg, p.o.) also suppresses rhEpo-mediated polycythemia and splenomegaly in BALB/c mice^[1].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> |

PROTOCOL

| | |
|---|--|
| Cell Assay ^[1] | <p>The antiproliferative activity of JAK2 inhibitors is determined by incubating cells for 72 hours (96 hours for MB-02 and MUTZ-8 cells) with an 8-point concentration range of NVP-BSK805 and cell proliferation relative to NVP-BSK805 is measured using the colorimetric WST-1 cell viability readout. Of each triplicate treatment, the mean is calculated and these data are plotted in XLfit 4 to determine the half-maximal growth inhibition (GI₅₀) values^[1].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> |
| Animal Administration ^[1] | <p>Mice^[1]</p> <p>Concomitantly with NVP-BSK805 treatment, female BALB/c mice receive daily s.c. injections (in 100 μL saline buffer) of 10 units of rhEpo for 4 consecutive days. Controls are injected corresponding volumes of saline buffer. Mice are sacrificed 24 hours after the final dose and total blood, spleen, and bone marrow are taken for further analysis. Animals are 8 to 10 weeks of age at treatment start (20-25 g body weight) and are kept under optimal hygienic conditions with free access to food and water^[1].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> |

CUSTOMER VALIDATION

- Patent. US20180263995A1.

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REFERENCES

[1]. Baffert F, et al. Potent and selective inhibition of polycythemia by the quinoxaline JAK2 inhibitor NVP-BSK805. *Mol Cancer Ther.* 2010 Jul;9(7):1945-55.

[2]. Cheon JH, et al. The JAK2 inhibitors CEP-33779 and NVP-BSK805 have high P-gp inhibitory activity and sensitize drug-resistant cancer cells to vincristine. *Biochem Biophys Res Commun.* 2017 Sep 2;490(4):1176-1182.

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