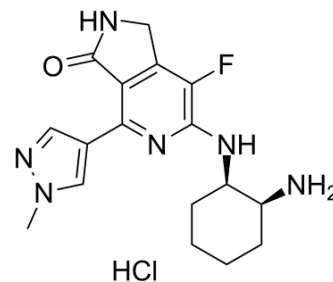


## TAK-659 hydrochloride

<b>Cat. No.:</b>	HY-100867A
<b>CAS No.:</b>	1952251-28-3
<b>Molecular Formula:</b>	C <sub>17</sub> H <sub>22</sub> ClFN <sub>6</sub> O
<b>Molecular Weight:</b>	380.85
<b>Target:</b>	Syk; FLT3
<b>Pathway:</b>	Protein Tyrosine Kinase/RTK
<b>Storage:</b>	4°C, stored under nitrogen
	* In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



### SOLVENT & SOLUBILITY

#### In Vitro

H<sub>2</sub>O : 2 mg/mL (5.25 mM; ultrasonic and adjust pH to 3 with HCl)  
 DMSO : < 1 mg/mL (insoluble or slightly soluble)

Preparing Stock Solutions	Solvent Concentration	Mass		
		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	---	---	---

Please refer to the solubility information to select the appropriate solvent.

### BIOLOGICAL ACTIVITY

#### Description

TAK-659 hydrochloride is a highly potent, selective, reversible and orally available dual inhibitor of spleen tyrosine kinase (SYK) and fms related tyrosine kinase 3 (FLT3), with an IC<sub>50</sub> of 3.2 nM and 4.6 nM for SYK and FLT3, respectively. TAK-659 hydrochloride induces cell death in tumor cells but not in nontumor cells, and with potential for the treatment of chronic lymphocytic leukemia (CLL)<sup>[1][2][3][4]</sup>.

#### IC<sub>50</sub> & Target

IC<sub>50</sub>: 3.2 nM (Syk), 4.6 nM (FLT3)<sup>[1]</sup>

#### In Vitro

TAK-659 hydrochloride inhibits cellular proliferation in SYK-dependent DLBCL and FLT3-dependent AML cell lines<sup>[1][3]</sup>. TAK-659 hydrochloride (5 μM; 1-24 hours) induces Casp3 activation in the LMP2A/MYC cells which was readily apparent at 4 h and reached maximum levels at 8 h of treatment<sup>[4]</sup>. TAK-659 hydrochloride (0.01-10 μM; 1 hour) stimulates expression of phospho-Syk at Tyr525 and Tyr352 and phospho-ERK1/2 increased in Ramos cells<sup>[2]</sup>. MCE has not independently confirmed the accuracy of these methods. They are for reference only. Apoptosis Analysis<sup>[4]</sup>

Cell Line:	LMP2A/MYC cells
Concentration:	5 $\mu$ M
Incubation Time:	1 hour, 2 hours, 4 hours, 8 hours, 24 hours
Result:	Induced apoptosis in LMP2A/MYC lymphoma cells.

#### Western Blot Analysis<sup>[2]</sup>

Cell Line:	Ramos cells
Concentration:	0.01 $\mu$ M, 0.1 $\mu$ M, 1 $\mu$ M, 10 $\mu$ M
Incubation Time:	1 hour
Result:	Enhanced expression of phospho-Syk at Tyr525 and Tyr352 and phospho-ERK1/2 in stimulated Ramos cells.

#### In Vivo

TAK-659 hydrochloride (100 mg/kg/day; p.o.; daily, for 10 days) treatment totally abrogates splenomegaly and tumor development in LMP2A/MYC mice in both pretumor and tumor cell transfer experiments<sup>[4]</sup>.  
TAK-659 hydrochloride treatment kills tumor cells, but not host cells within the spleen and tumors<sup>[4]</sup>.  
TAK-659 hydrochloride treatment abrogates metastasis of tumor cells into bone marrow<sup>[4]</sup>.  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	LMP2A/MYC double transgenic mice <sup>[4]</sup>
Dosage:	100 mg/kg/day
Administration:	Oral gavage; for 10 days
Result:	Inhibited LMP2A-induced tumor cell survival in vivo.

## 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.
- [3]. Jie Yu, et al. Anti-tumor activity of TAK-659, a dual inhibitor of SYK and FLT-3 kinases, in AML models. *Journal of Clinical Oncology* 34, no. 15\_suppl.
- [4]. Cen O, et al. Spleen Tyrosine Kinase Inhibitor TAK-659 Prevents Splenomegaly and Tumor Development in a Murine Model of Epstein-Barr Virus-Associated Lymphoma. *mSphere*. 2018 Aug 22;3(4).

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

India Contact:  
Life Technologies (India) Pvt. Ltd.  
306, Aggarwal City Mall, Opposite M2K Pitampura, Delhi – 110034 (INDIA). Ph: +91-11-42208000, 42208111, 42208222, Mobile: +91-9810521400, Fax: +91-11-42208444  
Email: customerservice@lifetechindia.com Website: www.lifetechindia.com