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产品名称：TAK-659 (hydrochloride)
产品别名：TAK-659 hydrochloride

生物活性：

Description	TAK-659 hydrochloride is a potent, selective and orally available spleen tyrosine kinase (Syk) inhibitor with an $IC_{50}$of 3.2 nM.
IC_{50} & Target	IC50: 3.2 nM (Syk)[1]
In Vitro	In a cell proliferation assay, TAK-659 shows inhibition toward a SYK-dependent cell line (OCILY10). TAK-659 is shown to be sensitive toward FLT3-ITD dependent cell lines, MV4-11 and MOLM-13 while the WT FLT3 RS4-11 (ALL cell line) and RA1 (Burkitt's Lymphoma cell line) are not sensitive toward TAK-659. The sensitivity to TAK-659 is associated with mutations impacting SYK activity in B cell lymphomas, whereas TAK-659 is not cytotoxic for adherent primary or solid tumor cell lines[1]. TAK-659 inhibits the microenvironment-induced activation of Syk and downstream signaling molecules, without inhibiting the protein homologue ZAP-70 in T cells. Importantly, the pro-survival, proliferative, chemoresistant and activation effects promoted by the microenvironment are abrogated by TAK-659, which furthermore blocks CLL cell migration toward BMSC, CXCL12, and CXCL13[2].
In Vivo	TAK-659 is currently undergoing Phase I clinical trials for advanced solid tumor and lymphoma malignancies, a Phase Ib study in advanced solid tumors in combination with nivolumab, and PhIb/II trials for relapsed/refractory AML. TAK-659 blocks anti-IgD (immune-globulin D antibody) stimulated CD86 expression in mouse peripheral B cells in vivo. In the OCI-LY10 xenograft and DLBCL PHTX-95L (primary human tumor graft from DLBCL patient) mouse models, TAK-659 demonstrates potent tumor growth inhibition (TGI) after 20 days of treatment. In the FLT3-dependent MV4-11 xenograft model, TAK-659 shows tumor regression at 60 mg/kg daily after 20 days of dosing[1].
Solvent&Solubility	***In Vitro:*** **DMSO : < 1 mg/mL** (insoluble or slightly soluble) **H_2O : 2 mg/mL** (**5.25 mM;** ultrasonic and adjust pH to 3 with HCl)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.6257 mL	13.1285 mL	26.2571 mL
5 mM	0.5251 mL	2.6257 mL	5.2514 mL
10 mM	---	---	---

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80° C, 6 months; -20° C, 1 month (stored under nitrogen)。 -80° C 储存时，请在 6 个月内使用，-20° C 储存时，请在 1 个月内使用。

References

[1]. Lam B, et al. Discovery of TAK-659 an orally available investigational inhibitor of Spleen Tyrosine Kinase (SYK). Bioorg Med Chem Lett. 2016 Dec 15;26(24):5947-5950.

[2]. Purroy N, et al. Inhibition of BCR signaling using the Syk inhibitor TAK-659 prevents stroma-mediated signaling in chronic lymphocytic leukemia cells. Oncotarget. 2017 Jan 3;8(1):742-756.