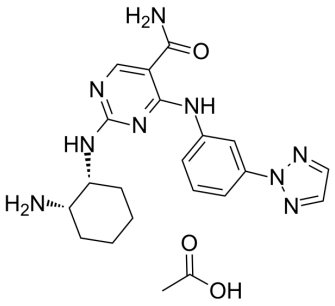
PRT062607 acetate

Cat. No.:	HY-15324
CAS No.:	1370261-98-5
Molecular Formula:	$C_{21}H_{27}N_9O_3$
Molecular Weight:	453.5
Target:	Syk; Syk; Src; Mixed Lineage Kinase; PAK; Pyk2; FAK; Apoptosis
Pathway:	Protein Tyrosine Kinase/RTK; MAPK/ERK Pathway; Cell Cycle/DNA Damage; Cytoskeleton; Apoptosis
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



BIOLOGICAL ACTIVITY

Description

PRT062607 (P505-15) acetate is an orally available Syk inhibitor (IC_{50}: 1 nM) that inhibits inflammation and induction Apoptosis. PRT062607 acetate exerts potent antitumor activity in tumor xenograft mouse models[1].[2].

IC_{50} & Target

Lck	PAK5
249 nM (IC_{50}, [2])	166 nM (IC_{50}, [2])

In Vitro

PRT062607 acetate also has significant activity against multiple kinases, with IC_{50}s of 81 nM (Fgr), 88 nM (MLK1), 123 nM (Yes), 139 nM (Flt3), 166 nM (PAK5), 192 nM (Lyn), 244 nM (cSRC), 249 nM (Lck), 108 nM (Pyk), 415 nM (FAK), 1.05 nM (ZAP-70) [1].

PRT062607 acetate (0.01-2 μM; 3 d) inhibits Phosphorylation of ERK(Y204), AKT(S473) and SYK(Y352) in Ramos cells, and inhibition of BLNK Tyr84 phosphorylation[1][2].

PRT062607 acetate (2 μM; 24 h) in SU-DHL6 cells Induces apoptosis in human whole blood[1].

In human whole blood, P505-15 can effectively inhibit B cell antigen receptor-mediated B cell signaling and activation (IC_{50}: 0.27 and 0.28 μM) and Fc receptor 1-mediated induced basophil degranulation (IC_{50}: 0.15 μM)[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis

Cell Line:	Ramos cells[1], SUDHL4 cells[2]
Concentration:	0.01, 0.025, 0.064, 0.16, 0.4, 2.5 μM
Incubation Time:	3 days
Result:	Resulted not entirely concentration-dependent and complete inhibition on ERK (Y204)and AKT (S473) phosphorylation, Lyn phosphorylation of SYK at Y352. Inhibited BLNK Tyr84 phosphorylation in a concentration dependent manner, while whitout inhibitory effect on Lyn activity. Potently inhibited BCR-mediated pERK Tyr204 in the Ramos B cell line, without suppressing PMA-mediated pERK Tyr204.

In Vivo

PRT062607 acetate produced dose-dependent anti-inflammatory activity in two rodent models of rheumatoid arthritis.

PRT062607 acetate (15, 30 mg/kg; po; bid; 5 d) causes SYK inhibition in mice and prevents BCR-induced splenomegaly in mice[1].

PRT062607 acetate (15 mg/kg; po ; bid; 5 d) SYK inhibition in mice prevents Ramos tumor formation in mouse xenograft models[1].

PRT062607 acetate (10-20 mg/kg; po; bid) prevents BCR mediated splenomegaly and significantly inhibited NHL tumor growth in xenograft models[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	anti-IgD Stimulated Mouse Inflammation Model[1]
Dosage:	10 mg/kg, 15 mg/kg, 20 mg/kg
Administration:	po; bid for 5 days
Result:	Suppressed mouse B-cell activation following stimulation with this anti-IgD.

Animal Model:	Ramos Tumor Xenograft Model in NOD/SCID mice[1]
Dosage:	15 mg/kg, 30 mg/kg
Administration:	po; bid; terminated when tumor weights began reaching approximately 1.5 mg, at which time tumors were excised and weighed.
Result:	Protected mouse from Ramos tumor growth in vivo.

CUSTOMER VALIDATION

- Proc Natl Acad Sci U S A. 2022 Oct 25;119(43):e2207280119.
- Int J Ophthalmol. 2022 Jul 18;15(7):1044-1052.
- Harvard Medical School LINCS LIBRARY

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REFERENCES

[1]. Spurgeon SE, 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 Feb;344(2):378-87.

[2]. Coffey G, et al. Specific inhibition of spleen tyrosine kinase suppresses leukocyte immune function and inflammation in animal models of rheumatoid arthritis. J Pharmacol Exp Ther. 2012 Feb;340(2):350-9.

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