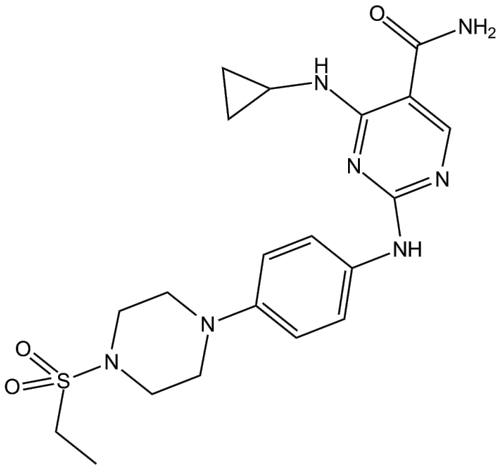
Product Data Sheet

Product Name: Cerdulatinib (PRT062070)
Cat. No.: GC11209

Chemical Properties

Cas. No.	1198300-79-6		
Chemical Name	4-(cyclopropylamino)-2-((4-(4-(ethylsulfonyl)piperazin-1-yl)phenyl)amino)pyrimidine-5-carboxamide		
SMILES	NC(C1=CN=C(NC2=CC=C(N3CCN(S(=O)(CC)=O)CC3)C=C2)N=C1NC4CC4)=O		
Formula	C20H27N7O3S	M.Wt	445.54
Solubility	≥ 22.3mg/mL in DMSO	Storage	Desiccate 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



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Protocol

Cell experiment [1]:

Cell lines	DLBCL (diffuse large B-cell lymphoma) cells: germinal center B-cell (GCB) subtype, activated B-cell (ABC) subtype.
Preparation method	Limited solubility. 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	6 h
Applications	Cerdulatinib induces apoptosis in both GCB and ABC cell lines by caspase 3 and PARP cleavage. Cerdulatinib also triggers apoptosis and cell cycle arrest in BCR-stimulated DLBCL cells. Cerdulatinib blocks JAK/STAT and BCR signaling in both ABC and GCB cell lines as well.

Animal experiment [2]:

Animal models	Female Lewis rats collagen-induced arthritis (CIA) model
Dosage form	Oral gavage twice daily.
Applications	3 mg/kg of Cerdulatinib suppresses the inflammation and reverses relative to pretreatment levels at 5 mg/kg. Cerdulatinib also dose-dependently leads to significant improvements in inflammatory infiltrate within the synovium and the integrity of the articular cartilage. Moreover, Cerdulatinib treatment affects anticollagen antibody formation and reduces 50% of circulating antibody titers at the 1.5, 3, and 5 mg/kg doses.

Caution: Product has not been fully validated for medical applications. For research use only.
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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. Ma J, Xing W, Coffey G et al. Cerdulatinib, a novel dual SYK/JAK kinase inhibitor, has broad anti-tumor activity in both ABC and GCB types of diffuse large B cell lymphoma. Oncotarget. 2015 Nov 5.

2. Coffey G, Betz A, DeGuzman F et al.The novel kinase inhibitor PRT062070 (Cerdulatinib)demonstrates efficacy in models of autoimmunity and B-cell cancer. J Pharmacol Exp Ther. 2014 Dec;351(3):538-48.

Background

Cerdulatinib (PRT062070) is a potent and selective inhibitor of Syk and JAK.[1]

The JAK/STAT cascade, which has been implicated in hematopoiesis and cytokine signaling, is present in humans and flies. Worms. The SYK/ZAP70 kinases play an important role in human T and B cell signaling.[3]

Cerdulatinib can induce apoptosis via down-regulation of MCL1 protein and PARP cleavage. Through the inhibition of RB phosphorylation and down-regulation of cyclin E,the Cerdulatinib can also block G1/S transition and cause cell cycle arrest. Further analyses of the cell signaling activities showed that STAT3 phosphorylation was sensitive to inhibition by cerdulatinib in ABC cell lines while phosphorylation of SYK, PLCg2, AKT and ERK is reported to be sensitive to inhibition by cerdulatinib in GCB cell lines.[2]

Cerdulatinib is effective in rodent models of B-cell lymphoma and autoimmune disease and has exhibited anti-tumor activity in genetically diverse B-cell lymphoma cell lines and is more effective than Syk- or Jak- selective inhibitors alone.[1]

References:

[1] Manish Patel , Pau Hamlin, MD, etal. , A Phase I Open-Label, Multi-Dose Escalation Study of the Dual Syk/Jak Inhibitor PRT062070 (Cerdulatinib) in Patients with Relapsed/Refractory B Cell

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Malignancies. Blood: 124 (21) ; December 6, 2014.
[2] Y. Lynn Wang, MD PhD, Jiao Ma, PhD, etal., SYK and STAT3 Are Active in Diffuse Large B-Cell Lymphoma: Activity of Cerdulatinib, a Dual SYK/JAK Inhibitor. Blood: 124 (21) ; December 6, 2014.
[3]Morrison DK, Murakami MS, Cleghon V. Protein kinases and phosphatases in the Drosophila genome. J Cell Biol. 2000 Jul 24;150(2):F57-62.

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