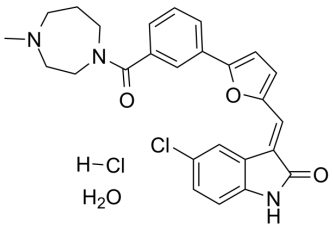
CX-6258 hydrochloride hydrate

Cat. No.:	HY-18095A
CAS No.:	1353858-99-7
Molecular Formula:	$C_{26}H_{27}Cl_2N_3O_4$
Molecular Weight:	516.42
Target:	Pim
Pathway:	JAK/STAT Signaling
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (48.41 mM; Need ultrasonic)

H_2O : 7.14 mg/mL (13.83 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9364 mL	9.6820 mL	19.3641 mL
5 mM	0.3873 mL	1.9364 mL	3.8728 mL
10 mM	0.1936 mL	0.9682 mL	1.9364 mL

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

In Vivo

1. Add each solvent one by one: 20% HP-β-CD in saline
   Solubility: 20 mg/mL (38.73 mM); Suspended solution; Need ultrasonic and warming and heat to 48°C
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.84 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.84 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CX-6258 hydrochloride hydrate is a potent and kinase selective pan-Pim kinases inhibitor, with IC_{50}s of 5 nM, 25 nM and 16 nM for Pim-1, Pim-2 and Pim-3, respectively[1].

IC_{50} & Target

IC50: 5 nM (Pim-1), 25 nM (Pim-2), 16 nM (Pim-3)[1]

In Vitro

CX-6258 causes dose dependent inhibition of the phosphorylation of two pro-survival proteins, Bad and 4E-BP1, at the Pim kinase specific sites S112 and S65 and T37/46, respectively[1].

CX-6258 treatment (12 mM, 3 h) treatment diminishes steady-state levels of ectopic NKX3.1 in PC3 cells[2].

CX-6258 treatment results in a significant reduction in NKX3.1 half-life[2].

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

Western Blot Analysis[1]

Cell Line:	MV-4-11 human AML cells.
Concentration:	0.1 μM, 1 μM, 10 μM.
Incubation Time:	2 hours.
Result:	Caused dose dependent inhibition of the phosphorylation of two pro-survival proteins, Bad and 4E-BP1, at the Pim kinase specific sites S112 and S65 and T37/46, respectively.

In Vivo

CX-6258 (50-100 mg/kg; p.o; daily; over a period of 21 days) exhibits robust in vivo efficacy in two Pim kinases driven tumor models[1].

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

Animal Model:	Nude mice, MV-4-11 xenograft models[1]
Dosage:	50 mg/kg, 100 mg/kg.
Administration:	Oral administration; once daily; over a period of 21 days.
Result:	Exhibited dose dependent efficacy, with a 50 mg/kg dose producing 45% tumor growth inhibition (TGI) and a 100 mg/kg dose producing 75% TGI.

REFERENCES

[1]. Mustapha Haddach, Jerome Michaux, Michael K, Discovery of CX-6258. A Potent, Selective, and Orally Efficacious pan-Pim Kinases Inhibitor. ACS Med. Chem. Lett., 2012, 3 (2), pp 135-139

[2]. Padmanabhan A, Gosc EB, Bieberich CJ. Stabilization of the prostate-specific tumor suppressor NKX3.1 by the oncogenic protein kinase Pim-1 in prostate cancer cells. J Cell Biochem. 2013 May;114(5):1050-7.

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