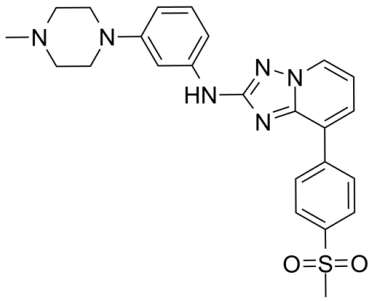
Data Sheet

Product Name:	CEP-33779
Cat. No.:	CS-3439
CAS No.:	1257704-57-6
Molecular Formula:	C24H26N6O2S
Molecular Weight:	462.57
Target:	JAK
Pathway:	Epigenetics; JAK/STAT Signaling; Stem Cell/Wnt
Solubility:	DMSO : 50 mg/mL (108.09 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

CEP-33779 is a novel, selective, and orally bioavailable inhibitor of **JAK2** with an **IC_{50}** of 1.8±0.6 nM. IC50 & Target: IC50: 1.8±0.6 nM (JAK2)[1] **In Vitro:** CEP-33779, at nontoxic concentrations, significantly sensitizes overexpression of P-glycoprotein overexpressing multidrug resistance cells to its anticancer substrates. CEP-33779 significantly increases intracellular accumulation and decreases the efflux of doxorubicin by inhibiting the overexpression of P-glycoprotein transport function[3]. **In Vivo:** CEP-33779 exhibits a favorable PK profile in nude mice, an iv half-life of 1 h, moderate distribution (Vd=2.6 L/kg), and measurable oral exposure with an estimated bioavailability of 33%. It demonstrates antitumor efficacy in the CWR22 xenograft model; oral dosing for 14 days at 30 mg/kg bid results in tumor stasis and partial regressions in 5/10 animals[1]. CEP-33779 administration results in an almost complete shrinkage of tumors in most animals; few remaining tumor nodules were small, poorly vascularized, and had a necrotic appearance. CEP-33779 suppressed activation of NF-κB in tumors[2].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [1]The kinase activity of baculovirus-expressed human JAK1, JAK2, or JAK3 is measured. Each 96-well Costar high binding plate is coated with 100 µL/well of 10 µg/mL neutravidin in TBS at 37 °C for 2 h, followed by 100 µL/well of 1 µg/mL 15-mer peptide substrate at 37 °C for 1 h. The kinase assay mixture (total volume=100 µL/well) consisting of 20 mM HEPES (pH 7.2), ATP (0.2 µM ATP for JAK1 and JAK2 and 0.1 µM ATP for JAK3), 1 mM $MnCl_2$, 0.1% BSA, and CEP-33779 (diluted in DMSO, 2.5% DMSO final in assay) is added to the assay plate. Enzyme is added and the reaction is allowed to proceed for 20 min at room temperature. Detection of the phosphorylated product is performed by adding 100 µL/well of diluted Eu-N1 labeled PY100 antibody. Samples are incubated at RT for 1 h, followed by addition of 100 µL enhancement solution. Plates are agitated for 10 min, and the fluorescence of the resulting solution is measured. IC_{50} values are determined[1]. **Animal Administration:** [1]Mouse: Nude mice bearing CWR22 xenografts are dosed orally with 55 mg/kg of CEP-33779 or a vehicle (PEG400). At 2, 6, and 24 h after dosing animals (3/group) are sacrificed, tumors are excised and plasma samples are prepared. Tumor extracts are prepared using Triton-based extraction buffer supplemented with inhibitors of proteases and phosphatases. Equal amounts of extracts are resolved on SDS-PAGE gels and STAT3 phosphorylation and expression are analyzed by Western blot using specific antibodies[1].

References:

[1]. Dugan BJ, et al. A selective, orally bioavailable 1,2,4-triazolo[1,5-a]pyridine-based inhibitor of Janus kinase 2 for use in anticancer therapy: discovery of CEP-33779. J Med Chem. 2012 Jun 14;55(11):5243-54.

[2]. Seavey MM, et al. Therapeutic efficacy of CEP-33779, a novel selective JAK2 inhibitor, in a mouse model of colitis-induced colorectal cancer. Mol Cancer

Ther. 2012 Apr;11(4):984-93.

[3]. Tang SJ, et al. CEP-33779 antagonizes ATP-binding cassette subfamily B member 1 mediated multidrug resistance by inhibiting its transport function. Biochem Pharmacol. 2014 Sep 15;91(2):144-56.

CAIndexNames:

[1,2,4]Triazolo[1,5-a]pyridin-2-amine, N-[3-(4-methyl-1-piperazinyl)phenyl]-8-[4-(methylsulfonyl)phenyl]-

SMILES:

O=S(C1=CC=C(C2=CC=CN3C2=NC(NC4=CC=CC(N5CCN(C)CC5)=C4)=N3)C=C1)(C)=O

Tel: 732-484-9848 Fax: 888-484-5008 E-mail: sales@ChemScene.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA