

Product Data Sheet

Product Name: A 419259

Cat. No.: GC35209

Chemical Properties

Cas. No. 364042-47-7

SMILES NC1=C2C(N([C@H]3CC[C@H](N4CCN(C)CC4)CC3)C=C2C5=CC=C(OC6=CC=CC=C6)C=C5)=NC=N1

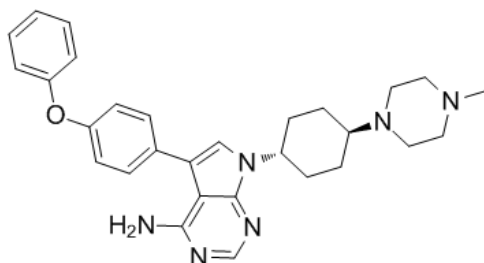
Formula $C_{29}H_{34}N_6O$ M.Wt 482.62

Solubility 55 mg/mL in water 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

Cell experiment [1]:

Cell lines	K-562 and Meg-01 cell lines
------------	-----------------------------

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Preparation Method	10⁴ cells were plated per well in 96-well plates for each day of a 4-day time course. Various concentrations of A 419259 or vehicle control were added to the wells (five wells per concentration per day) and the plates were incubated at 37°C. At each time point, one plate was centrifuged at 1500g for 10min to pellet the cells. Cells were washed with PBS, and calcein-AM was added to each well to a final concentration of 1mM. Plates were incubated in the dark at room temperature for 1h. The plates were then read at 485/530nm (excitation/emission) using a SpectraMax Gemini XS fluorescent plate reader and data were analysed with SoftMax Pro software
Reaction Conditions	0-1µM; 0-4d
Applications	A 419259 block Ph ⁺ leukemia cell (K-562 and Meg-01) proliferation in a dose dependent fashion.
Animal experiment [2]:	
Animal models	C57BL/6 mice
Preparation Method	C57BL/6 mice were injected intraperitoneally (i.p.) with 30mg/kg A 419259 or the vehicle control (DMSO/PBS) 24h and 12h before i.p. injection of 5mg/kg LPS or PBS. Mice were sacrificed after 3h, and the tissues were stored at -80°C and prepared for immunoblotting.
Dosage form	30mg/kg; i.p.; twice

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Applications	Mice treated with A 419259 showed reduced response to LPS, with lower amounts of secreted IL-1 β than in vehicle-treated mice. A 419259 could markedly decrease the inflammatory cells' infiltration in the liver. The protein levels of NLRP3 and caspase 1 (P20) in the liver decreased when the mice were treated with A 419259.
References:[1] Wilson MB, Schreiner SJ, Choi HJ, Kamens J, Smithgall TE. Selective pyrrolo-pyrimidine inhibitors reveal a necessary role for Src family kinases in Bcr-Abl signal transduction and oncogenesis. <i>Oncogene</i> . 2002;21(53):8075-8088.[2] Kong X, Liao Y, Zhou L, et al. Hematopoietic Cell Kinase (HCK) Is Essential for NLRP3 Inflammasome Activation and Lipopolysaccharide-Induced Inflammatory Response In Vivo. <i>Front Pharmacol</i> . 2020;11:581011.	

Background

A 419259 is a pyrrolopyrimidine Src family kinase inhibitor with IC₅₀ values of 9nM, <3nM and <3nM for the Src family members Src, Lck and Lyn, respectively^[1].

In vitro, A 419259 (0-1 μ M; 0-4d) blocked the proliferation and induced apoptosis of Ph⁺ leukemia cells (K-562 and Meg-01) in a dose-dependent manner, without markedly affecting Ph⁻ myeloid leukemia cells (TF-1 and HEL)^[1]. A 419259 (1 μ M; 16h) inhibited Lck and c-Src activity in self-renewing H1 hES cells^[2]. A 419259 (1 μ M; 24h) inhibited Src-related signaling, thereby affecting the differentiation of mouse embryonic stem cells (mESCs)^[3].

In vivo, A 419259 (30mg/kg; i.p.; twice) inhibited HCK/NLRP3 inflammasome signaling, reduced IL-1 β release and alleviated hepatic inflammation in LPS-induced mice^[4]. A 419259 (0.5mg/kg; i.p.; once every three days for three times) reduced phosphorylated Src levels in the spinal cord and skeletal muscle, improved motor function and extended lifespan in AR-97Q transgenic male mice^[5]. A 419259 (5mg/kg; i.v.; once) significantly inhibited tumor growth and reduced tumor weight in CD-1 mice bearing CAL51 tumors^[6].

References:

[1] Wilson MB, Schreiner SJ, Choi HJ, Kamens J, Smithgall TE. Selective pyrrolo-pyrimidine inhibitors reveal a necessary role for Src family kinases in Bcr-Abl signal transduction and

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

oncogenesis. *Oncogene*. 2002;21(53):8075-8088.

[2] Zhang X, Simerly C, Hartnett C, Schatten G, Smithgall TE. Src-family tyrosine kinase activities are essential for differentiation of human embryonic stem cells. *Stem Cell Res*. 2014;13(3 Pt A):379-389.

[3] Meyn MA 3rd, Smithgall TE. Chemical genetics identifies c-Src as an activator of primitive ectoderm formation in murine embryonic stem cells. *Sci Signal*. 2009;2(92):ra64.

[4] Kong X, Liao Y, Zhou L, et al. Hematopoietic Cell Kinase (HCK) Is Essential for NLRP3 Inflammasome Activation and Lipopolysaccharide-Induced Inflammatory Response In Vivo. *Front Pharmacol*. 2020;11:581011.

[5] Iida M, Sahashi K, Kondo N, et al. Src inhibition attenuates polyglutamine-mediated neuromuscular degeneration in spinal and bulbar muscular atrophy. *Nat Commun*. 2019;10(1):4262.

[6] Cheung A, Opzoomer J, Ilieva KM, et al. Anti-Folate Receptor Alpha-Directed Antibody Therapies Restrict the Growth of Triple-negative Breast Cancer. *Clin Cancer Res*. 2018;24(20):5098-5111.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA