

Product Data Sheet

Product Name: PRT062607 Hydrochloride

Cat. No.: GC10499

Chemical Properties

Cas. No. 1370261-97-4

Chemical Name 4-((3-(2H-1,2,3-triazol-2-yl)phenyl)amino)-2-(((1R,2R)-2-aminocyclohexyl)amino)pyrimidine-5-carboxamide hydrochloride

SMILES NC(C1=C(NC2=CC(N3N=CC=N3)=CC=C2)N=C(N[C@H]4[C@H](N)CCCC4)N=C1)=O.Cl

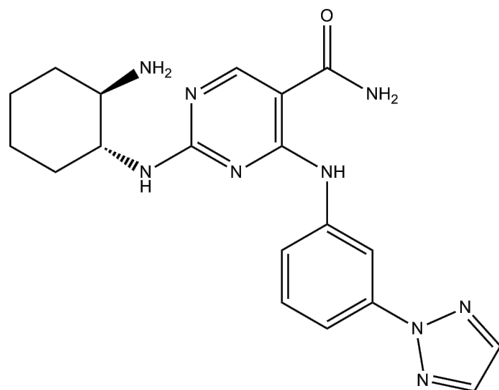
Formula $C_{19}H_{24}ClN_9O$ M.Wt 429.91

Solubility ≥ 21.5 mg/mL in DMSO, ≥ 83.2 mg/mL in Water 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.

Structure



HCl

Protocol

Cell experiment: [1]

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

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

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Cell lines Primary B-cells, SU-DHL6 cells

Preparation method The solubility of this compound in DMSO is >10 mM. 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.

Reaction Conditions 1 µM, 24 hours

Applications To compare the relative sensitivity of primary versus tumor B-cells, the mixing experiments in which SU-DHL6 was combined with human whole blood and treated with P505-15 were performed. Under these conditions, whereas the tumor B-cell line underwent apoptosis in response to SYK inhibition, primary B-cells did not.

Animal experiment: [1]

Animal models NOD/SCID mice injected with Ramos cells

Dosage form Oral administration, 10, 15, or 20 mg/kg, twice daily

Applications A statistically significant reduction in average tumor weight was achieved in all dosing groups relative to vehicle control. It revealed that submicromolar concentrations of P505-15 prevented tumor formation by an aggressive NHL cell line in mice.

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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] Spurgeon S E, Coffey G, Fletcher L B, et al. The selective SYK inhibitor P505-15 (PRT062607) inhibits B cell signaling and function in vitro and in vivo and augments the activity of fludarabine in chronic lymphocytic leukemia. *Journal of Pharmacology and Experimental Therapeutics*, 2013, 344(2): 378-387.

Background

PRT062607 Hydrochloride is a highly selective and novel SYK inhibitor with IC₅₀ value of 1 nM. Spleen tyrosine kinase (SYK) is a cytoplasmic tyrosine kinase and primarily expressed in hematopoietic cells including B-cells.

PRT062607 Hydrochloride is an orally bioavailable SYK inhibitor and its affinity for SYK is at least 80-fold greater than other kinases. In NHL cell lines, PRT062607 Hydrochloride inhibits SYK activation and induces caspase dependent apoptosis. Also, PRT062607 Hydrochloride inhibited SYK and caused apoptosis of the tumor B-cell line [1].

PRT062607 Hydrochloride effectively antagonize CLL cell survival after BCR triggering. Moreover, they inhibit the secretion of the chemokines CCL3 and CCL4 by CLL cells, and leukemia cell transfer toward beneath stromal cells, the tissue homing chemokines CXCL13 and CXCL12 [2].

In a mouse xenograft model, mice dosed with all three concentrations (twice daily with 10, 15, or 20 mg/kg) of PRT062607 Hydrochloride were protected from Ramos tumor growth [1].

References:

[1]. Spurgeon SE, Coffey G, Fletcher LB, et al. The selective SYK inhibitor P505-15 (PRT062607) inhibits B cell signaling and function in vitro and in vivo and augments the activity of fludarabine in chronic lymphocytic leukemia. *J Pharmacol Exp Ther*, 2013, 344(2): 378-387.

[2]. Hoellenriegel J, Coffey GP, Sinha U, et al. Selective, novel spleen tyrosine kinase (Syk) inhibitors suppress chronic lymphocytic leukemia B-cell activation and migration. *Leukemia*, 2012, 26(7): 1576-1583.

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